Lymph node dissection is not associated with outcome after nephroureterectomy for upper tract urothelial carcinoma.

**Objective:** To determine if performing a lymph node dissection (LND) is associated with a better outcome than not performing a LND in patients undergoing nephroureterectomy (NU) for upper tract urothelial carcinoma (UTUC).

**Methods:** Using the Surveillance, Epidemiology, and End Results (SEER) database, 2824 patients were identified who underwent NU for UTUC who had staging information available. Survival outcomes were compared between patients who had a LND and were shown to be node negative (pN0) and those who did not undergo a LND (pNx). Outcomes were also compared after correcting for variables such as tumor stage, grade, age, gender, primary tumor location, type and year of surgery.

**Results:** Estimated 5-year cause-specific mortality (CSM) after NU was not significantly different for pN0 and pNx patients (81.2% and 77.8%, respectively). This remained true across all sub-set analyses and after adjustment for all covariates.

**Conclusions:** There was no association between doing a LND and demonstrating no evidence for lymph node metastases (pN0) relative to not performing a dissection (pNx).

**Reviewer's Comments:** It is now quite clear that in the setting of locally advanced bladder cancer, the standard of care at the time of radical cystectomy is to also perform a proper, thorough bilateral pelvic lymphadenectomy. However, the situation in the setting of upper tract urothelial carcinoma is more clouded. The biggest single problem is lack of standardization. There is no agreement whether a lymphadenectomy should be done, or on the template or bounds for a lymphadenectomy if one is done. The disease itself is not as common, so reported series are all smaller than those found for bladder cancer. There is also no standardized reporting system to reflect quality of a lymphadenectomy if one is done. All of these impact the quality of data reported across institutional series and in larger data sets such as SEER. This paper by Lughezzani and colleagues is commendable for seeking to tackle this difficult question in this SEER-based analysis. They also deserve credit for acknowledging the shortcomings of many studies that are attempting to address this important problem, including their own. The current study suggests that perhaps there is no advantage to doing a LND dissection if one compares pN0 to pNx patients. However, the authors properly point out that this could be due to a number of different factors, most of which include all the shortcomings just listed. So, does this study provide the answer we are looking for? Unfortunately, the answer at the moment is no, so for now the individual urologist will have to use his or her judgment as to whether a LND is warranted for any given patient. (Reviewer-Peter E. Clark, MD).

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**Keywords:** Lymphadenectomy, Nephroureterectomy, Upper Tract Urothelial Carcinoma

**Print Tag:** Refer to original journal article
Pazopanib Improves Progression-Free Survival in Advanced Kidney Cancer

Pazopanib in Locally Advanced or Metastatic Renal Cell Carcinoma: Results of a Randomized Phase III Trial.
Sternberg CN, Davis ID, et al:
J Clin Oncol 2010; 28 (February 20): 1061-1068

Pazopanib improves progression-free survival compared to placebo in patients with advanced clear cell renal cell carcinoma.

**Objective:** To evaluate the safety and efficacy of pazopanib, an oral angiogenesis inhibitor, in advanced kidney cancer.

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

**Participants:** 435 patients with locally advanced or metastatic renal cell carcinoma (RCC).

**Methods:** Histology had to be either pure or predominant clear cell RCC. Patients were either treatment naïve or had failed prior cytokine therapy. Patients were randomized 2 to 1 pazopanib to placebo.

**Results:** Of patients, 233 (54%) were treatment naïve. Patients randomized to pazopanib had a longer median progression-free survival compared to patients randomized to placebo (9.2 months vs 4.2 months, respectively). This was also true in both the treatment naïve and prior cytokine treated sub-groups. Overall objective response rate was 30%, with the vast majority partial responses. Complete responses occurred in 1% of patients on pazopanib. Median duration of response was >1 year. Toxicity was generally manageable, with the most common adverse events being diarrhea, hypertension, changes in hair color, nausea, anorexia, and vomiting. There was no meaningful difference in quality of life in the pazopanib treated patients relative to placebo.

**Conclusions:** Pazopanib improves progression-free survival and objective response in patients with advanced clear cell RCC compared to placebo with acceptable toxicity.

**Reviewer's Comments:** Available treatment options for patients with advanced or metastatic renal cell carcinoma have expanded dramatically over the last several years. Advances in kidney cancer biology have led to a range of new agents including the angiogenesis inhibitors such as sunitinib, sorafenib, and bevacizumab (plus interferon) as well as inhibitors of the mTOR pathway such as temsirolimus and everolimus. Now added to this list is another angiogenesis inhibitor, pazopanib. Characteristics are analogous to those seen in the published randomized trials of sunitinib versus placebo, so the ongoing trial comparing those agents is the next logical step. Issues that remain unanswered at this point, however, continue to be the question of what is the best sequence of agents to use and how to best risk stratify patients in the modern era. There is also a need to identify agents that have proven efficacy in non-clear cell renal cell carcinoma. Those issues aside, this trial was successful and has now led to approval of pazopanib for clinical use. (Reviewer-Peter E. Clark, MD).

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Keywords: Clear Cell Renal Cell Carcinoma, Metastatic, Pazopanib, Tyrosine Kinase Inhibitor

Print Tag: Refer to original journal article
Prompt decompression of infected hydronephrosis is a critical issue; the method of obtaining this can be ureteral stent or percutaneous nephrostomy.

**Background:** Consensus-based guidelines and expert opinion suggest that percutaneous decompression of an infected hydronephrosis is safer than retrograde instrumentation.

**Objective:** To identify the optimal method of decompression of infected hydronephrosis.

**Design:** Systematic review.

**Methods:** Databases were queried for publications pertinent to the management of urinary tract infection and/or urosepsis in the face of obstructive hydronephrosis. A second search was performed to document complication rates of the procedures.

**Results:** Only 2 high-level randomized prospective studies (Level 1b evidence) were identified (82 patients total). Neither demonstrated superiority with regards to efficacy of resolution of the obstruction or resolution of sepsis. One additional retrospective study (Level 2c evidence) reported similar systemic inflammatory responses after decompression with nephrostomy tube versus ureteral stenting (59 patients total); however, stone size was significantly larger in the nephrostomy group. Overall major complication rate was 4% for nephrostomy tube, but was poorly documented for ureteral stenting.

**Conclusions:** There is no evidence to support a hypothesis that ureteral stenting is more hazardous in the setting of infected hydronephrosis.

**Reviewer's Comments:** The authors clearly identify an area where our literature is sorely lacking and further research is required. A multi-institutional randomized trial evaluating not only traditional measures of success (renal function, serum white count, postoperative fever), but also strict criteria for the systemic inflammatory response and bacteremia, is warranted. They rightly point out that timely decompression is the most critical consideration and the decision may be driven by the relative anesthetic risk associated with the procedure or the after-hours availability of the urologist/radiologist. (Reviewer-Manoj Monga, MD).
New Evidence Suggests Routine Antibiotics Not Always Necessary for SWL

Fever After Shockwave Lithotripsy--Risk Factors and Indications for Prophylactic Antimicrobial Treatment.

Duvdevani M, Lorber G, et al:

J Endourol 2010; 24 (February): 277-281

Routine antibiotics may not be needed for middle and distal ureteral stones if no ureteral stent or nephrostomy tube is present; with the small portion of patients treated with shockwave lithotripsy, routine prophylaxis remains warranted.

**Background:** The American Urological Association (AUA) Best Practices guideline recommends routine antibiotic prophylaxis for extracorporeal shockwave lithotripsy (SWL). In contrast, the European Association of Urology guidelines recommend prophylaxis only in cases of ureteral stents, urethral catheters, nephrostomy tubes, or infection stones. 

**Objective:** To identify risk factors for fever after SWL.

**Design:** Retrospective chart review.

**Participants:** >15,000 patients treated with the Dornier HM-3 lithotripter over 22 years.

**Methods:** Patients treated for stones >2 cm were excluded. A urine culture was obtained 7 to 10 days prior to SWL and UTI treated with culture-specific antibiotics. Patients with persistent bacteriuria were treated with 24 to 48 hours of parenteral antibiotics after the SWL. Patients with stones >15 mm underwent ureteral stenting or nephrostomy tube placement. All patients with an indwelling ureteral stent or nephrostomy tube received 1 preoperative dose of parenteral antibiotic. All patients were monitored in the hospital for 24 hours after SWL and had a urine culture within 24 hours of the procedure.

**Results:** 14% of patients received preoperative antibiotics for a positive urine culture. Even with a positive urine culture immediately after SWL, risk of postoperative fever (>38°C) was only 1.4%. Significant predictors of fever included positive urine culture, indwelling nephrostomy or ureteral stent, renal or upper ureteral stone treatment, or preoperative urinary tract infection or sepsis.

**Conclusions:** Selective antibiotic prophylaxis for SWL is recommended.

**Reviewer's Comments:** At first glance, this paper suggests that the AUA statement regarding prophylactic antibiotics at the time of shockwave lithotripsy deserves further scrutiny. However, the great majority of stones treated with SWL in the United States are renal and proximal ureteral stones; this study confirms they may benefit from preoperative antibiotic prophylaxis. As ureteroscopic approaches to ureteral stones have been demonstrated to be more efficacious and more cost effective, the use of SWL in this subset of patients would be less common. The AUA statement for prophylaxis is based on Level 1a evidence -- a meta-analysis of 8 randomized prospective controlled trials. As such, a single perioperative dose of antibiotics at the time of SWL remains warranted. (Reviewer-Manoj Monga, MD).

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Keywords: Lithotripsy, Fever, Antibiotics

Print Tag: Refer to original journal article
Objective: To evaluate the prognostic value of serum creatinine level (CR) at presentation and nadir level after transurethral valve ablation for posterior urethral valves (PUV).

Design: Retrospective review.

Methods: Children with a history of PUV treated with valve ablation from 1987 to 2004 were identified. Assessment included CR assessments and imaging studies.

Results: 120 cases were identified presenting at a mean age of 2 years (range 1 month to 15 years). Mean follow-up was 4.4 years (range 2 to 12 years). Of patients, 44 (37%) developed renal insufficiency (RI). Significantly less RI was seen in those with initial and nadir CR <1.0 mg/dl ($P <0.05$). When initial CR was <1.0 mg/dl, RI developed in 22% versus 63% when >1.0 mg/dl. When nadir CR was <1.0, 24% developed RI compared to 84% when >1.0 mg/dl. When glomerular filtration rate was calculated initially, it was 34 in those who went on to RI and 117 in those with normal renal function.

Conclusions: CR values before and after valve ablation have prognostic value. Specifically, CR <1.0 mg/dl is associated with a low rate of later RI.

Reviewer's Comments: This study reconfirms older data. What makes the study unique is that all patients underwent valve ablation, whereas many other studies included vesicostomy or upper tract diversions. The institution studied is a tertiary center, so many presented after catheter drainage, therefore index CR values are somewhat arbitrary; nonetheless, all improved after valve ablation. This information is valuable in counseling families regarding future risk for RI and 1.0 mg/dl is certainly an easy number to retain. (Reviewer- John Gatti, MD).

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Keywords: Creatinine Renal Insufficiency, Renal Function, Urethra, Valve, Valve Ablation

Print Tag: Refer to original journal article
Urinary stones in children are more prevalent in girls aged <13 years in the North Central United States.

**Objective:** To evaluate incidence of admissions to pediatric hospitals for urinary stone disease.

**Design:** Retrospective study.

**Methods:** Patients aged <18 years hospitalized for urinary stones from 2002 to 2007 using the Pediatric Health Information System (PHIS) database were identified. This includes data from 41 participating freestanding children's hospitals in the United States.

**Results:** Of 2.7 million hospitalizations, nearly 4000 were for urinary stones in children. Stones admissions were more common in girls (1.5 females to 1.0 males). Mean age was 12 years with over half of admits being aged <13 years. Of patients, 88% were white, and the North Central region had the most hospitalizations for stones. An increase in stone admissions was noted in the summer months (August to September). Also noted over the study period was an increase in the use of tamsulosin for expulsive therapy, despite its off-label use for this purpose in children.

**Conclusions:** Children with stones account for 1 in 685 pediatric hospitalizations in the United States. Risk factors include female gender, age <13 years, white race, and North Central location.

**Reviewer's Comments:** This study is extremely interesting with an increase in stone admission compared to historical value, but no significant change in admissions over the 6 years assessed. The PHIS database does not include any outpatient encounters, outpatient surgery, or hospitalizations <24 hours. Therefore this data set likely grossly underestimates the number of children suffering from urolithiasis. A side note is the increasing use of tamsulosin over the time span of this study despite it not being FDA approved for expulsive therapy in children. (Reviewer-John Gatti, MD).

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**Keywords:** Pediatrics, Epidemiology, Urolithiasis

**Print Tag:** Refer to original journal article
Appropriate preoperative selection of patients based upon specific pre-intervention criteria may decrease overall utilization of urodynamics.

**Objective:** To assess in which groups of women undergoing interventions for stress urinary incontinence (SUI) could urodynamics be safely omitted in order to decrease utilization of urodynamics in an appropriate fashion.

**Design:** Post hoc analysis of previously studied patients in prospective trials.

**Methods:** Women undergoing surgical intervention for SUI and preoperative urodynamics were evaluated for factors in their medical history and physical examination, as well as findings on urodynamics, which might stratify the population into low- and high-risk groups for failure of intervention if urodynamics were not performed. Patients utilized for this data set came from prospective evaluations of either retropubic or obturator placement of transvaginal tapes done at a referral hospital in Holland over 8 years.

**Results:** 437 women underwent interventions during this time frame of whom 381 women were considered to be uncomplicated and who had also undergone preoperative urodynamics. Multivariate logistic regression assessment was performed on criteria from medical history and physical examination and also factors from urodynamics including the presence of low urethral function (<20 cm of water maximum urethral closure pressure) and presence of detrusor activity. This population is a stratification of individuals more likely to benefit from preoperative urodynamics by age (≥53 years); those who had a prior incontinence surgery history and who are also aged ≥29 years; and those who had complaints of nighttime voiding and were aged ≥36 years.

**Conclusions:** If interventionalists considered these findings, approximately 29% of patients could have exclusion of urodynamic evaluation without the factors indicated being present. This is an interesting article as it deals with concerns regarding the utilization of urodynamics and populations where urodynamics may or may not be beneficial. National guidelines do exist which suggest that women with typical symptomatic SUI do not require preoperative urodynamics (National Health Service, United Kingdom). Whether or not these findings alone are significant enough to exclude urodynamics was explored by this paper.

**Reviewer's Comments:** The paper does identify using more complicated logistic regression model populations that may or may not be at greater risk for complications. Also, it reports outcomes after stress incontinence evaluation, and therefore, who may or may not need urodynamics dependent upon the presence or absence of these factors. (Reviewer-Roger R. Dmochowski, MD).
Bladder Wall Thickness Does Not Differentiate OAB Patients

Transabdominal Ultrasonography of Detrusor Wall Thickness in Women With Overactive Bladder.

Chung S-D, Chiu B, et al:

BJU Int 2010; 105 (March): 668-672

Ultrasonographic-determined bladder wall thickness does not distinguish amongst women with either symptomatic or asymptomatic overactive bladder simply based upon morphometric measurement.

Objective: To assess clinical utility of bladder wall thickness (BWT) as a method for noninvasive determination of women with overactive bladder (OAB).

Design: Prospective assessment.

Participants: 122 OAB symptomatic women.

Methods: Participants were undergoing voiding, bladder evaluation, transabdominal ultrasonography, and urodynamics as predictive of their baseline symptoms. Women were either with OAB dry or wet as compared to a group of women in a control group (no OAB symptoms). All patients completed a 3-day voiding diary to distinguish between continent versus incontinent status with OAB; transabdominal ultrasound was also performed at standardized bladder volumes and also at maximal bladder capacity by catheter infusion and natural filling. Urodynamics were further done to classify urinary dysfunction in 88 patients. Average population age was 58 years. Normal controls constitute 39 patients. Of patients, 44 women had dry OAB and 39 had wet OAB. Of women who underwent urodynamics, 28 had no findings, 30 had increased bladder sensation (lower volume at first desire), and 30 had demonstrative detrusor overactivity. There was no difference in BWT at established volumes between symptomatic subgroups and controls at 250 to 300 cc bladder-fill volume. At bladder capacity, incontinent OAB patients had increased bladder wall thickness as compared to controls. Bladder capacity was greater in normal controls as compared to those with OAB.

Conclusions: BWT, as measured by transabdominal ultrasonography, did not distinguish between patients who were asymptomatic versus those who were symptomatic, but did show a difference between patients with normal versus abnormal urodynamic findings. Bladder wall thickness was determined to not be a useful diagnostic test for detrusor overactivity.

Reviewer's Comments: This is a well-done, prospective assessment of women with symptoms versus normal controls. There had been much discussion as to the value of abdominal ultrasonography for purposes of detecting BWT. This study clearly shows that there is no statistical difference amongst symptomatic and asymptomatic patients. BWT will continue to be assessed as its validity for predictability of detrusor overactivity and OAB symptomatology. (Reviewer-Roger R. Dmochowski, MD).

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Keywords: Bladder Wall Overactive Bladder, Ultrasound, Urodynamics

Print Tag: Refer to original journal article
In overweight patients with Type 2 Diabetes, weight loss intervention is effective in mitigating the worsening of erectile function.

**Background:** Obesity and sedentary lifestyle are important risk factors for erectile dysfunction (ED). Risk of ED is 30% lower in men who report >16 metabolic equivalents (METs) hours per week compared to sedentary men.

**Objective:** To examine the effect of lifestyle intervention on erectile function (EF) in men with diabetes mellitus (DM).

**Methods:** All men were participants in the Look AHEAD (Action for Health in Diabetes) study which examined the effect of lifestyle intervention on cardiovascular morbidity and mortality in >5000 overweight Type 2 diabetics. Men from the Look AHEAD study sites who were sexually active at baseline were asked to complete the International Index of Erectile Function (IIEF) at baseline and then at 1 year, with the changes in weight, physical fitness, and ED at 1 year compared between men who were randomly assigned to either a lifestyle intervention or a control condition. Primary eligibility included Type 2 DM, age 45 to 74 years, and BMI ≥25 kg/m2.

**Results:** Completion rate was comparable between the intensive lifestyle intervention (ILI) group at 81.8%, and controls at 82.7%. ILI lost more weight at 1 year than controls (9.9% versus 0.6%, \( P < 0.001 \)). ILI also had better changes in HgbA1c, blood pressure, and high density lipoprotein cholesterol. There was a significant difference between groups for changes in ED, as scores changed from 17.3 at baseline to 18.6 in ILI, while they remained stable in controls. After adjusting for baseline differences in EF score, there was only a trend for men in the ILI to have greater increases in EF than controls. However, 20% of controls reported worsening of their EF, with 57% staying the same and 23% reporting improvements. Distribution in ILI was different, with only 8% reporting worsening, 70% staying in the same group, and 22% reporting improvements. Using an increase of 2 or 3 units as a criterion for "clinically meaningful" changes, the authors found no difference in the proportion of men reporting improvements, but significantly smaller percentage of men in ILI compared to controls with worsening of ≥2 units. Thus, weight loss intervention was effective in mitigating the worsening of EF in controls.

**Conclusions:** In this sample of older, overweight men with Type 2 DM, weight loss produced only small improvements in EF, but the benefit of weight loss helped preserve performance. Despite changes in weight and fitness, which were substantial, IIEF scores only slightly increased in ILI compared to controls.

**Reviewer's Comments:** Potential problems with this paper include a possible regression to the mean and the very modest change in symptoms, meaning that those men with great amounts of weight loss were not associated with greater improvement in EF suggesting a possible ceiling effect. However, this was a trial with high participant retention. (Reviewer-Kevin T. McVary, MD).

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Keywords: Erectile Dysfunction, Obesity, Weight Loss, Type 2 Diabetes

Print Tag: Refer to original journal article
Orgasmic Function Increases Over Time Following Radical Prostatectomy

Postoperative Orgasmic Function Increases Over Time in Patients Undergoing Nerve-Sparing Radical Prostatectomy.

Salonia A, Gallina A, et al:

J Sex Med 2010; 7 (January): 149-155

Postoperative orgasmic function improves over time following bilateral nerve-sparing radical prostatectomy.

**Background:** Attention has been given to postoperative erectile function (EF) and incontinence following bilateral nerve-sparing radical prostatectomy (BNSRP). However, orgasmic function has not been assessed. Orgasmic modifications like absence, and alteration in intensity and pain are common following RP. Additionally, men may complain of postoperative orgasm-associated incontinence (climacturia).

**Objective:** To prospectively assess orgasmic function (OF) over time in men undergoing a BNSRP.

**Participants/Methods:** Baseline data were obtained from 334 men, consecutively operated, sexually active, with prostate carcinoma, undergoing a BNSRP.

**Results:** 71.3% showed preoperative normal EF, 8.7% showed mild ED, 1.8% showed mild to moderate ED, 2.7% had moderate ED, and almost 10% showed severe ED. EF domain noticeably increased over time after initially dropping postoperatively. OF also improved over time, reaching a peak at the 48-month time point. Analysis showed an association between patients' IIEF OF at 12, 24, and 36 months of follow-up, and that OF increased with the recovery of the EF score. OF decreased with age and with the improvement of incontinence. OF also increased with EF domain and with use of phosphodiesterase type 5 inhibitors (PDE5-I).

**Conclusions:** OF increased postoperatively over time with improvement of EF and decreased with age and with continence improvement. Of note, 14% of patients reported pain during orgasm. Analysis also shows that patient age was inversely correlated with OF at the 12-month time point, but after that it did not appear to contribute much to the OF. Of patients, 10% who claimed they were potent had severe ED preoperatively. One should remember that evaluation just prior to surgery in terms of sexual function has shown not to be accurate.

**Reviewer's Comments:** Whether or not the IIEF is the ideal metric for measuring OF is a matter of debate, because only 2 questions are devoted to any aspect of this. This study has a small sample size, and data were not segregated according to the use of PED5-I. Contribution of psychological distress that may impact was also not measured. It is not clear if partner function may impact OF as this was not assessed. (Reviewer-Kevin T. McVary, MD).

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Keywords: Erectile Dysfunction, Sexual Function, Prostate Cancer

Print Tag: Refer to original journal article
Coffee May Improve Cholesterol

**Effects of Coffee Consumption on Subclinical Inflammation and Other Risk Factors for Type 2 Diabetes: A Clinical Trial.**

Kempf K, Herder C, et al:

Am J Clin Nutr 2010; 91 (April): 950-957

Large intakes of coffee daily may be associated with a lower risk of subclinical inflammation.

**Background:** Coffee consumption has been associated with a lower risk of liver, neurological, prostate, and various other diseases, especially type 2 diabetes. A variety of mechanisms have been theorized as to why this is the case; a reduction in oxidative stress and inflammation are 2 of the more common.

**Objective:** To determine the impact of moderate to high regular coffee intakes on a variety of health markers and inflammation.

**Design:** Single-blind, 3-stage clinical trial.

**Participants:** 47 habitual (4 cups a day) coffee drinkers.

**Methods:** Participants were 23% male with a mean body mass index of 29.2 kg/m2 and mean age of 54 years. Participants stopped drinking coffee for 1 month, then in the second month they consumed 4 cups of filtered coffee per day, and in the third month 8 cups of filtered coffee a day. Blood samples were analyzed by a variety of methods to determine the extent of coffee intake during various time periods.

**Results:** A variety of healthy coffee-derived compounds significantly increased, including caffeine and chlorogenic acid (healthy anti-inflammatory compound), with filtered coffee intake. A variety of inflammatory markers were significantly reduced including interleukin-18, while other insulin sensitivity compounds such as adiponectin significantly increased. All positive changes occurred during the 8 cups of filtered coffee per day interval including a significant high density lipoprotein (HDL) cholesterol increase by a mean of 3 points. No changes were observed in glucose metabolism.

**Conclusion:** Coffee intake seems to have positive impacts on subclinical inflammation and HDL, but without an impact on glucose.

**Reviewer’s Comments:** Okay, let me get this straight. Drinking 8 cups of coffee a day reduces the risk of subclinical inflammation? What about the impact of that much coffee on your speech, heart rate, your ability to get any sleep or run a 100-yard dash (not mentioned in this manuscript). I think the greater point is that, since I have been in urology, there has been an assault on all things tasty and fun and associated with some quality of life. Alcohol, eggs, fat in your diet, sugar, coffee, soda pop, artificial sweeteners, etc. Millions of dollars spent to convince patients that somehow abandoning the things near and dear to your heart needs to be done to save your heart. All I have to say is enjoy your coffee and other so called evils of life now because the deli line of life gets a little shorter every day regardless of what you do. Also, there is no shred of evidence to suggest that these members of the food police that try to control everything you eat and drink have ever been accurate in their predictions of what does and does not impact your health. (Reviewer-Mark A. Moyad, MD, MPH).

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Keywords: Coffee, Subclinical Inflammation, Type 2 Diabetes

Print Tag: Refer to original journal article
There are plenty of good dietary sources of selenium, so an individual selenium dietary supplement is not necessary.

**Background:** Selenium deficiency exists in some areas of the world (China and the United Kingdom) and selenium excess exists in other countries (the United States). Dietary recommended intakes of selenium vary depending on the country because there is no general consensus on how much selenium is needed to saturate blood levels.

**Objective:** To test the dose-response relationship for selenium from a combination of diet and supplements sources.

**Design:** Randomized double-blind, placebo-controlled intervention.

**Participants:** 119 healthy men, aged 50 to 64 years, living in the United Kingdom.

**Methods:** A daily selenium-enriched yeast tablet containing 50, 100, or 200 µg selenium, selenium-enriched onion meals (50 µg/day), or an un-enriched meal was consumed for 12 weeks. Primary outcome was change in platelet glutathione peroxidase activity and in plasma selenium and selenoprotein P concentrations (all parameters of optimum selenium status).

**Results:** Mean baseline plasma selenium concentration for all subjects increased significantly by 10 weeks in all groups. Intakes of selenium of 50 to 200 µg were adequate to provide optimal blood levels of selenium. Markers of selenium status, especially selenoprotein P, increased in response to all selenium interventions.

**Conclusions:** Plasma selenoprotein P appeared to be the most useful marker of selenium intake because it responded to a variety of different dietary or supplemental types of selenium. Optimal levels of selenium occurred at the daily food and beverage intake of 55 µg/day (recommended daily allowance), in addition to 50 µg/day from an outside source.

**Reviewer's Comments:** It is easy to get selenium (20 to 50 µg/day) from healthy and non-healthy food and beverage sources. Thank goodness, for example, a cheeseburger and fries gives me about 30 µg of selenium. However, my favorite source of selenium is simply healthy fatty fish, such as tuna or salmon (30 to 60 µg per serving). In fact, one theory as to why some of the healthiest fish contain low levels of mercury is because they are also high in selenium, which may detoxify or block the absorption of methyl-mercury (just a theory). The bottom line, ladies and germs, is that if your multivitamin contains much more than the recommended daily allowance of selenium (about 55 µg) I would be careful. In fact, any multivitamin that contains >100 µg of selenium should be avoided completely based on this study. Selenium toxicity includes fatigue and nail loss which, when last I checked, is not fun! (Reviewer-Mark A. Moyad, MD, MPH).

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Keywords: Selenium, Diet, Supplements

Print Tag: Refer to original journal article
Radical Prostatectomy Associated With Better Metastasis-Free Survival Than Radiation

Metastasis After Radical Prostatectomy or External Beam Radiotherapy for Patients With Clinically Localized Prostate Cancer: A Comparison of Clinical Cohorts Adjusted for Case Mix.

Zelefsky MJ, Eastham JA et al:

J Clin Oncol 2010; 28 (March): 1508-1513

Although metastases were rare, patients with localized prostate cancer who underwent radical prostatectomy had lower risk of developing metastases than men who had radiotherapy.

Objective: To compare the risk of developing metastases in men with clinically localized prostate cancer treated with radical prostatectomy (RP) versus external beam radiotherapy (EBRT).

Design: Retrospective cohort study.

Methods: Included were men with clinically localized prostate cancer who underwent RP or EBRT to doses of ≥81 Gy. Salvage therapy was given to a subset of each cohort, but was given sooner to RP patients (median 13 months) after initial therapy than EBRT patients (median 69 months). Risk of metastasis-free survival was compared after controlling for multiple covariates.

Results: The estimated 8-year freedom from metastasis rate for both RP and EBRT patients was 97% and 93%, respectively. After adjusting for case mix, patients with intermediate risk disease were 3.3% less likely to develop metastases while for high-risk patients, the difference was 7.8%.

Conclusions: Developing metastases is rare after both RP and EBRT for localized prostate cancer. Patients with the highest disease risk who underwent RP had a lower risk of developing subsequent metastatic progression than EBRT patients. However, a number of confounders could have influenced these results.

Reviewer's Comments: The age-old debate continues: what is the best way to treat localized prostate cancer, surgery or radiation? To date, we do not have a proper randomized trial to answer this question, nor are we likely to anytime soon. In the mean time, therefore, studies such as this one by Zelefsky are the best data we have available. The strengths of this analysis are that there are >1000 patients in each cohort, all were treated by experts in the field, and EBRT patients all received a reasonably high dose of radiation, >81 Gy. However, despite these strengths and a carefully done analysis, the study still risks being confounded by variables and biases we can't account for. As an example, EBRT patients were less likely to get salvage therapy, and when they did it was often much later. Is it possible that giving salvage androgen deprivation later influenced results more than initial therapy? Similarly, EBRT patients did not have their nodes irradiated, while the RP patients all had a lymphadenectomy. Is it possible this made a difference? Finally, EBRT patients got only a short course of hormone therapy even if they were high risk. Recent trials have suggested that high-risk patients fare better if EBRT is combined with a long course of hormone therapy. Perhaps this accounts for the difference between cohorts. Therefore, even though this is a thoughtful and well-executed cohort study, it cannot escape the fundamental short fall of all retrospective cohort studies and still leaves the basic question incompletely answered. (Reviewer-Peter E. Clark, MD).

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Keywords: Radical Prostatectomy, External Beam Radiotherapy, Metastasis, Prostate Cancer

Print Tag: Refer to original journal article
Abiraterone Acetate Shows Activity in Docetaxel-Treated Prostate Cancer

Phase II Multicenter Study of Abiraterone Acetate Plus Prednisone Therapy in Patients With Docetaxel-Treated Castration-Resistant Prostate Cancer.

Danila DC, Morris MJ et al:

J Clin Oncol 2010; 28 (March): 1496-1501

Abiraterone acetate showed significant activity in men with castrate-resistant prostate cancer who progressed after docetaxel.

Objective: To test the safety and efficacy of abiraterone acetate (AA) plus prednisone in men with castrate-resistant prostate cancer (CRPC) who had failed prior therapy with docetaxel.

Design: Open label phase II study.

Participants: 58 men with CRPC.

Methods: All participants had failed prior therapy with docetaxel, and 27 had received ketoconazole in the past. Men were treated with a combination of AA plus prednisone. Efficacy and safety were assessed using prostate-specific antigen (PSA) changes, radiographic imaging, and measuring circulating tumor cell (CTC) numbers.

Results: 36% of patients had a ≥50% decline in serum PSA. Among men previously treated with ketoconazole, this was higher at 45%. Over one fourth of men had an improvement in their performance status and one third of patients with pretreatment abnormal CTC counts normalized those counts after therapy. Toxicity was generally mild with no grade 4 events noted.

Conclusions: AA plus prednisone is well tolerated and shows promising activity in this population of men with CRPC who had failed prior docetaxel. This regimen is recommended to go onto phase III testing.

Reviewer's Comments: There was a time when men with advanced prostate cancer who were failing androgen deprivation were said to have androgen independent disease. It is now recognized that this was a misnomer. Tumors in men with CRPC are not independent of the androgen receptor in the vast majority of cases, and one of the best manifestations of this is the trial presented by Danila et al. The drug abiraterone acts by blocking the synthesis of neo-androgens anywhere in the body, including the androgens, which we now know are often made inside prostate cancer cells themselves. Even in heavily pretreated men who have failed multiple therapies, including standard androgen deprivation and docetaxel, interrupting androgen receptor function is still relevant and therapeutically beneficial. Another interesting point to take away from this study is the observation that those men who had also failed ketoconazole in the past fared worse than those who had never received this drug. While that observation is preliminary, it will be interesting to see if it holds up in the larger phase III trial that is currently ongoing. Finally, this is one of the first published trials to examine the utility of CTC as a marker of response. While again preliminary, future data on the performance metrics of this test are eagerly anticipated since the failings of PSA as a surrogate for treatment efficacy in men with CRPC is now well appreciated. (Reviewer-Peter E. Clark, MD).

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Keywords: Abiraterone Acetate, Cytochrome P450, Docetaxel, Castrate-Resistant Prostate Cancer, Androgen Receptor

Print Tag: Refer to original journal article
Risk of Transfusion After PCNL Is Low

Factors Affecting Blood Loss During Percutaneous Nephrolithotomy Using Balloon Dilation in a Large Contemporary Series.

Tomaszewski JJ, Smaldone MC, et al:

J Endourol 2010; 24 (February): 207-211

Objective: To identify variables associated with bleeding and transfusion after percutaneous nephrolithotomy (PCNL).

Design: Retrospective chart review.

Participants: 225 patients undergoing PCNL from 2000 to 2008.

Methods: Mean stone size was 3.5 cm, with 65% either full or partial staghorn calculi. Access was obtained in 90% of cases at the time of PCNL by the urologist. The Boston Scientific NephromaxTM or Bard X-Force® balloon was utilized for tract dilation. Multiple accesses were used in 5% of patients. Nephrostomy tubes (10F to 22F) were left at the end of all procedures for a median of 2 days. Postoperative imaging consisted of CT scan (75%) or KUB (25%).

Results: Stone-free rate was 80%. Secondary procedures included nephroscopy (25%), shockwave lithotripsy (6%) and ureteroscopic lithotripsy (12%). Pulmonary complication rate was 3%, transfusion rate was 1%, and risk of needing embolization was 1%. In <5% of procedures using the Nephromax, tract dilation was insufficient, and fascial incision needles were required to incise retroperitoneal scarring; this was not encountered with the Bard X-Force. Due to the low number of patients requiring transfusion, no perioperative predictive variables were identified.

Conclusions: Risk of transfusion after contemporary PCNL is low.

Reviewer's Comments: The findings reported confirm a recent study from the University of Western Ontario that the contemporary risk for transfusion after PCNL is 1%. Though this may reflect improvements in surgical technique and instrumentation, it may also reflect a more stringent approach to postsurgical anemia compared to the 1980's when transfusion rates for PCNL were >15%. Indeed, as most patients in this study who required transfusion proceeded to angioembolization, it suggests that transfusion is now reserved for those with critical bleeding. The authors note a fairly high secondary procedure rate, but with this were able to obtain a final stone-free rate of 98%. (Reviewer-Manoj Monga, MD).

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Keywords: Percutaneous Nephrolithotomy, Transfusion

Print Tag: Refer to original journal article
The Lithoclast Master and low-energy Holmium laser were the most efficient and effective lithotrites for percutaneous management of large proximal ureteral stones.

Objective: To compare the efficacy of different intracorporeal lithotripters during percutaneous nephrolithotomy (PCNL) for proximal ureteral stones.

Design: Retrospective chart review.

Participants: 192 patients with proximal ureteral calculi (mean size 16mm) and severe hydronephrosis treated from 2003 to 2007.

Methods: Stones were fragmented with either the pneumatic lithotripter, Swiss Lithoclast master (pneumatic/US combination), or Holmium Laser. Holmium laser technique was divided into low-energy (0.5 to 1.0J, 6 to 10Hz) and high-energy (1.0 to 3.0J, 10 to 30Hz). PCNL was performed after sequential tract dilation to 22F using metal dilators. A 20.8F rigid nephroscope was utilized without a nephrostomy sheath. A 365 micron laser fiber was used with the Holmium laser. A 12F nephrostomy was placed and removed after 5 days. Stone-free rates were determined by KUB at 1 month, at which point the double-J ureteral stent was removed. Intravenous urography and ultrasound was performed at 1 year to evaluate for complications.

Results: Operating time was 30 minutes shorter (80 minutes) for the Lithoclast and low-energy Holmium laser; stone-free rates were higher for these two modalities (90% vs. 80%). Ureteral strictures developed in 6% of patients on follow-up; however, 16% of patients undergoing high-power Holmium laser developed stricture.

Conclusions: The Swiss Lithoclast and low-energy Holmium laser are the preferred lithotrites for large proximal ureteral stones treated by PCNL.

Reviewer's Comments: The authors do not comment on their use of basket devices for fragment removal. They comment that one deterrent to pneumatic lithotripsy is the large fragments that are formed, requiring "time-consuming" extraction. Indeed, the absence of a nephrostomy sheath in their surgical technique suggests that active fragment extraction is not performed. As such, this may impact their findings of higher efficacy for lithotripters that either form smaller fragments (low-energy Holmium laser) or actively extract stone fragments (ultrasonic component of the Lithoclast). The finding of a higher ureteral stricture rate with high-energy Holmium laser is an important contribution to the literature. The authors do not report their selection of calix for percutaneous access; one would anticipate a high percentage of upper and middle calyces to facilitate access to the proximal ureter with a rigid nephroscope. For centers selecting a lower calyceal access and the use of a flexible endoscope, the low-energy Holmium laser would come out on top. (Reviewer-Manoj Monga, MD).

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Keywords: Proximal Ureteral Stone, Percutaneous Nephrolithotomy, Intracorporeal Lithotripsy

Print Tag: Refer to original journal article
Febrile UTI Rare After Ureteroneocystostomy

Whittam BM, Thomasch JR, et al:
J Urol 2010; 183 (February): 688-692

Background: Recent studies have suggested that open ureteroneocystostomy (UNC) may have an increased rate of febrile urinary tract infection (FUTI) compared to endoscopic techniques for the treatment of reflux.

Objective: To determine the rate of FUTI after UNC.

Design: Retrospective chart review.

Methods: 395 patients having undergone UNC for primary reflux from 2002 to 2007 were identified. Demographic, diagnostic, and operative data were reviewed. A Cox proportional hazards model was used to assess predictors of subsequent FUTI.

Results: UNC was performed in 395 patients (673 ureters). Mean age was 58 months and grade 3 reflux most common (41%). Incidence of FUTI was 4.6% at a mean follow-up of 15 months. Of 18 patients with FUTI, 12 underwent voiding cystourethrogram and 5 were found to have persistent reflux. Postoperative dysfunctional elimination syndrome was a significant predictor of FUTI (HR 3.8, P =0.02) occurring in 15% of toilet-trained children. Age, reflux grade, surgical technique and preoperative dysfunctional elimination syndrome were not predictive.

Conclusions: FUTI after UNC is relatively uncommon and may be lower than previously reported. Postoperative dysfunctional elimination syndrome is a significant risk factor for FUTI.

Reviewer's Comments: The authors report a low incidence of FUTI after UNC. Recent comparisons have suggested that endoscopic treatment of reflux may be associated with lower rates of subsequent FUTI, but the incidence herein described is quite comparable. The study is limited by its limited follow-up and retrospective nature which may have resulted in underreporting of infections. The take-home point is that those with postoperative dysfunctional elimination syndrome are at risk for subsequent infection, and the urologist's work may be far from done at the end of the operation. (Reviewer-John Gatti, MD).

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Keywords: Urinary Tract Infection, Dysfunctional Elimination Syndrome, Ureteroneocystostomy

Print Tag: Refer to original journal article
Objective: To determine impact of testicular torsion on late hormonal function of the testis.

Design/Participants/Methods: A chart review was performed identifying 20 patients with a history of testicular torsion; 8 had undergone orchiectomy, 12 detorsion and orchiopexy. At a mean of 5 years later (mean age 13.6 years), patients were assessed for hormonal function including follicle-stimulating hormone (FSH), luteinizing hormone (LH; before and after hormonal stimulation with gonadotropin-releasing hormone), testosterone, and inhibin B levels. Testicular size was assessed and semen analysis was obtained in children aged ≥18 years. An age-matched control group of normal boys was used for inhibin B comparison. Inhibin B is a marker of Sertoli cell function and spermatogenesis.

Results: 6 orchiopexy patients were noted to have late atrophy with 2 undergoing excision of the remnant testis. Serum basal FSH, LH, and testosterone levels were normal in both torsion groups (orchiectomy and orchiopexy). Inhibin B levels were significantly lower in the torsion groups when compared to controls (35 vs 64 pg/ml), but were similar between orchiopexy and orchiectomy groups (30 vs 41 pg/ml). There was significant correlation with inhibin B, testosterone, and testicular volume in both groups. Semen analyses were obtained on 7 boys, of which 6 had abnormal fertility index (3 of 3 after orchiectomy, 3 of 4 after orchiopexy).

Conclusions: Testicular torsion can result in decreased hormonal function. The type of surgical approach (orchiopexy vs orchiectomy) does not impact these results.

Reviewer's Comments: This study objectively assesses the outcome of testicular torsion with regard to late hormonal function. Although endocrine function was preserved, semen parameters and inhibin B were abnormal. It is unclear why the orchiopexy and orchiectomy groups were no different. Factors such as an autoimmune insult from exposure to antigenic substances after ischemic damage, abnormal baseline function, or reflex vasoconstrictive ischemia of the contralateral testis at the time of torsion may contribute. It is important for families to know that whether the testis is salvaged or not, fertility impairment may ultimately occur. (Reviewer-John Gatti, MD).

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Keywords: Fertility, Torsion, Testis, Inhibin B, Testicular Function

Print Tag: Refer to original journal article
Long-Term Results of Transureteroureterostomy Appear Beneficial

Transureteroureterostomy Revisited: Long-Term Surgical Outcomes.
Iwaszko MR, Krambeck AE, et al:

J Urol 2010; 183 (March): 1055-1059

Transureteroureterostomy appears to have outcomes which are beneficial for the patient irrespective of site of involvement and primary indications.

**Objective:** To assess long-term durability and functionality of transureteroureterostomy as a reconstructive technique in a group of chronically followed individuals.

**Design:** Retrospective chart review over approximately 22 years.

**Participants:** 63 individuals at a single institution undergoing transureteroureterostomy.

**Methods:** Average treatment age was a relatively young 31.5 years. Of patients, 21 (33%) had transureteroureterostomy performed for malignant indications and 42 (67%) had benign indications. There is a relatively equal distribution between right to left and left to right anastomoses and 21 individuals also had some form of concurrent urinary diversion. Of patients, 16 (25%) had received abdominal radiation prior to the intervention. Also, 15 (23.8%) individuals had postoperative complications of significance and these complications were more common in those who had had diversion undertaken for a primary indication of malignancy.

**Results:** Mean follow-up was 5.8 years. Of 56 patients who had long-term imaging follow-up, 54 (96.4%) had a non-obstructed anastomosis and 2 (3.0%) had obstructed anastomosis. Renal function was relatively well preserved in the study population. Of patients, 8 developed subsequent urolithiasis requiring multiple endourological interventions. Overall, 6 individuals required surgical re-intervention for obstruction or other revision indications (10.3%).

**Conclusions:** Recurrent stricture, distal obstruction, and stone disease do occur in a small percentage of individuals undergoing transureteroureterostomy, but most of these individuals were managed without significant consequence. The option of transureteroureterostomy remains facile and reasonable for individuals needing unilateral urinary diversion due to a variety of indications.

**Reviewer’s Comments:** Long-term outcomes for urologic procedures are becoming more commonly reported. Transureteroureterostomy, because of its relative rarity, lacks these long-term outcomes. This is an interesting paper because of its assessment of these outcomes. The authors cumulatively review all potential problems related to this procedure at a relatively reasonable time frame postoperatively. Certainly, problems with recurrent stone disease may continue to haunt at least some of these individuals. This article is an important consideration in terms of the evidence supporting the use of transureteroureterostomy. (Reviewer-Roger R. Dmochowski, MD).

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Keywords: Ureter, Ureteral Obstruction, Reconstructive Surgical Procedures

Print Tag: Refer to original journal article
Pelvic organ prolapse has a strong association with functional symptomatology including overactive bladder symptoms.

**Objective:** To analyze published articles for purposes of determining relationship between overactive bladder (OAB) symptomatology and/or detrusor overactivity with pelvic organ prolapse.

**Design:** Meta-analysis of relevant studies.

**Methods:** Papers related to combined symptomatology and presentation of pelvic organ prolapse and OAB were assessed from Medline and Embase data sources. Only articles that included both pelvic organ prolapse and OAB symptomatology were included. Results of prolapse surgery were considered without concomitant results of stress incontinence surgery.

**Results:** There appeared to be no relationship between the compartment or stage of pelvic organ prolapse and actual presence of OAB symptoms. OAB symptoms appeared to be present irrespective of prolapse magnitude (stage) or compartment involved. Interventions for pelvic organ prolapse including both surgical and nonsurgical managements appeared to improve OAB symptoms to some degree dependent upon author definition. There do not appear to be any predictive factors, however, where OAB symptoms will resolve or not with intervention. Detrusor overactivity is concomitantly present with pelvic organ prolapse and will resolve in a range of patients; although, postoperative detrusor overactivity does persist in a substantial percentage of patients dependent upon reported trial. There does appear to be a trend toward bladder outlet obstruction in some women (based upon urodynamics) being a possible deciding factor for OAB/detrusor overactivity symptomatology.

**Conclusions:** A causal relationship between OAB and pelvic organ prolapse apparently does exist. The mechanism for this, however, is as of yet, not completely defined.

**Reviewer's Comments:** This is a meta-analysis of the literature dealing with one of the common functional abnormalities associated with overactive bladder symptomatology and detrusor overactivity. This, along with colorectal dysfunction and sexual dysfunction, are the 3 primary functional issues associated with pelvic organ prolapse. The actual causative factor related to these functional symptoms is unclear; however, bladder outlet obstruction may have at least a partial contributory component to them. (Reviewer-Roger R. Dmochowski, MD).

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Keywords: Detrusor Overactivity, Overactive Bladder, Pelvic Organ Prolapse, Pessary

Print Tag: Refer to original journal article
Testosterone Therapy Appears Beneficial to Patients With Deficiencies

Symptomatic Response Rates to Testosterone Therapy and the Likelihood of Completing 12 Months of Therapy in Clinical Practice.
Rhoden EL, Morgentaler A:

J Sex Med 2010; 7 (January): 277-283

In a study by Rhoden and Morgentaler, two thirds of men who started testosterone therapy completed 12 months, and their symptoms were more likely libido and erectile dysfunction combined.

Background: There is awareness in the health impact of testosterone deficiency (TD), and therefore the benefits of testosterone supplementation (TS). This has been shown to improve libido, erectile function, and different aspects of body composition. There is little information in the literature regarding acceptability, compliance, and the symptomatic benefits of replacement in a routine clinical setting.

Objective: To investigate outcomes of TS in a consecutive series of men diagnosed with TD.

Design: Retrospective review.

Methods: The primary goal was to address what percentage of men complete 12 months of treatment, and what are the clinical features of those men. Testosterone and free testosterone were obtained during clinic hours, ranging from 8 AM to 5 PM. Additional visits were scheduled if TS was suboptimal. Patients were reevaluated at 3 months, and if having symptom improvement, were encouraged to continue; those without were not. Those with an indeterminate response were encouraged to continue for ≥3 months.

Results: Mean patients age was 58.4 years. Of patients, 63% completed 12 months of therapy, all of whom reported symptomatic benefits; 26.8% discontinued treatment prior to 12 months after reporting either minimal or no benefit; 10% of men were lost to follow-up. Initial mode of therapy was injection, and over time converted to topical gels. Following injections, 46.8% tried gel treatments and 72.7% of these found this treatment adequate and continued on with the gel. The balance tried the gel and decided to switch back to the injection. Not surprisingly, baseline testosterone and free testosterone levels were improved with supplementation, and baseline testosterone levels were significantly lower for those men who eventually responded compared to non-responders. Of patients, 5 developed hematocrit >54%, 1 developed urinary retention, 1 was identified with prostate malignancy, and 1 developed gynecomastia.

Conclusions: Of note, two thirds of men who started therapy completed 12 months, and of these “responders”, symptoms were more likely libido and erectile dysfunction combined. They also had lower baseline levels of testosterone. The percentage responding was similar to those whose testing was performed in the morning or the afternoon, suggesting that in men aged >40 years, the timing of testosterone measurement is not critical.

Reviewer’s Comments: This is a retrospective review of a clinical population, not a randomized controlled trial. Most patients were being treated for symptoms relating to some aspect of sexual health. No questionnaire data were used. This report was done during the period of gel introduction, and thus there was an alteration in treatment pattern because of that. Mean prostate-specific antigen increased by 16% over this period, but not statistically significant. (Reviewer-Kevin T. McVary, MD).

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Keywords: Testosterone Replacement Therapy, Hypogonadism, Aging

Print Tag: Refer to original journal article
Currently, objective evidence does not support the use of any natural aphrodisiac for male or female sexual dysfunction.

**Background:** Patients frequently ask about the use of natural aphrodisiacs. **Objective:** To review natural aphrodisiac agents that patients may ask about. **Discussion:** (1) Ambrein is a non-plant natural aphrodisiac and very common in the Middle East. It is found in the gut of sperm whales. Only animal studies have been done with this particular agent, and it is thought to stimulate pituitary secretion of luteinizing hormone (LH), leading to an increase in serum testosterone. (2) Bufo Toad is a hallucinogen, related medically to serotonin. No mechanism is known. It is assumed to have central effect because of the accompanying hallucinogenic properties. (3) Spanish Fly comes from a beetle known as Lytta vesicatoria. It contains up to 5% of cantharidin that irritates animal tissues, inhibits phosphodiesterase and phosphatase activity and causes vasal congestion. Contrary to popular belief, these actions are not female-specific, and side effects include renal toxicity and gastrointestinal bleeding. (4) Tribulus terrestrus, a perennial plant with worldwide distribution, has some evidence for erectile dysfunction (ED) impact, yet limited to animal studies that show significant improvement in erectile function after oral administration. (5) Horny Goat Weed (Epimedium herba) has been used as an energy and ED enhancing drug in traditional Chinese medicine. The active agent is icariin which increases intercavernosal pressure (animal models) and the expression of inducible and neuronal nitric oxide synthases. (6) Ginseng refers to the species Panax which contain ginsenosides. Limited information is available from 28 randomized controlled trials. Meta-analysis revealed that ginseng improved sexual performance more than placebo, but many of these reports did not report on the nature of placebo, and therefore definitive conclusions are difficult. Mechanism is unknown, though animal studies suggest that it can increase nitric oxide. (7) Chocolate (cacao) is thought to have an impact on mood. It is known to stimulate serotonin and flavonoids in the central nervous system, modulating female genital sexual functioning. Several studies in females report a positive influence from chocolate. Solid conclusions are difficult to be reached. (8) Alcohol is known to have depressant effects of the central nervous system, increasing levels of the inhibitor neural transmitter, gamma amino butyric acid. Chronic alcohol use significantly decreases the odds of ED in most of the cross-sectional studies, yet there are contradictory results from other epidemiologic studies, making a solid conclusion regarding aphrodisiac unreliable. **Conclusions:** Currently, objective evidence does not support the use of any natural aphrodisiac for male or female sexual dysfunction. **Reviewer’s Comments:** Aphrodisiacs are used by men complaining of various degrees of ED and by potent men. There is little evidence from the literature to recommend the usage of any of these agents. The toxic effect of these agents is not known. Sexual medicine specialists should warn their patients. (Reviewer-Kevin T. McVary, MD.)

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Keywords: Sexual Dysfunction, Phytotherapy, Alternative Therapy, Erectile Dysfunction

Print Tag: Refer to original journal article