

# Advances in Sexual Medicine

*Highlights from the 2007 Winter Meeting of the Sexual Medicine Society of North America, December 6-9, 2007, Chicago, IL*

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The Sexual Medicine Society of North America held its winter scientific meeting in Chicago in December 2007. The meeting covered most of the issues that are related to sexual medicine, with “state of the art” lectures, scientific sessions with both poster and podium presentations, and debates between experts in a number of disciplines.

### Dietary Factors and Erectile Dysfunction

On the first day of the meeting, Dr. Kevin McKenna<sup>1</sup> from Northwestern University Medical Center (Chicago, IL)

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Reviewed by John P. Mulhall, MD, Memorial Sloan-Kettering Cancer Center, New York, NY, and Jacob Rajfer, MD, University of California at Los Angeles, Los Angeles, CA.

discussed some of the dietary factors relating to the development of the metabolic syndrome. There is evidence to suggest that there is a relationship between low testosterone, as one may develop from either aging or diabetes, and the metabolic syndrome. Dr. McKenna provided basic scientific evidence that high fructose in our foods may be 1 of the major culprits in the development of the metabolic syndrome in man. Fructose ingested is converted directly into low-density lipoprotein and fat, in addition to leading to insulin-resistance dyslipidemia. Because fructose does not induce a satiety effect, many foods that are made with fructose (eg, many soft drinks) do not fill one up, and we keep eating more and more until satiety takes effect. This probably explains why there is a correlation between fructose consumption and the preva-

lence of obesity. It is presumed that high-fructose diets lead to an increase in oxidative stress, and this leads to a loss of neurons and smooth muscle in the penis, which ultimately leads to erectile dysfunction (ED). In addition, because the penis is the “observation post” for what is taking place inside the vascular system, it makes sense that there is a strong correlation between ED and cardiovascular disease. Indeed, this was a theme that was constantly being repeated throughout the meeting (ie, that ED may be a marker for underlying cardiovascular disease, and vice versa).

### Stem Cell Therapy

Dr. Tom Lue<sup>2</sup> from the University of California, San Francisco, presented a lecture on the use of stem cells for the treatment of sexual dysfunction. The idea of using stem cells to replenish

the “penile tissues” makes therapeutic sense, given that the majority of cases of ED are due to the loss of corporal smooth muscle and an increase in corporal fibrosis. As such, a number of investigators have used different stem cells to accomplish this, despite the current federal ban on the use of embryonic stem cells in the United States. Because stem cells from other parts of the body (eg, bone marrow, fat, and skeletal muscle) are used to make corporal smooth muscle cells, certain issues such as the oncogenicity of these cells need to be resolved before they are made ready for “prime time.”

### Phosphodiesterase Type 5 Inhibitors

A topic of interest at the meeting was the use of daily phosphodiesterase type 5 (PDE-5) inhibitors. Are they safe? Are they effective? What are the indications? Rajfer and associates<sup>3</sup> (University of California at Los Angeles) reported on the long-term safety and efficacy of tadalafil 5 mg daily for 1 to 2 years. The data were obtained from 2 open-label extension studies, 1 for 12 months (n = 234) and 1 for 2 years (n = 238). The mean improvement in erectile function domain (EFD) score for the 1- and 2-year patient groups was 10 and 8, respectively. After a washout period of 4 weeks without tadalafil, the mean EFD score returned to baseline (pretreatment). The adverse events profiles were very similar to that seen with on-demand 10-mg and 20-mg dosing. Thus, the investigators have shown in this analysis that daily tadalafil dosed at 5 mg is well tolerated and results in statistically significant and clinically meaningful improvements in erectile function.

Elsewhere at the meeting, Dr. Christian Stief<sup>4</sup> (Ludwig-Maximilians-University, Munich, Germany) discussed 3 other disorders for which

daily PDE-5 inhibitors might ultimately be used: Peyronie’s disease (PD), benign prostatic hyperplasia (BPH), and overactive bladder (OAB). For PD, the use of PDE-5 inhibitors is as an antifibrotic compound, whereas for BPH and OAB it is probably used both as an antifibrotic and as an enhancer of smooth muscle function. Before the daily use of these compounds for treatment of PD, OAB, and BPH can be recommended, large, randomized, placebo-controlled studies in each of these disorders will be required.

increase in the proportion of patients answering yes to SEP3, compared with a 10% increase with placebo. Assessing the normalization of the erectile function domain score at 8 hours, the investigators showed that there were 6 times as many men in this category when sildenafil was used compared with placebo. This study demonstrates nicely what we have known as clinicians for quite some time: that is, that sildenafil is a drug whose efficacy lasts 8 to 12 hours after dosing.

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Dr. Arthur Burnett<sup>5</sup> from Johns Hopkins in Baltimore, MD, presented his work on sickle cell and priapism. His theory is that priapism is due to a dysregulation of the PDE-5 enzyme in the penis and that treatment with PDE-5 inhibitors causes an increase in cyclic guanosine monophosphate in the tissues of the penis, which in turn leads to normal functioning of the PDE-5 enzyme. Dr. Burnett used a mouse model to support his hypothesis, and from his observations Dr. Burnett’s group has espoused chronic PDE-5 inhibitor therapy for patients with recurrent priapism. Preliminary studies in a small group of patients treated with daily PDE-5 inhibitors seem to support their theory.

Steidle and colleagues<sup>6</sup> (Indiana University School of Medicine, Indianapolis, IN), reviewing data from 2 randomized, double-blind, placebo-controlled trials, assessed the efficacy of sildenafil citrate at 8 hours after dosing. Using the Sexual Encounter Profile question 3 (SEP3) (“Were you able to have an erection that lasted long enough to have successful intercourse?”), they showed that at 8 hours after dosing there was a 50% to 60%

### Spinal Cord Injury

A fascinating lecture was given by Dr. John Kessler, Chair of Neurology at Northwestern University, who presented his work on repair of spinal cord injury. Dr. Kessler<sup>7</sup> has identified why injury to the spinal cord does not lead to regeneration of the neural fibers that are injured or transected. Simply stated, when an injury occurs in the neural tissue there is formation of a glial scar that acts as a blocker for regenerating or sprouting neural fibers. Dr. Kessler has identified certain gels that will inhibit such glial scars and promote healing of the injured fibers. He presented some fascinating videos of rodents that received this gel in the injured area of the spinal cord and had remarkable improvement in their motor and sensory function compared with nontreated animals.

### Diabetes Mellitus and ED

Another topic that was covered at the meeting was the relationship between diabetes mellitus (DM) and ED. Dr. Kanchan Chitale<sup>8</sup> from the University of Washington (Seattle, WA) discussed the differences between type 1 (insulin deficiency) and type 2

(insulin excess) and looked at the response of the autonomic nervous system in erectile function. Her group determined that the endothelium-independent (neuronal nitric oxide) and endothelium-independent (acetylcholine) response in type 1 and type 2 DM was impaired in the rat penis. However, the sympathetic response (vasoconstriction) was impaired in type 2 but not in type 1 DM. This suggested to the investigators that future therapy for ED in men with DM may be different depending on the type of DM.

out use of Hegar, Brooks, or Dilamezinsert dilators. When proximal fibrosis was encountered (difficult passage of the Furlow), the Metzenbaum scissors was used. Fifty-two patients were studied. None had undergone prior implant surgery. In only 8% of patients was proximal Metzenbaum scissors placement necessary. There were no adverse events, including infection at 3 to 6 months post-operatively. Operative time was subjectively evaluated, as was the degree of penile bruising. The trend in penile

were for 10 minutes, whereas the ChlorPrep scrub was for 3 minutes. Patients in the povidone-iodine, Hibiclens, and ChlorPrep groups had 40%, 10%, and 40% skin bacterial growth before skin preparation, respectively. However, no patient had any bacteria grown from skin swabs obtained at the completion of the case. This simple yet informative study demonstrates that our current approaches to pre-penile implant surgery surgical preparation are excellent means of sterilizing the scrotal skin. This study was limited by an absence of randomization and patient comorbidity profile as a predictor of pre-scrub skin bacteria positivity. It would also be interesting to know for how long after surgical scrub the skin is likely to show no bacterial growth.

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Can ED be prevented? Can it be reversed? Does interventional therapy with insulin affect the prevalence of ED in type 1 diabetics? Dr. Hunter Wessells<sup>9</sup> from the University of Washington reviewed the Diabetes Control and Complication Trial/Epidemiology of Diabetes Intervention and Complication Study and showed that by careful control of serum glucose with insulin therapy the incidence of ED was reduced in diabetic men from 23% to 8%. The study could not answer the question of whether ED could be prevented, but it did show that its onset could be delayed by careful control of the serum glucose.

### Penile Implant Surgery

Wilson and colleagues<sup>10</sup> assessed the need for corporal dilation during placement of the new AMS 700 MS 3-piece inflatable penile prosthesis (American Medical Systems, Minnetonka, MN). The investigators used a technique that allowed distal but not proximal placement of a Metzenbaum scissors. This was followed by passage of the Furlow inserter with-

implant surgery is toward maneuvers that shorten operative time. This has the advantages of perhaps further reducing infection rates and allowing a greater number of cases to be performed on the surgeon's operating list. On the other hand, without the use of such novel operative strategies, penile implant surgery in a patient with no prior implant surgery should take no more than 45 to 60 minutes. Shortening this time is not likely to further reduce infection rates.

Carrion and coworkers<sup>11</sup> (University of Miami School of Medicine, Miami, FL) studied skin bacteria growth after surgical prepping before implant surgery. Three groups using different preparations were studied: povidone-iodine (28 patients), chlorhexidine (Hibiclens, Mölnlycke Health Care US, Norcross, GA) (22 patients), and combined chlorhexidine and alcohol (ChlorPrep, Enturia, Leawood, KS) (20 patients) (70 patients total). Skin cultures (aerobic and anaerobic) were obtained after skin shaving but before surgical incision and preparation and then at the completion of the case. Povidone-iodine and Hibiclens scrubs

### Radical Prostatectomy and Erectile Function

Muller and associates<sup>12</sup> (Weill Medical College of Cornell University, New York, NY) studied 258 patients after radical prostatectomy (RP) treated with intracavernosal injection therapy with trimix (papaverine 30 mg/mL, phentolamine 1 mg/mL, and prostaglandin E1 10 µg/mL). Patients were separated into 2 groups: those using more than 50 U trimix ("VL"; n = 126) and those receiving less than 15 U trimix ("no VL"; n = 132). This segregation was based on prior work from this group suggesting that men using more than 50 U of trimix uniformly have venous leak. Differences were sought between the "VL" and the "no VL" groups. Variables analyzed included age at surgery, comorbidity profile, self-reported preoperative erectile function, neurovascular preservation at surgery, and time to presentation for ED management after RP. The subjects in the "VL" group were significantly older (60 vs 56 years;  $P < .01$ ) and presented for injection therapy later (13 months vs

9 months;  $P < .05$ ) than those in the “no VL” group. There was no clinically meaningful difference in baseline erectile function. Furthermore, there was no significant difference between these groups in comorbidity profile or degree of neurovascular preservation. Fifty-five percent of both groups had bilateral and 22% unilateral nerve sparing. In a multivariate logistic regression analysis, using the significant variables to predict the diagnosis of venous leak, age was the only variable that remained significant in the model (relative risk 1.08; 95% confidence interval, 1.04–1.12;  $P < .01$ ). This study interestingly undermines the role of non-nerve-sparing surgery in the genesis of venous leak after RP but emphasizes the importance of age at the time of RP as a predictor of poor erectile function outcomes.

Burnett and Trinity<sup>13</sup> (Johns Hopkins) analyzed the impact of erythropoietin (EPO) administration in an unblinded, nonrandomized study on erectile function recovery in men undergoing RP who were fully potent preoperatively. This study was based on animal data suggesting that erythropoietin was a neuromodulatory agent facilitating neuroregeneration. The 2 groups were matched for baseline erectile function and comorbidity profiles. Patients were followed with Sexual Health Inventory for Men (SHIM) questionnaire assessment at 3-month intervals. Fifteen patients elected to use EPO (single dose of 40,000 IU on day of operation), and 21 did not use EPO. At 3 months after surgery there was a statistically but not clinically meaningful difference in SHIM scores between the 2 groups. However, at 12 months after RP, the

EPO group had higher SHIM scores without and with PDE-5 inhibitor use compared with the non-EPO group (12 vs 5 and 14 vs 7, respectively). Clearly, the size of this study and its nonrandomized nature limit the conclusions that can be drawn; however, there is a signal supported by animal data that EPO may have a neuroprotective or neuroregenerative role and may play a part in the future management of the RP patient.

### Grading Erectile Hardness

There has been a recent revival in interest in the grading of erectile hardness. Goldstein and colleagues<sup>14</sup> (Alvarado Hospital, San Diego, CA) assessed the correlation between the erection hardness score (EHS) and the ability to have successful sexual intercourse. The EHS is a 5-point scale assessing penile rigidity during intercourse (0 = no erection, 1 = tumescent but not firm, 2 = firm but not firm enough for penetration, 3 = firm enough for penetration but not fully rigid, and 4 = fully rigid). Data were obtained on 307 subjects who were part of a sildenafil citrate double-blind, placebo-controlled trial. Comparing patients with EHS 2 and EHS 3, the latter were 42 times more likely to have successful intercourse compared with the former. Comparing patients with EHS 3 and EHS 4, the latter were 324 times more likely to have successful intercourse compared with the former. This study supports the earlier data that EHS correlated well with improvement in psychosocial outcomes and demonstrates the importance of erection hardness. The EHS is a useful tool for the assessment of baseline erectile function as well as response to treatment. ■

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