European Society for Sexual Medicine

Issue 32 – January 2015

ESSMToday

ESSM NEWSLETTER

www.essm.org

HIGHLIGHTS FROM THE EDITION

CONTACT
ESSM Secretariat
Via G. Ripamonti 129 – 20141 Milano, Italy
Phone: +39–02–56 601 625
Fax: +39–02–70 048 577
Email: admin@essm.org

IMPRINT
Publisher: ESSM
Editor-in-Chief: Juan I. Martinez-Salamanca
Layout: CPO HANSER SERVICE

Contents

Welcome Address

I am delighted to welcome you to this **2014 / 2015** Issue of the ESSM newsletter. We have in our society great things coming soon.

We would like to congratulate again all ESSM members and staff for their great work organizing our next Meeting in Copenhagen. As you may know, this event is really important for our society, so please “start spreading the news” between your colleagues and friends, to bring as much people as you could. The meeting contents will be outstanding, the members of the scientific team, leaded by **Dr. Albersen**, were working really hard to get there.

In this issue, we have included an interesting interview with a pioneer and world-class expert in Sexual Medicine, **Prof. F. Giuliano**. We cover main topics – highlights have presented at AUA Orlando Meeting 2014 prepared by **Dra. Egui** and myself, along with our classic sections by my associate editors **Dr. Mondaini**, **Dr. Angulo** and **Dr. Vozmediano**.

Also, we add two very interesting Key from Kols collaborations regarding Penile Cancer done by **Salvatore Sansalone** and Testosterone & Cardiovascular Health done by **Dr. Corona** and **Prof. Maggi**. I hope you will enjoy reading it.

Finally, I would like to thank you all for your continued support of our society and I look forward to seeing you in Copenhagen in February.

My very best
Juan I. Martínez-Salamanca

Interview with Prof. Giuliano

by Dr. Juan I. Martinez-Salamanca (JIMS)

Dr. Juan I. Martínez-Salamanca
Hospital Universitario Puerta de Hierro-Majadahonda Universidad Autónoma de Madrid
Department of Urology

msalamanca99@hotmail.com

Prof. François Giuliano
Neuro-uro-andrology, Dept of physical medicine and rehabilitation
Raymond Poincare hospital 104 boulevard R. Poincare
92380 Garches, France

francois.giuliano@uvsq.fr

François Giuliano has a specialist urological practice at the Academic hospital of Garches in France which focuses on sexual health and non malignant diseases of the lower urinary tractin neurologic patients. He is Professor of Therapeutics at the University of Paris West. He has chaired numerous postgraduate courses and lectured on a variety of topics in male sexual dysfunction and pathologies of the lower urinary tract.

Prof. Giuliano's major research interests include pathophysiology, diagnosis and management of sexual dysfunctions and of benign prostatic hyperplasia and urinary incontinence and co-morbidities such as endothelial dysfunction.

He has an extensive experience conducting clinical trials and is a recognized authority on the study of male urology and sexual medicine.

He is actively involved in experimental research investigating the pharmacological mechanisms controlling ejaculation, erectile, female sexual and lower urinary tract functions. This research involves an integrated approach, using neuro-anatomical, neurophysiological, biochemical, and pharmacological techniques.

Prof. Giuliano is a widely published author in peer-reviewed journals, and has edited and contributed to several books. He is associate editor of Journal of Sexual Medicine and involved in the production of guidelines and care pathways.

He is a member of professional organizations and holds leadership positions at the European and the International Societies for Sexual Medicine and is vice chairman of the International Consultation of Sexual Dysfunctions.

He is internationally recognized for his expertise in the experimental approach to neurophysiology and in the clinical management of erection, ejaculation and lower urinary tract functions and, has won several national and international awards.

Having you here it is a real pleasure and honor not only for me but also for all ESSM Members.

JIMS: Prof. GIULIANO could you make us a brief journey throughout your professional background?
I am a urologist by training. I have worked in the dept of urology of the academic hospital of Bicêtre, in the South of Paris during 17 years practicing general urology and gradually specializing in sexual medicine. Then I have moved to a hospital dedicated to neurologic patients and my daily practice is currently mostly focused on the urogenital dysfunctions of spinal cord injured patients or patients suffering from multiple sclerosis. In parallel I have always dedicated a significant amount of time to experimental research.

JIMS: During you dilated career, which has led to the passage from "Andrology" to "Sexual Medicine", and what do you prefer "Sexual Medicine" or "Men´s Health"?
I have always been more involved in managing male sexual dysfunction rather than with infertility. Sexual health is actually a important part of urogenital Men's Health that should not limited to testosterone replacement therapy.

JIMS: What do you think the role of the urologist should be in the field of basic research in Sexual Medicine? And what are our major challenges?
The clinician with a specialization in urology is the perfect candidate to bridge the gap between basic scientists and the many remaining challenges in clinical practice in sexual medicine including ejaculatory disorders, severe erectile dysfunction with a poor response to PDE5 inhibitors, orgasmic problems …Urologist knows the anatomy and the physiology of the male sexual organs and functions respectively.

JIMS: Prof. GIULIANO PDE5 Inhibitors (tadalafil) have been approved in U.S. and Europe for patients with ED & LUTS, which do you consider being the ultimate role of this drug in all treatment options of this group of patients?
There is strong evidence that daily tadalafil has a similar efficacy when compared to alpha blocking agents for male LUTS. I suspect this can be related to an effect on nitrergic bladder afferent pathways. I regret that there is almost no data available regarding efficacy of PDE5 inhibitors on neurogenic detrusor overactivity via a modulation of the micturition reflex targeting the bladder sensory innervation. There is no question that in patients with LUTS and ED tadalafil should be the preferred treatment option from both an efficacy and a tolerability perspective.

JIMS: In the field of Men´s LUTS in which you worked and contributed very hardly, what do you think are the main challenges to achieve?
The registered pharmacological mechanisms of action have mild symptomatic efficacy. Which is lacking is much more effective compounds maybe with a dual or even triple mechanisms of action which could also act on the erectile tissue targeting the ageing process of the lower urinary and genital tracts. There is a variety of mechanisms of action which should deserve

Interview with Prof. Giuliano

investigation including Rho kinase inhibitors, guanylate cyclase activators, compounds tragetting the bladder afferences.

JIMS: Prof. GIULIANO, regarding the latest controversy about Testosterone Replacement Therapy & Cardiovascular Risk, what is your personal opinion about that?

I believe that testosterone replacement should be used appropriately and with caution. This story reminds me about the Women health initiative (WHI) that led in the US to a significant decrease in the use of hormonal supplementation in post menopausal women. It was reported that most of men receiving testosterone in the US do not have clinically meaningful low testosterone.

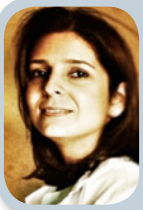
JIMS: And last but not least, which do you consider the most important challenges for our specialty (Sexual Medicine) and for our society (ESSM) in the next 5 years?

The level of knowledge regarding the physiology of male sexual response including the neurophysiology and pharmacology of ejaculation, the physiology of orgasm is still limited. We must remember that this is after and in parallel having achieved significant progress in the physiology of penile erection that effective treatments for ED have been developed. Apart from premature ejaculation, ejaculatory disorders and orgasmic problems remain unmet medical needs. ESSM has tremendously supported the development of good medical practices during the last 20 years. Ultimately European patients have benefit of better care from well trained sexual medicine physicians thanks to ESSM. The main challenges for the next 5 years, but I am afraid it will last longer, is in my opinion to design a disease modifying treatment for ED instead of symptomatic treatments and to increase the knowledge regarding ejaculatory disorders. This can achieved by engaging more scientists within sexual medicine.

It was a great pleasure to interview you; I am convinced that your points of view, fruits of a lifetime devoted to your work, will be highly appreciated by our readers. Thanks once again.

AUA 2014 Men's health highlights

by Alejandra Egui



María Alejandra Egui Rojo MD
Department of Urology
Hospital Universitario de Fuenlabrada
Madrid, Spain

Email: dra_eguirojo@hotmail.com

In this issue, we discuss the most outstanding works in the field of treatment of BPH/LUTS and recent advances in the field of sexual health, which were presented at the American Urological Congress 2014, celebrated in Orlando Florida (USA) in May, 2014. In order to extend the content provided, as in previous installments, for each work commented, the corresponding identification number is indicated in brackets, to be able to easily locate it on the conference website.

With respect to the treatment of BPH, highlights a surge in basic research, which brings two new natural compounds (phytotherapy) with posible therapeutic effect on this condition: the Honokiol and Seroitae. Similarly, research on possible new therapeutic targets stands as the enzymes Arginase and Rac.

The first study, discusses the role of Honokiol, a constituent of Magnolia, on prostatic smooth muscle (MP19-08). Honokiol and Magnolol two lignan constituent of Magnolia are used in traditional Japanese medicine. The aim of this study was to analyze the effects of these two components in the contraction of human prostate tissue and the viability of stromal cells. An in vitro assay was performed in organ bath studies with prostate tissue obtained from radical prostatectomy specimens. Contractions were induced by noradrenaline, phenylephrine or by electric field stimulation. Viability was determined by stromal cells cultures. The authors concluded Honokiol may interfere with the dynamic component of bladder outlet obstruction by inhibition of prostate smooth muscle contraction, and with the static component promoting the stromal cell apoptosis. Randomized placebo-controlled trials needed to determine the potential clinical applications based Honokiol extract treatments.

The second study evaluates the efficacy Seoritae extract to reduce the weight and suppress the proliferation of the prostate (MP19-13). The Seoritae (SE) is a variety of soybean and traditional natural food in Korea. In this paper, an analysis was performed to determine if the ES has a beneficial effect on reducing prostate weight a rat model of BPH.

Sprague-Dawley rats were divided into four groups: control, BPH, BPH and two groups were treated with SE (BPH+SE1 and BPH+SE2). All rats with BPH (BPH/HBP HBP SE1 and SE2) underwent bilateral orchiectomy and then were induced prostatic hyperplasia by administration of testosterone enanthate for 5 weeks. BPH+ SE groups received daily oral doses of SE for 5 weeks. Regarding the results, BPH group showed a marked increase in prostate weight than in the control group, whereas rats in the BPH/SE groups showed a decreased prostate weight. Similarly, the activity of 5-alpha reductase in serum and prostate were significantly higher in the BPH group compared to controls and it was reduced in the groups treated with HBP/SE. The concentration of caspase-3 (a marker of apoptosis) was significantly increased in BPH group compared to the control group, and it was decreased in the groups treated with SE. These results suggest that SE is effective to reduce the volume, and suppressing the proliferation of the prostate, which may play a role in the treatment of BPH. However, the most important limitation of this study is that the work was made in an animal model.

In respect of novel therapeutic targets, this study examined the Arginase enzyme as a possible modulator of nitric oxide (NO) activity (MP19-02). In the cell, arginase enzymes (Arg) counteract the production of NO by degrading the amino acid L-arginine, considered the major substrate of the nitric oxide synthases (NOS).
Currently, the distribution of Arg in the human prostate is unknown. This paper, evaluates by in-vitro immunochemical analysis, the expression of Arg in the transition zone (TZ) of the prostate. The results concluded that Arg I (one of the two types of arginases studied), is located together with other key proteins in the signaling of cyclic GMP in the TZ of the human prostate. These findings support the hypothesis that Arg can modulate in a negative manner the activity of the NO system in the TZ and support the role of signaling via NO-cGMP in the prostate.

Another interesting work regarding possible future therapeutic targets, it was presented by Dr Thomas Kunit et al (Munich. Germany) (MP 19-09), where studied the role of compound NSC23766 (Rac inhibitor monomeric GTPase) in the regulation of smooth muscle tone of the periurethral prostate tissue. Rac is a major regulator of smooth muscle tone outside the lower urinary tract. This analysis evaluates the effect of NSC23766 on periurethral prostatic tissue obtained from patients undergoing radical prostatectomy (n = 27). The results showed that NSC23766 inhibited the contraction induced by phenylephrine and noradrenaline in human prostate samples. In Western blot analysis revealed bands with the expected size for Rac1 in prostate tissue, prostatic stroma and glands. Rac1 was located in smooth muscle cells and epithelial tissue. The results suggest that the pathophysiology of LUTS may be affected by RAC regulation of smooth muscle tone in the lower urinary tract, constituting a potential therapeutic target.

Another topic that has reached interest in the field of BPH, is the association of this condition with other entities, specifically with the metabolic syndrome, which has been implicated in several diseases. In this sense Russo et al (PD 25-09) presented a work where the association between non alcoholic fatty liver disease (NAFLD) and the risk of moderate/severe LUTS was studied. The role of insulin resistance (IR) as a predictive factor of moderate to severe LUTS was also studied. A cross-sectional study involving 544 patients with LUTS assessed by IPSS was performed. Diagnosis

AUA 2014 Men's health highlights

of Metabolic syndrome was defined according to the criteria of the International Diabetes Federation. The NAFLD diagnosis was assessed by hepatic ultrasound, performed by a radiologist (blinded) according to the hepatic steatosis index (HSI). A higher value of 0.36 in the HSI was considered diagnostic of NAFLD. The analyses of the results found that the presence of hepatic steatosis was greater in patients with severe LUTS compared with patients with moderate and mild LUTS (37.62% vs. 36.07% and 34.69% respectively, $p < 0.01$). In logistic regression analysis, HSI values above 0.36 were found to be an independent predictor for moderate to severe LUTS, after adjustment of the presence of metabolic syndrome (OR = 2.92, $p < 0.01$). They concluded that those subjects with metabolic syndrome and HSI> 0.36 in ultrasound, showed up to 2 times more likely to have moderate or severe LUTS compared with patients diagnosed with metabolic syndrome. The authors conclude that this work found new associations between hepatic steatosis, metabolic syndrome and LUTS. Those subjects with NAFLD (indicator of metabolic syndrome) should be considered as a risk group to develop moderate to severe LUTS.

Also there have been developments regarding the treatment of LUTS / BPH. Here, we highlight two works:

The first examines the role of behavioral therapy as a significant treatment option for nocturia in men (PD 23-10). An analysis in 72 patients was performed, comparing changes in nocturia, sleep, and quality of life as a result of a new multicomponent behavioral therapy + exercise (M-BET), a therapy with active comparator (α-blocker tamsulosin 0.4 mg), and a combination of α-blocker with M-BET. The authors concluded that behavioral therapy alone or combined with α-blockers showed statistically significant reductions in nocturia and favorable effects on quality of life, sleep and other annoyances. These results suggest that the behavioral therapy can provide a significant treatment option in men with nocturia.

The second paper present an analysis of the results of combined treatment with tadalafil / finasteride for the treatment of erectile dysfunction and/or BPH-LUTS (PD 23-04). This post-hoc analysis identified the proportion of patients achieving a minimum level of improvement in erectile function and / or BPH-LUTS when co-administered tadalafil 5 mg once a day and finasteride once a day (TAD / FIN). The results showed that over 50% of patients treated with TAD / FIN and placebo / FIN showed a clinically significant improvement in LUTS / BPH. The majority of sexually active patients with ED treated with base TAD / FIN showed improvement in erectile function. It is important to note that not only patients with LUTS / BPH and DE experienced a significant improvement in erectile function, but also those without ED. The authors conclude that further studies are needed to accurately assess the benefits of this therapeutic combination.

With regard to the research conducted in the field of sexual health, first we focus on the field of clinical research, where we discuss three interesting papers, about the search for future therapeutic targets:

In the first study (MP 47-13), the role of stimulation of Calcium-activated potassium (KCa) channels as a treatment strategy in patients with ED was investigated. Previously it has been observed that the KCa stimulation enhances the vasodilatory capacity of PDE5 inhibitors. This paper evaluates the impact of the modulation of KCa in neurogenic regulation of cavernous smooth muscle tone. Copora cavernosa samples of both rats and human were obtained. Organ chamber was performed with both tissue samples and the response to electrical stimulation was measured, demonstrating reproducible contractions and frequency-dependent used in the corpus cavernosum of the rat. Blocking the large-conductance KCa (BK) markedly potentiated the contractions. These results were similar to those obtained with samples of human corpus cavernosum.

The results indicate that BK participates in regulation of neurogenic control of cavernosal smooth muscle tone. The pharmacological stimulation of these channels would favor relaxant responses. Therefore, BK stimulation might be reasonable to treat ED, especially in situations involving imbal-

anced regulation of neurogenic control.
The second paper study the increase in Rho kinase 2 an increase of synthetic smooth muscle-specific marker expression observed in the corpus cavernosum of patients with severe ED (MP 47 20). Clinical research has shown upregulation of the RhoA / Rho protein kinase (ROCK) pathway, (specifically ROCK2 isoform) in the corpus cavernosum (CC) of animal models of erectile dysfunction. In other vascular diseases, activation of ROCK results in contractile phenotypic change of smooth muscle cells (SMCs) to synthetic SMCs (for example, myofibroblasts). This analysis assessed whether these phenotypic changes were happening in the SMCs of the CC of patients with severe ED. Fourteen samples of human corpus cavernosum of patients with ED undergoing penile prosthesis implantation were analyzed and compared with 5 samples of cavernous tissue from healthy men, obtained by core biopsy. In both tissues, the expression of mRNA coding for ROCK 1, ROCK2, MYH11 (heavy chain kinase SMCs) and aSMA (SMC alpha-actin) the latter present in the contractile muscle cells (healthy) were assessed. The findings provide evidence of phenotypic changes in the CC of the SMCs of ED patients, suggesting that chronic inhibition of ROCK 2 interfere with these changes, and it may be a future therapeutic target for prevention of the DE. ROCK inhibitors for the treatment of cardiovascular disease are currently under development.

The third paper discusses the preliminary results of the use of stem cells derived from human adipose tissue in the treatment of Peyronie's disease (PD). (PD 21-01). The aim of this study was to evaluate the effects of a local injection of stem cells derived from human adipose tissue (hADSCs) in a rat model of PD in chronic phase. The results showed that in a rat model of chronic EP, ADSC injections in the tunica albuginea partially reversed the fibrosis and restored the ratio of collagen III / I to normal. The success of this pioneering study may indicate a new approach to the future of clinical research, however, in this study no data were reported about the improvement of penile curvature, which is the reason for patient consultation

It also highlights the progress towards new therapeutic regimens used in both the DE, and premature ejaculation (PE). Here, we discuss the most outstanding studies:

The first paper investigates the management of erectile dysfunction induced by diabetes with a combination of PDE5 inhibitors and strict glycemic control (MP 47-11). Recent research has indicated that the DE-induced diabetes (DM) can be effectively controlled by strict control of glycemia, as well as chronic treatment with PDE5 inhibitors. To this end, experimental work was performed in rat model (control, DM, DM treated with insulin, DM treated with PDE5 inhibitors and DM treated with insulin and PDE5 inhibitors).

The analysis of the results concluded that the diabetic rats showed decreased in erection parameters compared to normal rats. The combination of both treatments PDE5 inhibitors and glycemic control with insulin show a restoring erectile function, producing a greater effect compared to insulin treatment alone or PDE5 inhibitors alone. Multiple mechanisms (including apoptosis, endothelial rehabilitation, Rho kinase pathway), may be responsible for the additional effects. Evidence postulates that improved glycemic control in diabetic patients with ED can be beneficial. The results should be confirmed by clinical data.

The second paper, questions the role of sildenafil in rehabilitation after radical prostatectomy (RP) (MP 48-12). Sildenafil was considered an effective treatment for ED post RP. This study evaluated the patterns of recovery of erectile function after RP, and responses in 94 patients undergoing nerve sparing RP, treated with sildenafil 50 mg or placebo, from the first day after surgery and with a postoperative follow-up of 13 months. International Index of Erectile Function (IIEF), tumescence and nocturnal penile rigidity and the subjective assessment of the patient about erectile function were measured. The results show that the nightly use of sildenafil citrate does not provide a therapeutic benefit in the recovery of erectile function after RP. Regardless of treatment, both subjective and objective measures of erectile function improve with time.

The third paper investigates the impact of treatment with Silodosin 8 mg on sexual function in patients with BPH-LUTS treated with this drug (MP 40-15). This paper provides an analysis of sexual function in 137 patients diagnosed with LUTS / BPH treated with silodosin. Sexual function was assessed by IIEF orgasmic function (questions 9 and 10). With regard to the results, about 70% of patients with LUTS / BPH treated with silodosin reported anejaculation or hypospermia, and approximately 17% of men experienced impaired orgasmic function. Anejaculation found to be the cause of the interruption silodosin in 6% of patients. These robust findings reiterate previous evidence of deleterious effects of silodosin in the mechanisms that lead to the failure of ejaculation and decreased ejaculatory volume.

Finally, we discuss the study presented by Simsek et al, where perform a comparative analysis between Dapoxetine and paroxetine in the treatment of premature ejaculation (PE) (MP 48-18). This prospective analysis compared the safety and efficacy of paroxetine 20 mg daily versus dapoxetine (30 and 60 mg) in 150 patients diagnosed with PE. The results showed that although the dose of 30 mg dapoxetine not exceeded paroxetine results, treatment with 60 mg dapoxetine 1-3 hours before sexual intercourse results in a greater increase intravaginal ejaculatory latency time (IELT) respect to paroxetine. The authors conclude that treatment with 30 mg of dapoxetine demand does not exceed the daily treatment with paroxetine and suggests that the starting dose of dapoxetine treatment in cases of severe PE should be 60 mg.

Key from KOLS: Sexual outcomes after partial penectomy for penile cancer: Results from a multiinstitutional study

by Salvatore Sansalone and Valerio Iacovelli

Prof.Salvatore Sansalone
Senior Lecturer in Urology
Dept. of Experimental Medicine and Surgery
University Tor Vergata
Rome, Italy

salvatore.sansalone@yahoo.it

Valerio Iacovelli

valerio.iacovelli85@gmail.com

Penile cancer is an uncommon malignancy. For the more advance disease phase, aggressive therapy with partial or total penectomy is still the conventional and necessary treatment. Surgical treatment is inevitably mutilating and may cause a devastating effect on a man's self-image.

Considering the strong impact on patients' sexual life we evaluated sexual function and satisfaction after partial penectomy.

The patients in the present study (n=25) represented all those who attended our institutions and were diagnosed and treated for penile cancer during the period from October 2011 to November 2013. All patients underwent partial penectomy and were invited to a follow-up investigation at the out-patient clinic. Sexual pre-surgical baseline was calculated. The pre-operative IIEF (International Index of Erectile Function) scores were registered systematically. For the first domain, erectile function average score was 28.68 (range 24,5–30). Orgasmic function score was 9.86 (range 8.8–10). Sexual desire score was 8.75 (range 7.9–10). Intercourse satisfaction rate was 12.5 (range 11.8–14.5). Overall satisfaction rate was 9.01 (range 7.9–9.8).

Sexual outcomes of each patient were estimated by taking into consideration four standardized and validated questionnaires.

The **EDITS** questionnaire *(Erectile Dysfunction Inventory of Treatment Satisfaction)* was used to assess patients and partners 'treatment satisfaction. The EDITS Patient average rate was 74.97 (range 43.18–93.18); EDITS Partner average rate that was 73.25 (range 50–95.7).

The **IIEF 15** addresses the relevant domains of male sexual function that are erectile function, orgasmic function, sexual desire, intercourse satisfaction, and overall satisfaction. With regard to erectile function (IIEF 1-5,15), average score was 21.28 (range 12–29). Orgasmic function analyzed by questions 9 and 10 reached a score of 7.92 (range 2–10). Items 11 and 12 investigate about sexual desire; the average score was 7.16 (range 3–10). Intercourse satisfaction is described by items 6,7 and 8 and registered a score of 7.32 (range 0–14). The overall satisfaction average score (items 13,14) was 6.52 (range 4–10).

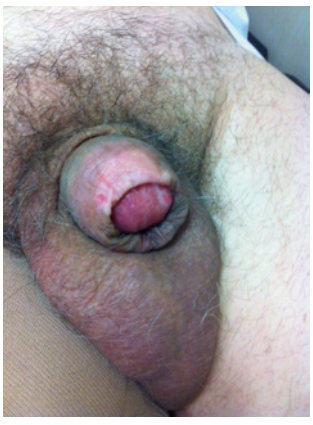
The **QEQ** questionnaire *(Quality of Erection Questionnaire)* evaluating patient himself in objective and truthful manner regarding his erection registered a score of 77.46 (range 33–91.6).

The **SEAR questionnaire** *(Self-Esteem and Relationship)* is divided in two domains. The first eight items of the SEAR questionnaire analyze the patient's sexual relationship. The overall score of SEAR 1–8 was 68.06 (range 28.12–96.8). The second domain of the SEAR is about confidence and has two subdomains self-esteem and overall relationship. SEAR 9–12 self-esteem score was 73.25 (range 43.75–100); SEAR 13–14 overall relationship score was 74.5 (range 25–100).

Although penile cancer is an uncommon malignancy, the majority of patients will have 5 years disease specific survival of over 90% despite local recurrence 25. Hence, these long term survivors will live with the sexual and psychosexual effects of their treatment. Inevitably, partial penectomy resulted in changes to both feelings of masculinity and perception of self and body image. These feelings may also have an emotional basis and be associated with unconscious fears from a "cracked" image of lover to reticence in showing the surgical site to the partner. Furthermore, for our young patient without partner, changed appearance was a major concern and a potential barrier to seeking new relationship.

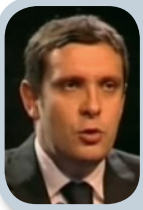
Although uncommon, penile cancer is a diagnosis with profound implications for men's sexual life. This study indicates a high percentage of patients and partners satisfaction about the surgical treatment with a promising results regarding recovery of sexual function, self-esteem and overall relationship satisfaction.

Pretreatment correct education and a proper multidisciplinary follow up may improve sexual outcome after partial penectomy.



Key from KOLS: Testosterone and cardiovascular risk

by Giovanni Corona, Mario Maggi



Dr. Giovanni Corona
Endocrinology Unit
Maggiore-Bellaria Hospital
Medical Department
Azienda-Usl Bologna
Bologna, Italy

jocorona@libero.it

Prof. Mario Maggi
Andrology and Sexual Medicine Unit
Department of Department of
Experimental, Clinical
and Biomedical Sciences
University of Florence
Florence, Italy
m.maggi@dfc.unifi.it

Cross-sectional epidemiological studies clearly show a significant relationship between low testosterone (T) and cardiovascular (CV) diseases (CVD) (1–3). However, longitudinal studies have failed to document an association between baseline low T and incident CVD (1–3). In addition, analysis of longitudinal trajectory patterns of elderly men in the Framingham Heart Study confirms the lack of association between low T and incident events (4). In contrast, a significant increase in risk of incident CV mortality for subjects with low T has been reported in one meta-analysis (1), while in another a non-significant trend was observed (2). It has also been suggested that the increased risk associated with low T could be limited to elderly subjects (3). Meanwhile, conditions associated with high CVD risk, such as obesity, metabolic syndrome (MetS), type 2 diabetes mellitus (T2DM) and dyslipidaemia, were all associated with incident hypogonadism, as demonstrated in the prospective population-based Study of Health in Pomerania (5–6). Hence, the relationship between hypogonadism and increased CV risk is at least multi-directional and, therefore, still a matter of debate. One possible interpretation of all the aforementioned data is that low T could be an adaptive condition in order to be more resilient, by sparing energy in an adverse state, as is the case for low three iodothyronine (T3) in the low T3 syndrome. Hence, the existence of a low T syndrome has been hypothesized (7). Alternatively, it can be speculated that CVD-associated hypogonadism represents a restraint to male fertility, thus limiting fatherhood in unhealthy conditions such as malnutrition, obesity or chronic illnesses.

Retrospective pharmaco-epidemiological studies might help in better clarifying this issues. A retrospective observational study from Seattle evaluated mortality rate in a series of 1031 T treated, compared with untreated hypogonadal (total T < 8.7 nmol/liter) male veterans (VA) greater than 40 years old (9). Over a mean follow-up period of 40.5 years, it was found that men receiving testosterone supplementation (TS; n=398) have a 39% decrease in mortality (HR 0.61; 95% CI 0.42–0.88), when compared to the untreated counterpart (9). Similar results have been reported in another retrospective study on type 2 diabetic subjects (10). However, these results must be interpreted cautiously because residual confounding may still be a source of bias, including the substantial risk of a primary selection bias due to the nonrandom assignment of T exposure. In addition, both studies used only all-cause mortality as the outcome and therefore the relevance of CV-related mortality was not captured. This gap was recently covered by another pharmaco-epidemiological survey conducted at the University of Texas Medical Branch at Galveston (US), examining 25,420 Medicare (the US's largest commercial health insurance) beneficiaries 66 years or older treated with T for up to eight years (11). The identified cohort was matched to 19,065 T nonusers at a 1:3 ratio. The study found that TS was not linked with any increased risk for heart attack (hazard ratio [HR] = 0.84; 95% CI = 0.69–1.02). In contrast, men at greater risk for heart problems who used T actually had a lower rate of heart attacks than similar men who did not receive this treatment. In apparent contrast with the aforementioned findings are two other, recently published, pharmaco-epidemiological studies (12–13). The first retrospectively evaluated a cohort of 8,709 VA, who had undergone coronary angiography between 2005 and 2011 showing low T levels (T<10.4 nmol/L). Among men who were receiving any form of TS, 25.7% had MACE, or died from any cause, versus 19.9% of those who did not receive hormonal therapy, with a hazard ratio of 1.29 (95% CI 1.04–1.58; P=0.02), which was not substantially affected by adjusting for confounders (12). Although the study presented many flaws, due to its retrospective design and to the little information on the VA database, it has received much attention in the lay media. One of the main criticisms of the study was based on an improper exclusion from analysis of 1132 men who had received a T prescription after experiencing a CV event (myocardial infarction or stroke, 14). Quite unexpectedly, the author's answer indicated "an incorrect notation" regarding this value (15). In particular, they asserted that the numbers of men excluded for this reason was 128, not 1132 after the data revision. This is an 89% error rate, involving >1000 individuals. In addition, 100 women were erroneously included in the original group of 1132 individuals. Considering that the main results could have been flawed by the gross study design and execution, a letter recommending retraction of the article by Vigen et al (12) has been submitted to the Editor-in-Chief of JAMA (16). The document was supported by several professional Societies (including the International Society for Sexual Medicine and International Society for the Study of Aging Male), and more than 100 scientists from 24 countries (16).

Another retrospective study, funded by the National Institutes of Health, investigated, in a large health-care database from Truven Health Analytics, the rate of nonfatal myocardial infarction in 56,000 middle-aged and older men, who were prescribed TS (13). The study reported a doubling in the risk of heart attack among men aged 65 years and older and a two- to three-fold increased risk in younger men with a preexisting history of heart disease, but not in those without CV events (13).

This contradictory scenario was further complicated in 2010, when the Testosterone in Older Men with Mobility Limitations (TOM) trial was

ESSM

European Society for Sexual Medicine

The European Society for Sexual Medicine (ESSM) is a not-for-profit, multidisciplinary, academic and scientific organisation dedicated to male and female sexual health and dysfunction.

Benefits of Becoming an ESSM Member

- ESSM offers its members a permanently updated web-site with different forums and a monthly update of the whole scientific literature of Sexual Medicine, Andrology and related medical disciplines.
- ESSM provides its members quarterly newsletter, ESSM Today which features the most recent news in the field of Sexual Medicine and focuses on key topics of interest to physicians in the field.
- ESSM has supported the creation of the Multidisciplinary Joint Committee on Sexual Medicine (MJCSM) that is working under the auspices of the European Union of Medical Specialists (UEMS). MJCSM's objectives are to study, promote and harmonize the highest level of Sexual Medicine in Europe – both on the basic and postgraduate level. The MJCSM will determine the standards for training and assessment in Sexual Medicine. Successful candidates will be awarded on behalf of the MJCSM the title of "Fellow of European Committee on Sexual Medicine (FECSM).
- Since 2007 ESSM has offered interested ESSM members the participation in a course of the European School of Sexual Medicine. Since 2013 the course is held in Budapest with the participation of more than 30 students from all over the world, supervised by the School Directors Yacov Reisman and Francesca Tripodi.
- Besides this structured course ESSM offers at its annual congresses both instructional courses related to topics of interest in Sexual Medicine and Master Courses covering the key contents of the ESSM educational program.
- ESSM provides to its members important research grants which all members are welcome to apply for according to eligibility criteria. These are intended to further research into any aspect of Sexual Medicine and are awarded with a maximum of EUR 30.000,00 each for a maximum of 18 months project duration.
- ESSM recognizes that basic scientists who are not actively engaged in clinical work in sexual medicine field may have had difficulty finding funds to attend the ESSM Annual Congresses.
- Fellowship support options are available either on individual application, supported by the National Affiliated Societies or by applying to different initiatives supported by the ESSM and open for members to apply upon invitation.

Take Your Chance – Become a Member of ESSM, Now!

Seize the day, or in Latin Carpe diem and become a member of ESSM now, to take all the advantages and benefits of ESSM membership.
There are two levels of ESSM membership available:

ESSM/ISSM Membership
A combined ESSM/ISSM membership (annual fee 160 EUR) for both Sexual Medicine Societies (ESSM/ISSM) including all ESSM and ISSM membership related services, including a subscription to the Journal of Sexual Medicine which is the monthly journal of the ISSM (International) and ESSM (European), and is the leading Journal in the field of Sexual Medicine. In addition there are reduced registration fees for all ISSM/ESSM related congresses.

ESSM only Membership
ESSM only membership (annual fee 50 EUR – reduced to 25 EUR for residents in training) which includes the ESSM official Scientific and Social periodical, the „ESSM Today", full access to the new comprehensive ESSM website:

www.essm.org

(including regularly updated scientific material, monthly updated literature reviews, the most recent guidelines, lecture recordings and presentations from past ESSM congresses), the opportunity to participate in the ESSM educational programs, and to apply for scientific and support grants and a reduced fee for the ESSM annual congress.

Formal ESSM membership applications can either be submitted directly to the ESSM or through one of the national ESSM affiliated societies. The ESSM Executive Committee is responsible for the approval of the membership application.

ESSM Annual Membership Fees (January to December)

Combined ESSM/ISSM Fee incl. JSM Journal	EUR 160
ESSM only Fee	EUR 50*

* A reduced fee EUR 25 is available for residents in training against proof of evidence.

European Society for Sexual Medicine
ESSM SECRETARIAT
Daniela Pajola | Via Ripamonti 129 | 20141 Milano, Italy
phone: +39 02–56601 625 | fax: +39 02–70048 577
email: admin@essm.org

published (17). Although improved physical function was noted (including leg- and chest-press strength and stair climbing while carrying a load), the TOM trial was ended early on, because of an imbalance in respiratory, dermatological and, most important, CV events between the two arms (CV events: T = 23 vs. placebo=5). In this randomized clinical trial (RCT), the authors randomized men aged 65 years or older (mean age 74±5) with limitations in mobility and total T levels between 3.5 and 12.1 nmol/L or free T <173 pmol/L to placebo or supra-physiological dose of T gel (100 mg daily) for six months, to assess the effect of TS on exercise tolerance. The cohort consisted of elderly community-dwelling men with a high prevalence of hypertension, obesity, diabetes, dyslipidemia, and known CVD. In addition, the TOM trial used a very broad definition of CV events, which are not adjudicated (17).Yet, the diversity of the cardiac events that occurred and the lack of their structured ascertainment strongly limit the clinical value of the study. Moreover, the population studied (frail men) and the utilization of high T dosages (double the recommended dose) further limit the study's generalizability.

Systematic reviews and meta-analyses are often considered as the highest level of evidence for evaluating interventions in healthcare and as a particularly useful tool in addressing questions for which multiple data sources are conflicting, or when there is a variety of reports with low statistical power, because pooling data can improve power and provide a convincing result. In 2013, Xu et al., (18) suggested a possible increased CV risk associated with TS. The authors meta-analyzed studies lasting 12 weeks or more and clearly reporting all CV-related events including 27 trials, enrolling 2,994 men. The forest plot indicates that TS increased the risk of CV events, with an OR=1.54 [1.09−2.18], which was even higher (OR=2.06 [1.34-3−17]) when results were categorized according to a positive pharmaceutical industry funding. However, it should be recognized that the primary outcome considered was "composite CV events", defined as anything reported as such by the study's authors including "peripheral edema" and "self-reported syncope". An overly broad definition of CV endpoints, inappropriately reported as "CV-related" by the investigators, increases the statistical power of the analysis, but, on the other hand, can be grossly misleading due to the heterogeneity and limited reliability of diagnostic criteria used to attribute these events to being drug-related. In our opinion, the assessments of CV safety of any therapy should be based on the incidence of major adverse cardiac events (MACE), which are easier to detect and less controversial in diagnosis. Xu et al., (18) meta-analysis was in contrast with three previous ones (19−21), showing neither a significant difference between the T and placebo groups for all incident CV events, nor for each type of event (CV death, fatal and non-fatal myocardial infarction, revascularization procedures, arrhythmia, cerebrovascular events), except the aforementioned increase in hematocrit over 50%, which was significantly more prevalent in the T group.

We recently performed the last, updated, systematic review and meta-analysis of RCTs on TS (14), using a more conventional definition of CV events similar to that used by regulatory authorities to verify the safety of newly registered drugs (www.fda.gov/Drugs/). We included all RCTs enrolling men and comparing the effect of TS vs. placebo on different endpoints giving CV-related events by study arm without any arbitrary restriction, even if CV events were not the principal endpoints. The principal outcome of this analysis was to examine the effect of TS, as compared to placebo, on the incidence of a new MACE. MACE was defined as the composite of CV death, non-fatal myocardial infraction and stroke, and acute coronary syndromes and/or heart failure reported as serious adverse events (www.fda.gov/Drugs/). Secondary outcomes included all CV-related events defined as anything reported as such by the authors of the individual studies. When meta-analyzing the largest number of studies collected so far (75 trials enrolling 5,464 subjects), we (14) did not observe any increase in CV risk associated with TS either when composite or single CV end-points were considered. In particular, the use of TS was not associated with any significant difference in the incidence of MACE with respect to placebo (MH-OR:1.01[0.57;1.77]; p=0.98). It should be recognized that although our data suggest no clear sign of risk in the short term, no information on possible long-term TS effects are available. Interestingly, when the CV effect of TS was categorized according to the baseline study population characteristics, we observed a protective role of TS in subjects with metabolic disease (14). This is not a surprise because, by meta-analyzing the available evidence, we previously demonstrated that TS is associated with an improvement of fat mass and glycometabolic control in subjects with T2DM and MetS (8). Similar results have been more recently confirmed by other authors (22).

Recently, the European Medicines Agency's Pharmacovigilance Risk Assessment Committee after completing an European Union-wide review of testosterone-containing medicines, concluded that evidence about the risks of these medicines in terms of serious side effects on the heart is inconsistent. The committee considered that the benefits of TS continued to outweigh its risks, but recommended that T-containing medications should only be used where hypogonadism has been confirmed by signs and symptoms, as well as laboratory tests.

Read the review here:
(http://www.ema.europa.eu/ema/index.jsp?curl=pages/medicines/human/referrals/Testosterone-containing_medicines/human_referral_prac_000037.jsp&mid=WC0b01ac05805c516f).

In conclusion, whereas it is clear the absence of any relationship between TS and increased CV risk, whether TS might represent a new strategy in improving metabolic profile and body composition, and thus reducing the risk of heart disease, needs also to be confirmed in larger and longer studies.

Key from KOLS: Testosterone and cardiovascular risk

References

1. Corona G, Rastrelli G, Monami M, Guay A, Buvat J, Sforza A, Forti G, Mannucci E & Maggi M. **Hypogonadism as a risk factor for cardiovascular mortality in men: A meta-analytic study.** Eur J Endocrinol. 2011;165: 687-701
2. Araujo AB, Dixon JM, Suarez EA, Murad MH, Guey LT &Wittert GA. Clinical review: **Endogenous testosterone and mortality in men: A systematic review and meta-analysis.** J Clin Endocrinol Metab. 2011;96: 3007-19.
3. Ruige JB, Mahmoud AM, De Bacquer D & Kaufman JM. **Endogenous testosterone and cardiovascular disease in healthy men: A meta-analysis.** Heart. 2011; 97, 870-5.
4. Haring R, Teng Z, Xanthakis V, Coviello A, Sullivan L, Bhasin S, Murabito JM, Wallaschofski H, Vasan RS. **Association of sex steroids, gonadotrophins, and their trajectories with clinical cardiovascular disease and all-cause mortality in elderly men from the Framingham Heart Study.** Clin Endocrinol (Oxf). 2013;78:629-34.
5. Torkler S, Wallaschofski H, Baumeister SE, Völzke H, Dörr M, Felix S, Rettig R, Nauck M, Haring R. **Inverse association between total testosterone concentrations, incident hypertension and blood pressure. Aging Male.** 2011;14:176-82.
6. Schipf S, Haring R, Friedrich N, Nauck M, Lau K, Alte D, Stang A, Völzke H, Wallaschofski H. **Low total testosterone is associated with increased risk of incident type 2 diabetes mellitus in men: Results from the Study of Health in Pomerania** (SHIP). Aging Male. 2011;14:168-75.
7. Corona G, Rastrelli G, Maseroli E, Fralassi N, Sforza A, Forti G, Mannucci E, Maggi M. **Low testosterone syndrome protects subjects with high cardiovascular risk burden from major adverse cardiovascular events.** Andrology. 2014;2:741-7.
8. Corona G, Rastrelli G, Maggi M. **Diagnosis and treatment of late-onset hypogonadism: Systematic review and meta-analysis of TRT outcomes.** Best Pract Res Clin Endocrinol Metab. 2013;27:557-79.
9. Shores MM, Smith NL, Forsberg CW, Anawalt BD & Matsumoto AM. **Testosterone treatment and mortality in men with low testosterone levels.** J Clin Endocrinol Metabol. 2012; 97, 2050–2058.
10. Muraleedharan V, Marsh H, Kapoor D, Channer KS, Jones TH. **Testosterone deficiency is associated with increased risk of mortality and testosterone replacement improves survival in men with type 2 diabetes.** Eur J Endocrinol. 2013;169:725-33.
11. Baillargeon J, Urban RJ, Kuo YF, Ottenbacher KJ, Raji MA, Du F, Lin YL, Goodwin JS. **Risk of Myocardial Infarction in Older Men Receiving Testosterone Therapy. Ann Pharmacother.** 2014 Jul 2. pii: 1060028014539918. [Epub ahead of print]
12. Vigen R, O'Donnell CI, Barón AE, Grunwald GK, Maddox TM, Bradley SM, Barqawi A, Woning G, Wierman ME, Plomondon ME, Rumsfeld JS & Ho PM. **Association of testosterone therapy with mortality, myocardial infarction, and stroke in men with low testosterone levels.** JAMA. 2013; 310: 1829-36.
13. Finkle WD, Greenland S, Ridgeway GK et al. I**ncreased risk of non-fatal myocardial infarction following testosterone therapy prescription in men.** PLoS One. 2014; 9, e85805.
14. Corona G, Maseroli E, Rastrelli G, Isidori AM, Sforza A, Mannucci E, Maggi M. **Cardiovascular risk associated with testosterone-boosting medications: A systematic review and meta-analysis.** Expert Opin Drug Saf. 2014;13:1327-51.
15. **Deaths and cardiovascular events in men receiving testosterone** JAMA 2014;311:963
16. Morgentaler AD for the Androgen Study Group. **Letter to JAMA asking for retraction of misleading article on testosterone therapy.** Available at: *www.androgenstudygroup.org/component/content/article?id=90:letterto-jama-asking-for-retraction-ofmisleading-article-on-testosterone-therapy*. [Last accessed 3 November 2014]
17. Basaria S, Coviello AD, Travison TG, Storer TW, Farwell WR, Jette AM, Eder R, Tennstedt S, Ulloor J, Zhang A, Choong K, Lakshman KM, Mazer NA, Miciek R, Krasnoff J, Elmi A, Knapp PE, Brooks B, Appleman E, Aggarwal S, Bhasin G, Hede-Brierley L, Bhatia A, Collins L, LeBrasseur N, Fiore LD, Bhasin S. **Adverse events associated with testosterone administration.** N Engl J Med. 2010;363:109-22.
18. Xu L, Freeman G, Cowling BJ, **Schooling CM. Testosterone therapy and cardiovascular events among men: A systematic review and meta-analysis of placebo-controlled randomized trials.** BMC Med. 2013;11:108.
19. Calof OM, Singh AB, Lee ML, Kenny AM, Urban RJ, Tenover JL, Bhasin S. **Adverse events associated with testosterone replacement in middle-aged and older men: A meta-analysis of randomized, placebo-controlled trials.** J Gerontol A BiolSci Med Sci. 2005;60:1451-7.
20. Haddad RM, Kennedy CC, Caples SM, Tracz MJ, Boloña ER, Sideras K, Uraga MV, Erwin PJ, Montori VM. **Testosterone and cardiovascular risk in men: A systematic review and meta-analysis of randomized placebo-controlled trials.** Mayo Clin Proc. 2007;82:29-39.
21. Fernández-Balsells MM, Murad MH, Lane M, Lampropulos JF, Albuquerque F, Mullan RJ, Agrwal N, Elamin MB, Gallegos-Orozco JF, Wang AT, Erwin PJ, Bhasin S, Montori VM. Clinical review 1: **Adverse effects of testosterone therapy in adult men: A systematic review and meta-analysis.** J Clin Endocrinol Metab. 2010;95:2560-75
22. Cai X, Tian Y, Wu T, Cao CX, Li H, Wang KJ. **Metabolic effects of testosterone replacement therapy on hypogonadal men with type 2 diabetes mellitus: A systematic review and meta-analysis of randomized controlled trials.** Asian J Androl. 2014;16

Have you read? Best of the Best: Basic Research

by Javier Angulo

Javier Angulo, PhD
Associate Editor
Departamento de Investigación
IRYCIS Hospital Universitario
Ramón y Cajal
Madrid, Spain

javier.angulo@hrc.es

Aging and ED – Oxidative stress and hypercontractility

Oxidative stress associated with middle aging leads to sympathetic hyperactivity and downregulation of soluble guanylyl cyclase in corpus cavernosum

Sila FH, Lanaro C, Leiria LO, Rodrigues RL, Davel AP, Claudino MA, Toque HA, Antunes E.
Am J Physiol Heart Circ Physiol 2014, pii: ajpheart.007.2013 - Sep 12 [Epub ahead of print].

Aging is the main independent risk factor for cardiovascular disease but also for erectile dysfunction (ED). Specifically, vascular aging is a determinant factor for cardiovascular disease and ED in the elderly. Reactive oxygen species (ROS) are physiologically produced at basal rate into the vascular wall in a controlled regulated manner. Eventually, different physiological and pathophysiological stimuli can generate acute increases in oxidative stress that influence cellular processes and signaling. In this regard, the concentrations of ROS may increase in pathological situations, as a consequence of either an increased ROS production and/or a reduction in the antioxidant defenses, since Denham Harman formulated the free radical theory of aging, the role of oxidative stress in the aging process and aging-related diseases is widely accepted. Aging vasculature generates an excess of ROS, superoxide and hydrogen peroxide, that compromise vascular function and facilitate the formation of the deleterious radical, peroxinitrite. Main sources of ROS are mitochondrial respiratory chain and NADPH oxidases although NOS uncoupling could also account for ROS generation. Although the role of ROS in ED in diabetic and aging animal models has been shown, mainly related to NO/cGMP pathway, Silva and collaborators focused on the impact of middle-aging and oxidative stress on adrenergic contraction of cavernosal tissue. They compared contractions elicited by electrical field stimulation (EFS) and norepinephrine in corpus cavernosum (CC) from 3.5-months old (young) and 10-month old (middle-aged). Cavernosal ROS levels and expressions of tyrosine hydroxylase (TH, a marker of adrenergic neurons) and α_1/β_1 subunits of soluble guanyly clycase (sGC) were also evaluated in both groups of animals.

Neurogenic contractions were enhanced in cavernosal tissue from middle-aged rats and this effect was accompanied by an increase in TH mRNA levels, suggesting a pre-synaptic hyperactivation. However, post-synaptic stimulation of adrenergic receptors with phenylephrine resulted in greater contractions in cavernosal tissue from middle-aged rats. This was not associated with an alteration on the expression of α_1A-adrenoceptors while a reduction in the protein levels of α_1/β_1 sGC subunits was observed in CC from middle-aged rats. ROS generation was significantly increased in CC from middle-aged rats. The involvement of ROS in sympathetic hypercontractilty and altered expression in CC from middle-aged rats was confirmed by the restoration of ROS levels and normalization of TH and sGC expressions by a 4-week treatment with the NADPH oxidase inhibitor, apocynin.

The authors propose the **reduction of oxidative stress by dietary antioxidants as a strategy to treat ED in aging population.** The mention of dietary antioxidants is interesting and is probably due to the controversial results obtained with the administration of pharmacological amounts of exogenous antioxidants in large aging population studies. Although epidemiological studies usually show prevention of cardiovascular events in subjects with higher **consumption of natural antioxidants in the diet** (Mediterranean diet, nuts, ß-carotens, etc.), large studies have frequently displayed no effects with respect to vascular health **by exogenous administration of antioxidants to aging subjects** or even a worse outcome in some cases. This could be related to the **physiological role that ROS play in vascular system** and experts propose therapies aimed **to preserve/recover systems responsible for cellular response to oxidative stress in aging** rather than to administer exogenous antioxidants. On the other hand, this work support the concept of **vascular aging as a modifiable risk factor for ED** changing the old view of the vascular aging as a non-modifiable risk factor.

Diabetic ED – Obesity and insulin resistance

Bariatric surgery improves the cavernosal neuronal, vasorelaxation, and contraction mechanisms for erectile dysfunction as a result of amelioration of glucose homeostasis in a diabetic rat model

Choi YS, Lee SK, Bae WJ, Kim SJ, Cho HJ, Hong SH, Lee JY, Hwang TK, Kim SW.
PLoS One 2014, 9: e104042.

Type 2 diabetes and obesity are two closely related conditions that are associated with the development of erectile dysfunction (ED). Diabetes and obesity are also known to have an impact on vascular function and represent a risk factor for cardiovascular disease. In addition to adoption of healthy lifestyle, bariatric surgery is the treatment indicated for morbid obesity. Bariatric surgery has been shown to ameliorate systemic vascular function and to reverse sexual dysfunction in obese patients. However, the mechanisms involving this positive effect are not well defined. In this sense, Choi and collaborators propose normalization of glucose disposal as the mechanism responsible for beneficial effects of bariatric surgery in obese diabetic subjects. For this purpose they used an animal model of type 2 diabetes and obesity: The Otsuka Long-Evans Tokushima Fatty (OLETF) rat. They performed a duodenal-jejunal bypass in the rats which would be similar to stomach-sparing, proximal, Roux-en-Y bypass surgery in humans. A sham-operated group was used for comparison. Bariatric surgery resulted in a moderate but significant weight loss four weeks after operation. In addition, the bariatric surgery group displayed a

Have you read ? Best of the Best: Basic Research

marked improvement in oral glucose tolerance test (OGTT) either with respect to pre-surgery or to sham-operated group post-surgery values. In comparison to sham-operated, animals undergoing bariatric surgery had enhanced in vivo erectile responses to cavernosal nerve stimulation and higher smooth muscle/collagen ratio in corpus cavernosum. The surgical therapy also resulted in increased eNOS and nNOS expression in corpus cavernosum while reduced cavernosal Rho-kinase expression and content of 8-oxo-2'-deoxyguanosine (8-OHdG), a marker of DNA damage induced by oxidative stress. Authors suggest that bariatric surgery restores glucose homeostasis in type 2 diabetic obese rats increasing eNOS and nNOS while reducing Rho-kinase expressions in corpus cavernosum. These effects would be responsible for improving vascular structure and recovering erectile function.

The study by Choi and co-workers support other evidences suggesting that insulin resistance is an important deleterious condition for endothelial and vascular function. In fact, it has been demonstrated that endothelial function is impaired in microvasculature of morbid obese subjects with insulin resistance (HOMA-IR > 3.8) but **is preserved in equally obese subjects but with normal insulin sensitivity** (El Assar et al. J Transl Med 2013). Furthermore this study also points to increased ROS generation as responsible for endothelial dysfunction in insulin resistant obese subjects.

Although the relationship between bariatric surgery and insulin sensitivity is not completely elucidated (mere weight loss? fat mass reduction?), the study by Choi and collaborators suggests that the **reversal of insulin resistance would normalize ROS generation and restore vascular and cavernosal alterations, promoting the recovery of erectile function**. It should be noted that **Rho-kinase is ROS-sensitive** and antagonizes NO/cGMP pathway. As the authors acknowledge as limitations of the study, **more extensive metabolic analysis, further physical determinations** could delineate the impact of bariatric surgery on metabolic status and vascular and cavernosal functions. In addition, **the impact of bariatric surgery on the level of androgens and estrogens** related to erectile function represents an interesting issue to address in the future.

Diabetic ED – Progression of diabetes and oxidative stress

Role of oxidative stress-induced systemic and cavernosal molecular alterations in the progression of diabetic erectile dysfunction
Castela A, Gomes P, Domingues VF, Paíga P, Costa R, Vendeira P, Costa C.
J Diabetes 2014, doi: 10.1111/1753-0407.12181 – Jun 9 [Epub ahead of print].

Pathophysiology of diabetic ED is multifactorial, consisting predominantly of vascular and neurological insults as a result of hyperglycemia-induced metabolic derangements. Accumulation of ROS due to increased generation and/or decreased detoxification by endogenous systems outstands as a main mechanism causing reduced availability of NO in vascular and erectile tissues leading to ED in diabetes. In fact, an exaggerated reduction of NO availability has been proposed as responsible for the lack of adequate response to PDE5 inhibitors in diabetic ED.

Although the association of diabetic ED with oxidative stress is clear, Castela and collaborators have investigated systemic and cavernosal oxidative stress with the progression of diabetes and the modifications produced in corpus cavernosum that could compromise tissue homeostasis and erectile function. They have paid attention to hydrogen peroxide (H_2O_2), a ROS less studied in cavernosal pathophysiology in favour of the most analyzed superoxide. H_2O_2 is generated after dismutation of superoxide and by other enzymatic reactions and, in contrast to superoxide, diffuses across membranes. The authors used a model of type 1 diabetes induced by streptozotocin in rats. Systemic and cavernosal oxidative stress parameters were analyzed in early (2 weeks) and late (8 weeks) stages of diabetes. They found increased accumulation of H_2O_2 in urine from diabetic rats at early stage that was maintained after 8 weeks of diabetes. Plasmatic glutathione reduced/oxidized ratio (GSH/GSSG), as an index of endogenous antioxidant capacity, was conserved at early stage of diabetes but was significantly reduced at late stage, suggesting an imbalance in the systemic redox status towards the promotion of oxidative damage. In cavernosal tissue from diabetic, H_2O_2 significantly increased at the late stage of diabetes. Furthermore, there was an increase in nitrosative stress (which is driven by reactive nitrogen species (RNS) such as peroxinitrite radical) in diabetic corpus cavernosum at late stage of diabetes as demonstrated by the increase in 3-nitrotyrosine-modified proteins (a modification that compromise protein function) in cavernosal tissue from these animals, located predominantly in cavernosal smooth muscle. Finally, this redox imbalance favoring oxidant modifications is associated with a reduction in the expression of eNOS, an enzyme of NO/cGMP pathway that is key for adequate erectile function.

Castela and co-workers conclude that **increased cavernosal oxidative stress, augmented protein oxidative damage and decreased eNOS expression are the deleterious events occurring with the progression of diabetes and contributing to ED**. They highlight the relevance of **preventive antioxidant therapy** to overcome such events. In line with the first article commented in this section, it would be pertinent to bring here the concept of **promoting endogenous antioxidant response** of cavernosal tissue as an alternative to the administration of exogenous antioxidants. However, this work also opens interesting questions such as that raised by the detection of **eNOS in cavernosal smooth muscle** and its down-regulation by diabetes: Is this enzyme relevant to cavernosal smooth muscle function and penile erection? On the other hand, it should be interesting to define **the mechanism linking oxidative stress to eNOS down-regulation**: Is it mediated by redox factors such as Rho-kinase? or is it a simple consequence of ROS- or RNS-induced endothelial apoptosis?

Have you read? Best of the Best: Clinical

A brief summary of the best papers and abstracts published in the main journals related to Sexual Medicine **by Nicola Mondaini**

Dr. Nicola Mondaini
Associate Editor
Department of Urology
Ospedale Santa Maria Annunziata
(Ponte a Niccheri)
Via dell'Antella, 58 – Bagno a Ripoli
Florence, Italy
mondatre@hotmail.com

ERECTILE FUNCTION

Lifestyle modifications and erectile dysfunction: What can be expected?

Maiorino MI et alt: Asian J Androl. 2014 Sep 9.

Erectile dysfunction (ED) is a common medical disorder whose prevalence is increasing worldwide. Modifiable risk factors for ED include smoking, lack of physical activity, wrong diets, overweight or obesity, metabolic syndrome, and excessive alcohol consumption. Quite interestingly, all these metabolic conditions are strongly associated with a pro-inflammatory state that results in endothelial dysfunction by decreasing the availability of nitric oxide (NO), which is the driving force of the blood genital flow. Lifestyle and nutrition have been recognized as central factors influencing both vascular NO production, testosterone levels, and erectile function. Moreover, it has also been suggested that lifestyle habits that decrease low-grade clinical inflammation may have a role in the improvement of erectile function. In clinical trials, lifestyle modifications were effective in ameliorating ED or restoring absent ED in people with obesity or metabolic syndrome. Therefore, promotion of healthful lifestyles would yield great benefits in reducing the burden of sexual dysfunction. Efforts, in order to implement educative strategies for healthy lifestyle, should be addressed

FERTILITY

Factors affecting spermatogenesis upon gonadotropin-replacement therapy: A meta-analytic study

Rastrelli G et alt: Andrology. 2014 Oct 1.

A meta-analysis was performed to systematically analyse the results of gonadotropin and GnRH therapy in inducing spermatogenesis in subjects with hypogonadotropic hypogonadism (HHG) and azoospermia. An extensive Medline and Embase search was performed including the following words: 'gonadotropins' or 'GnRH', 'infertility', 'hypogonadotropic', 'hypogonadism' and limited to studies in male humans. Overall, 44 and 16 studies were retrieved for gonadotropin and GnRH therapy, respectively.

Of those, 43 and 16 considered the appearance of at least one spermatozoa in semen, whereas 26 and 10 considered sperm concentration upon gonadotropin and GnRH, respectively. The combination of the study results showed an overall success rate of 75% (69–81) and 75% (60–85) in achieving spermatogenesis, with a mean sperm concentration obtained of 5.92 (4.72–7.13) and 4.27 (1.80–6.74) million/mL for gonadotropin and GnRH therapy, respectively. The results upon gonadotropin were significantly worse in studies involving only subjects with a pre-pubertal onset HHG, as compared with studies involving a mixed population of pre- and post-pubertal onset [68% (58–77) vs. 84% (76–89), $p = 0.011$ and 3.37 (2.25–4.49) vs. 12.94 (8.00–17.88) million/mL, $p < 0.0001$; for dichotomous and continuous data, respectively].

A similar effect was observed also upon GnRH. No difference in terms of successful achievement of spermatogenesis and sperm concentration was found for different FSH preparations. Previous use of testosterone replacement therapy (TRT) did not affect the results obtained with gonadotropins. Finally, a higher success rate was found for subjects with lower levels of gonadotropins at the baseline and for those using both human chorionic gonadotropin and FSH. Gonadotropin therapy, even with urinary derivatives, is a suitable option in inducing/restoring fertility in azoospermic HHG subjects. Gonadotropins appear to be more efficacious in subjects with a pure secondary nature (low gonadotropins) and a post-pubertal onset of the disorder, whereas previous TRT does not affect outcome.

HPV

Awareness and knowledge of human papillomavirus-related diseases are still dramatically insufficient in the era of high-coverage vaccination programs

Capogrosso P et alt: World J Urol. 2014 Sep 2

Assess knowledge and awareness concerning human papillomavirus (HPV) infection, HPV-associated diseases, and the existence of a specific vaccine among non-HPV-screened Caucasian-European adults after the market introduction of HPV vaccines. A cohort of 934 consecutive patients seeking their first medical help for uroandrologic purposes anonymously completed a 17-item questionnaire related to HPV. Data were compared with those of an age-comparable cohort of nurses (controls; n = 172). Knowledge and awareness of HPV infection were reported in 564 (51%) and 735 (66.5%) participants, respectively. Overall, 51.3% participants were informed that HPV is sexually transmitted, but most reported not being aware that HPV infection can be associated with anogenital warts (61.7%), female genitalia (46.6%), penile (58.5%), and oropharyngeal cancer (79.7%). Only 36.5% of the participants were informed regarding the existence of a specific vaccine. HPV knowledge was retrieved through the media and/or the Internet, at school, doctors, and relatives or friends in 395 (35.7%), 155 (14%), 97 (8.8%), and 88 (8.0%) participants, respectively.

Multivariable analyses showed that female gender [odds ratio (OR) 3.08; $p < 0.001$; 95% confidence interval 2.18–4.35] and educational status [high school diploma versus primary-secondary (OR 1.61; $p = 0.03$; 1.04–2.51); university degree versus primary-secondary (OR 2.89; $p < 0.001$; 1.83–4.57)] were significantly associated with awareness of HPV.Only approximately half of the participants reported knowing what HPV infection is, even after the approval and market introduction of the HPV vaccine. Awareness about the existence and availability of a HPV vaccine was even lower.

Have you read ? Best of the Best: Clinical

PENILE SURGERY

Penile prosthesis surgery in out-patient setting: Effectiveness and costs in the "spending review" era

Mondaini N et alt: Arch Ital Urol Androl. 2014 Sep 30;86(3):161-3

Penile implant patients are required to remain in the hospital after the operation for monitoring, antibiotic and analgesia administration. Cost containment, however, has resulted in the increased use of ambulatory surgery settings for many surgical procedures. Few studies have studied the feasibility of performing penile prosthesis insertion in an outpatient setting.

The results are controversial and nowadays, in the most of centers that deal with prosthetic surgery, patients are still hospitalized.The aim of our investigation was to compare the feasibility of the performance as well as the complication profiles of penile implant surgery performed in an in-patient and an outpatient setting at a single center by a single surgeon.From January 2009 to June 2014, 50 patients of the same uro-andrological unit underwent penile prosthesis implantation performed by a single surgeon (N.M.). Twenty implantations were performed in an ambulatory day surgery setting.

Effectiveness and costs of outpatient setting versus the in-patient setting of the penile prosthesis surgery.There were some differences between the two groups in the intra-operative parameters, such as, operating time. Time lost from work was similar in both groups approximating 14 days. The mean number of analgesic pills ingested by the patients post-operatively was similar in both groups, averaging just under 25 pills per patient. There weren't post-operative complications in the outpatient group. Cost were 17% less in outpatient clinic.The outpatient setting for this surgery is safe and effective even in patients with comorbidities or in case of secondary procedures. Costs are reduced by 17%.

Peyronie's disease

Experience in the use of collagenase clostridium histolyticum in the management of Peyronie's disease: Current data and future prospects

Egui Rojo MA et alt: Ther Adv Urol. 2014 Oct;6(5):192-7

Peyronie's disease (PD) is a chronic wound-healing disorder characterized by formation of fibrous inelastic scarring of the tunica albuginea resulting in a variety of penile deformities. In most cases, PD is accompanied by a physical and psychological impact. Xiaflex® is an injectable collagenase clostridium histolyticum (CCh) preparation consisting of a predetermined mixture of two distinct collagenases. Recently, the US Food and Drug Administration (FDA) approved Xiaflex® for the nonsurgical treatment of men with PD with curvature of 30° or more and tangible scar tissue plaque in their penis.This article presents a comprehensive review of the updated information on the use of Xiaflex® for the nonsurgical treatment of PD.Mean improvements in penile curvature ranging from 29% to 34% and in bother domain scores have been reported. The majority of the reported adverse effects are mild or moderate and 79% resolve without intervention.The combined results of these trials have led to the FDA approval of CCh for the treatment of PD. However, the long-term effects and results need further investigation, with large follow-up series. Considering these results, future perspectives will probably result in the use of a combined or sequential therapy including CCh.

FSD

Perceptions of dyspareunia in postmenopausal women with vulvar and vaginal atrophy: Findings from the REVIVE survey

Freedman MA. Womens Health (Lond Engl). 2014 Jul;10(4):445-54

Symptoms of vulvar and vaginal atrophy (VVA), including dyspareunia and vaginal dryness, have a distinct negative impact on a woman's quality of life. The REVIVE survey highlighted the lack of awareness of VVA symptoms among postmenopausal women with vaginal symptoms, with many women reluctant to initiate discussions with their healthcare professionals despite the presence of vaginal symptoms. The REVIVE survey also provided insights into women's views of VVA treatments. Women reported displeasure with the vaginal administration route, lack of symptom relief with over-the-counter products, and concerns about the safety of estrogen therapies. With the high prevalence of VVA, obstetricians/gynecologists should become vigilant in identifying women with VVA by implementing screening and discussion of symptoms during routine office visits – providing patients with information about appropriate therapies based on the severity and impact of symptoms, keeping in mind individual preferences and perceptions.

MEETINGS AND EVENTS CALENDAR 2015

Dr. Raul Vozmediano-Chicarro
Associate Editor
Section of Andrology
Department of Urology
Carlos Haya University Hospital
Malaga, Spain

vozme@msn.com

January

Fertility 2015
January 7 – 9, 2015
Location: Birmingham, UK.
Website: www.fertility2015.org/

II Curso de cirugía protésica para la disfunción eréctil
23 January, 2015
Location: Barcelona, Spain
Website: www.aeu.es/Calendario.aspx

February

17th Congress of the European Society for Sexual Medicine
February 5 – 7, 2015
Location: Copenhagen, Denmark
Website: www.essm-congress.org

XVIII. Reunión Nacional del Grupo de Andrología
February 12 – 13, 2015
Location: Cadiz, Spain
Website: www.aeu.es/eventosgrupos.aspx

XVI. International Workshop on the Development and Function of the Reproductive Organs
February 14 – 16, 2015
Location: Münster, Germany
Website: www.reproworkshop2015.de

March

ENDO 2015 – The Endocrine Society
March 5 – 8, 2015
Location: San Diego, California, USA
Website: www.endo-society.org

The Best of ESHRE and ASRM
March 3 – 7, 2015
Location: New York, USA
Website: www.eshre.eu

63rd Annual Meeting of the Pacific Coast Reproductive Society
March 11 – 15, 2015
Location: Rancho Las Palmas Dr, Rancho Mirage, California, USA
Website: www.pcrsonline.org

30th Anniversary EAU Congress
March 20 – 24, 2015
Location: Madrid, Spain
Website: eaumadrid2015.uroweb.org

April 2015

XXIII. North American Testis Workshop
April 15 – 18, 2015
Location: Little America Hotel - Salt Lake City, Salt Lake Stadt, Utah, USA
Website: www.andrologysociety.com/Meetings/Testis-Workshop.aspx

American Society of Andrology 40th Annual Conference
April 18 – 21, 2015
Location: Salt Lake Stadt, Utah, USA
Website: dev.andrologysociety.org/Meetings/ASA-Annual-Meeting/Future-Meetings.aspx

EUROPEAN SOCIETY
FOR SEXUAL MEDICINE

17th CONGRESS OF THE EUROPEAN SOCIETY FOR SEXUAL MEDICINE

5 – 7 February 2015 | Copenhagen, Denmark

www.essm.org

1995 – 2015

© Jenny Thompson – fotolia.com

HOT TOPICS

- RT-02 ► ESSM-SMSNA friendship session: Penile rehabilitation: The fall of a myth?
- ML-01 ► Mindfulness interventions for treating sexual dysfunction: The science of finding focus in a multitask world
- ML-02 ► Scandinavian Society for Sexual Medicine lecture: Pornography. What does it do for sexuality?
- LV-01 ► Male sexual dysfunction (broad cast from Herlev hospital)
- RT-07 ► The dual model in transgender care
- RT-09 ► Is there a future for medical therapy of Peyronie's disease?
- RT-13 ► Debate: Testosterone supplementation: Safe for the heart?
- ML-07 ► What happened to good old Masters & Johnson? An update on pharmacological and non-pharmacological PE treatment in 2015
- RT-15 ► Panel discussion: Sexual side-effects of BPH treatment: Practical implications and prevention

Hosted by: Scandinavian Society for Sexual Medicine

17th Congress of the European Society for Sexual Medicine

5 – 7 February 2015 | Copenhagen, Denmark

Preliminary Program Schedule

Thursday, 5 February 2015

Time	Room 1	Room 2	Room 3	Room 4	Foyer/Hall
08:30	Congress Opening	PS-01 Male sexual dysfunction – medical	WS-01 Eurosian Andrology Summit – Update on Male Infertility Premature ejaculation, delayed ejaculation and un-ejaculation		**Registration Counter** 07:30–18:00
09:00	RT-01 Populations studies in sexual (dys)function			NS-01 Eurosian Andrology Summit – Update on male infertility (Turkish Society of Andrology)	**Exhibition** 10:00–20:00
10:00	Break/HP-01		WS-02 Difficult cases of erectile dysfunction		Highlighted Posters **HP-01** Miscellanous 10:00–10:30 in the Poster Area
11:00	ML-01 Mindfulness interventions for...				
12:00	RT-02 ESSM-SMSNA friendship session: Penile rehabilitation: The fall of a myth?	PS-02 Psychosexual perspectives ESSM-01 ESSM Grants: New opportunities for research funding	WS-03 Male genital surgery – how to deal with complications		**Poster Exhibition** 10:00–20:00
13:00	Break/Industry sponsored session				
14:00	VS-01 Surgical treatment of male infertility and sexual dysfunction	RT-03 Novel approaches to psychotherapy – EFS and ESSM interactive symposium	ESSM-02 Resident's corner and ESRU presentation of case studies	NS-02 SIA (Società Italiana di Andrologia) and FISS (Italian Federation of Scientific Sexology)	
15:00		RT-04 Female genital disorders and sexual health			
16:00	CM-01 Cases that matter 1	PS-04 FSD	PS-03 Male sexual dysfunction – surgery	NS-03 SFMS/AIUS French Societies	
17:00	ML-02 Pornography. What does it do for sex... ML-03 History of ESSM				
18:00	ESSM Opening Ceremony				
18:30	Networking Reception in the exhibition area from 18:30–20:00				

ABBREVIATIONS

RT	–	Round Table
ML	–	Master Lecture
WS	–	Workshop
VS	–	Video Session
LV	–	Live Surgery Session
ESSM	–	ESSM Session
PS	–	Podium Session
CM	–	Case Session
NS	–	National Session

17th Congress of the European Society for Sexual Medicine

5 – 7 February 2015 | Copenhagen, Denmark

Preliminary Program Schedule

Friday, 6 February 2015

Time / Room	Room 1	Room 2	Room 3	Room 4	Foyer/Hall
08:30					**Registration Counter** 08:00 – 18:00
09:00		**RT-05** Paraphilias and BDSM in sexual medicine	**WS-04** Hormonal difficulties with sexual consequences in man and women		**Exhibition** 08:30 – 17:00
10:00	**LV-01** **Live Surgery** Male sexual dysfunction	Break / HP-02			Highlighted Posters **HP-02** Pre-clinical perspectives 10:00 – 10:30 in the Poster Area
11:00		**RT-06** Bench-to-bedside: Premature ejaculation – a translational update 2015	**WS-05** Infertility and sexuality	**NS-04** AUIS/SFMS French Societies	
12:00	**ML-04** Award of Excellence				**Poster Exhibition** 08:30 – 17:00
13:00	Break / Industry sponsored session				
14:00	**RT-07** The dual model in transgender care	**RT-08** Toys and vibratory devices for joy and medical need	**PS-05** Male sexual dysfunction	**NS-05** MESSM – Middle East Society for Sexual Medicine	
15:00	**ML-05** Sex addiction: Moral...	Break / HP-03			Highlighted Posters **HP-03** Female sexual dysfunction 15:30 – 16:00 in the Poster Area
16:00	**RT**	**RT-09** Is there a future for medical therapy of Peyronie's disease?	**RT-10** Neurotransmitters, mood regulation and sexual behavior		
17:00					
18:00		ESSM Annual Business Meeting			
18:30					

Preliminary Program Schedule

Saturday, 7 February 2015

Time / Room	Room 1	Room 2	Room 3	Room 4	Foyer/Hall
08:30					**Registration Counter** 08:00–18:00
09:00	**V-02** Approaches to female and transgender genital surgery	**RT-11** Testosterone substitution and male sexual health	**WS-06** Vulvodynia, vestibulodynia and sexual pain disorders (diagnosis, examination and treatment)		**Exhibition** 08:30–17:00
10:00	Break/HP-04				Highlighted Posters **HP-04** Sexology, MSD 10:00–10:30 in the Poster Area
11:00	**ML-06** ESSM: Two decades of...				
12:00		**RT-12** Are male factor infertility and male sexual dysfunction linked?	**WS-07** How to improve patient satisfaction and compliance	**NS-06** ASESA – Asociacón Espagnola de Andrología/SPA – The Portuguese Society of Andrology	**Poster Exhibition** 08:30–17:00
13:00	Break/Industry sponsored session				
14:00	**RT-13** Debate: Testosterone supplementation: Safe for the heart?	**PS-06** Female sexual dysfunction	**PS-07** Basic science and translational	**NS-07** SSSM – Scandinavian Society for Sexual Medicine	
15:00	**ML-07** What happened to good old Masters &...				
16:00	Break/HP-05				Highlighted Posters **HP-05** Female sexual dysfunction 15:30–16:00 in the Poster Area
17:00	**RT-14** RT: Incontinence and FSD	**RT-15** Panel discussion: Sexual side-effects of BPH treatment: Practical implications and prevention	**PS-08** LGBT and gender		
18:00		Closing Ceremony			
18:30					

PAYMENT OF THE ESSM MEMBERSHIP FEE 2015

To be sent back to:
ESSM secretariat – c/o AIM Congress
Via Ripamonti 129 – 20141 Milano, Italy
www.essm.org

Phone: +39 02–56601 354
Fax. +39 02–70048 577
email: admin@essm.org

Membership goes from January to December

❑ New Member
❑ Member since: _____

Title:

Name: Surname:

Date of Birth: Nationality:

Position held:

Institution:

Postal address: ❑ home ❑ work

City: Zip code: Country:

Telephone: Fax:

Email:

First Specialty: Second Specialty:

Membership category:

❑ Full Member
❑ Associate Member

Membership type:

❑ Simple ESSM	EUR 50,00
❑ Combined ESSM + ISSM	EUR 130,00

Special interests/expertise in Sexual Medicine – for new members only

1.

2.

Scientific work (two most important – peer reviewed – publications) – for new members only

1.

2.

❑ Herewith confirms the payment of EUR 50,00 for the **ESSM membership** cost for the year 2015 by:
❑ Herewith confirms the payment of EUR 25,00 for the **ESSM membership FOR RESIDENTS IN TRAINING*** cost for the year 2015
❑ Herewith confirms the payment of EUR 130,00 for the **ESSM and ISSM membership** cost for the year 2015

* A letter of the Chairman of the Department is necessary

❑ Bank transfer to AIM Congress srl

Bank:	Banca Popolare di Milano – Ag. 24 – Milano, Italy	
Account N.:	000000024845	
Bank codes:	CIN	K
	ABI	05584
	CAB	01624
	IBAN	IT81K0558401624000000024845
	SWIFT/BIC	BPMIITM1024

Please clearly state in the reason of payment: ESSM fee + name and surname

❑ Credit Card: ❑ Visa ❑ American Express ❑ Master Card ❑ Eurocard

Credit Card number:

Expiration date: CVC Number

Holder

Holder's Signature

Privacy and treatment of personal data
In order to process your membership of the European Society for Sexual Medicine (ESSM) we will store your details in an electronic database. This information will be used to process your application only and will not be used for any other communications. The information will not be sold, lent or otherwise divulged to third parties, other than where it is necessary to process your application.

Should your membership application be successful, your details will be stored permanently in a database and you will have an account set-up within *www.essm.org* where you will be able to manage your personal details and renew your membership annually. These details will not be sold, lent or otherwise divulged to third parties other than to manage your membership, send you relevant information about ESSM events and services and provide any services you request from time to time. We may use your personal details to send you communications from third parties without divulging your details to them. If you choose the combined membership of ESSM/ISSM we will then pass your details to ISSM allowing them to register your membership and send you the Journal of Sexual Medicine. Other than the ISSM, your personal information will never be sent outside the EU other than to countries where this is allowed under EU laws.

Should you have any concerns about the use of your personal details, please email admin@essm.org or write to
AIM Congress Srl – AIM Group – Via Ripamonti 129, 20141 Milano – C.a. Ms. Lavinia Ricci
For your consent on data processing and communication as described in the above report:

Date Signature

For more information please visit www.essm.org

Announcement for the next Congress

SAVE THE DATE

17th Congress of the European Society for Sexual Medicine

5 – 7 February 2015 | Copenhagen, Denmark

www.essm-congress.org