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Welcome Address

I am delighted to welcome you to this **June 2016** Issue of the ESSM newsletter. We have great things coming soon in our society.

We would like to thank again all ESSM members, speakers, live-surgeons, moderators, ESSM staff, etc for the great meeting we held in Madrid last February. Almost1200 attending delegates representing 76 countries, top ten countries were Italy, Spain, United Kingdom, Turkey, Portugal, The Netherlands, Denmark, France, Germany and USA. On behalf Dr. Moncada and myself as chairmen were very proud and honored for all your compliments during the meeting.

All the scientific committee lead by Dr. Albersen did an outstanding, very well attended, job putting together a phenomenal scientific program.

In this issue, we have included an interesting interview with world-class expert in urologic reconstructive surgery **Dr. Rados Djinovic, who serves now as a chairman of ESGURS**. We cover main topic highlights published in our field, by my great Associate Editors (**Dr. Mondaini, Angulo & Vozmediano**).

Also, we add two very interesting Key from Kols collaborations regarding Premature Ejaculation by Paolo Verze and an update of the well-known "PROPPER Study" by Gerard Henry. We hope you will enjoy the reading.

Finally, I would like to thank all of you for your continued support to our society.

My very best Juan I. Martínez-Salamanca Editor-in-Chief





Interview with Dr. Rados Djinovic

by Juan I. Martínez-Salamanca



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Dr. Djinovic is an internationally known figure and world-class leader in the field of Sexual Medicine. He is an outstanding contributor to the field of sexual medicine as a researcher, patient advocate, educator, innovator and author. He serves as a Chairman of Sava Perovic Foundation & Chairman of EAU (European Association of Urology) Section of Genitourinary Reconstructive Surgeons Section (ESGURS). Rados Djinovic's foremost accomplishment was saving the Sava Perovic Art of urological surgery after the death of the preeminent Professor. Seven years mastering the art with Dr Perovic and six more years continually developing, expanding and advancing it has clearly shown the art gets supreme surgical results for patients.

Rados graduated a Doctor of Medicine at the University of Belgrade — School of Medicine in January 1999. He did his Internship and clinical training from March 1999 to March 2000 at the Clinical Center of Serbia in Belgrade. His General Surgery Residency from April 2000 to June 2005 was back at Professor Perovic's University of Belgrade School of Medicine.

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

JIMS: Dr. Djinovic, could you make us a brief journey throughout your professional background?

Well, there were not too many years in surgery (20 years now), but I would say pretty long mileage. I got interested in surgery early during my faculty — I started to assist surgeries at the age of 23, and spent all my spare time in the operating

rooms and ICU. At first I was working at general surgery department, assisting "major" procedures and then was moved to cardiac surgery for some time. In the meantime, I also passed ECFMG and wanted to continue my education in the USA, but fortunately I discovered Prof Perovic art of reconstructive urological surgery, and was completely seduced by its complexity and great diversity of procedures. He was a real workaholic and we operated every day (including weekends and holidays), all day long, often finishing surgeries at/after midnight. Also, we travelled a lot, doing demonstrating surgeries at many meetings throughout the world, solving the most difficult cases. It was very though training, but enabled me to learn a lot in a short time, what was crucial for my early maturation as a surgeon.

JIMS: During you dilated career, which has led to the passage from "Andrology" to "Sexual Medicine", but what about "Reconstructive Surgery"? How mix all together?

One of the keys of Sava's great success was the fact that he treated all genito-urinary problems, both in children and adults, males and females. Using the experience from one into another group of patients, he joined all of these separate fields and created, we can freely say, new subspecialty of Genito-Urinary Reconstructive Surgery. So for me was much easier, since I've got everything already prepared, on the "plate". The only real difficulty was to follow Sava in his enormous work. After his passing, we continued on the same track — treating all possible problems — from pediatrics (hypospadias, extrophies, cloacas, DSD, upper tract deformities) to adults (urethral problems, hypospadias, ED,

Peyronies, incontinence, congenital problems in adults, ureteral reconstruction, bladder enlargements), both in male and female patients (cystocoele, rectocoele, vaginal reconstruction, incontinence). Sava also made great advancement of transgender surgery, in both ways (M2F and F2M), and we are regularly treat both groups of patients. That diversity is actually the main challenge for me — every working day is different and require a lot of thinking — there is no routine surgery at our center.

JIMS: Now, reconstructive surgery is done by different specialist (urologist, general surgeons, pediatric surgeons, etc.), what do you think would be the ideal profile? And what are our major challenges?

I strongly believe, or better say I am convinced that it requires full dedication. It does not make much difference from which field one comes, but is important to fully dedicate to this field and learn its principles – first how to handle tissue with care and then to do reconstruction (plastic surgery experience is also very important), which is quite different from classical, "excisional" surgery. Sava started his career as a pediatric surgeon, and it was very important since he introduced this fine surgical technique in adult surgery. Major challenges today are, first of all to understand that this is a particular field of surgery, which differs significantly from classical urological surgery, and secondly to provide appropriate training to the ones interested to learn it. I think that we should create fellowship at European level with several specialized centers where fellows would have a chance to learn and gain necessary experience. It should be taken like with every new field of surgery that slowly evolved in the past.

JIMS: Dr. Djinovic, if you were not a surgeon, what would you be?

Very, very difficult question. Weird, but once upon the time I used to be pretty interested in astrophysics.



Interview with Dr. Rados Diinovic

JIMS: In the field of Peyronie's Disease, what do you think are the main challenges to achieve? How do you set expectations with your patients?

Good and reliable short and long-term results. Both surgeon and patient should be aware of severity and seriousness of Peyronie's disease — thus I advise grafting with simultaneous penile implant more and more often, what gives the most reliable long-term success and happy patients. And always explain in detail the procedure and what result (and potential complications, of course) can they expect.

JIMS: Dr. Djinovic, What do you most often wish you could say to patients, but didn't?

I always speak very directly and thoroughly, yet carefully to patients, making sure that they clearly understand the problem they have, treatment options and my proposal, as well as potential risks and complication.

JIMS: What is the most rewarding aspect of being a doctor?

The one that is the essence of being human -

ability to help others in the most sensitive part of their lives – health. A smile or hug from the child or satisfaction on the face of adult after successful treatment is priceless.

JIMS: Dr. Djinovic, training remains a challenge on this field, what is your personal opinion about that?

Well, I already said that we should understand that we should unite internationally and create a well organized fellowship program with training centers through official organizations, primarily EAU and ESSM. Patients deserve better treatment and young, ambitious doctors deserve a chance to learn.

JIMS: What is your most important piece of advice for doctors just starting out?

To follow their dreams, work hard and carefully, plan their career by smart select where to learn. Patience is mandatory. Everything else comes by itself.

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?

Well, ESSM already did a huge job — succeeded to uncover this important field of medicine, which was mainly taboo till not so long time ago. Now it becomes a world-wide known specialty with greatly improved standards of care. I think that ESSM should just continue on the same way, and maybe through some more support for creation of national societies.

JIMS: 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.

Thank you – the pleasure is all mine.





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



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Erectile dysfunction

Song SH et alt: Usage and perceptions of phosphodiesterase type 5 inhibitors among the male partners of infertile couples Clin Exp Reprod Med. 2016 Mar; 43(1):26-30.

We aimed to investigate the prevalence of erectile dysfunction (ED) and the usage of phosphodiesterase type 5 (PDE5) inhibitors for ED treatment in infertile couples.

A total of 260 male partners in couples reporting infertility lasting at least 1 year were included in this study. In addition to an evaluation of infertility, all participants completed the International Index of Erectile Function (IIEF)-5 questionnaire to evaluate their sexual function. The participants were asked about their use of PDE5 inhibitors while trying to conceive during their partner's ovulatory period and about their concerns regarding the risks of PDE5 inhibitor use to any eventual pregnancy and/or the fetus.

Based on the IIEF-5 questionnaire, 41.5% of the participants (108/260) were classified as having mild ED (an IIEF-5 score of 17–21), while 10.4% of the participants (27/260) had greater than mild ED (an IIEF-5 score of 16 or less). The majority (74.2%, 193/260) of male partners of infertile couples had a negative perception of the safety of using a PDE5 inhibitor while trying to conceive. Only 11.1% of men (15/135) with ED in infertile couples had used a PDE5 inhibitor when attempting conception.

ED was found to be common in the male partners of infertile couples, but the use of PDE5 inhibitors among these men was found to be very low.

The majority of male partners were concerned about the risks of using PDE5 inhibitors when attempting to conceive.

Penile Surgery

Otero JR et alt: Comparison of the patient and partner satisfaction with 700CX and Titan penile prostheses. Asian J Androl. 2016 Jan 22.

Most widespread three-component penile prosthesis models are 700CX™ and Titan®. Our purpose is to assess patient and partner satisfaction after the first implant. This is a multicenter, retrospective, nonrandomized study in which all patients who met the inclusion criteria between 2009 and 2013 were included. In total. 248 patients agreed to participate. To evaluate patient satisfaction, a validated but modified 11-question questionnaire was completed (EDITS); and a nonvalidated two-item questionnaire was given to the partner. Statistical analysis used an ordinal logistic regression model. Two hundred and forty-eight patients (194 with 700CX™ vs 54 with Titan®) and 207 couples completed the questionnaire (165 with 700CX[™] vs 42 with Titan®). Overall satisfaction was high. Both showed great reliability for sexual intercourse and high compliance with prior expectations. Most patients were able to manage the penile prosthesis correctly within 6 months. Postoperative penile shortening led to some dissatisfaction in 42% and 46% of cases (700CXTM/Titan®). Significant differences were found in three questions of patients' questionnaire. There were more patients satisfied with the 700CXTM (P = 0.0001). No patient with Titan® implant took longer than 6 months to optimal management. Only 4% of patients with 700CX™ implant were dissatisfied with the deflation, in contrast to 24% with the Titan® (P = 0.0031). Of the two partners' questions, one showed a statistically significant difference (P = 0.0026). It seems that group 700CX™ would recommend to re-implant the prosthesis with a greater tendency. The overall satisfaction was very high for both prostheses. The final aspect of the erected and flaccid penis was satisfactory, but both groups showed significant discontent with its final size. Partners' overall satisfaction was high.

Fertility

Sharma R: Cigarette Smoking and Semen Quality: A New Meta-analysis Examining the Effect of the 2010 World Health Organization Laboratory Methods for the Examination of Human Semen. Eur Urol. 2016 Apr 21.

Approximately 37% of men of reproductive age smoke cigarettes, with Europe having the highest tobacco use among all the World Health Organization (WHO) regions. Toxins from tobacco smoking can potentially affect sperm development and function, with a negative effect on semen parameters. Given the high prevalence of smoking and recent changes in the WHO laboratory methods for the examination of human semen, the role of this exposure in face of new WHO methods needs to be clarified. We conducted a systematic review, followed by a meta-analysis, to determine whether cigarette smoking affects human semen parameters. PubMed, Saint Joseph's University Discover, and Google Scholar were used to identify relevant studies published after release of the latest WHO methods for laboratory evaluation of human semen. Participants were from fertility/urologic clinics and andrology laboratories. The outcome measures were semen volume, sperm concentration, motility, and morphology, the parameters usually used in clinical settings to assess fertility. Twenty studies with 5865 participants were included in the meta-analysis. Exposure to cigarette smoking was associated with reduced sperm count (mean difference [MD]: -9.72×106/ml; 95% confidence interval [CI], -13.32 to -6.12), motility (MD: -3.48%; 95% CI, -5.53 to -1.44), and morphology (MD: -1.37%; 95% Cl, -2.63 to -0.11). Subgroup analyses indicated that effect size was higher in infertile men than in the general population and in moderate/heavy smokers than in mild smokers. The overall effect



Have you read? Best of the Best: Clinical

size on semen volume, sperm count, and motility remained similar when 2010 and earlier WHO manuals were used for semen analysis but was lower with regard to sperm morphology.

Our results suggest that cigarette smoking has an overall negative effect on semen parameters. The latest WHO laboratory methods for the examination of human semen had a minimal impact on the magnitude of effect size, thus confirming the observed negative effect of smoking on conventional semen parameters.

A new systematic review and meta-analysis comprising 5865 men shows that cigarette smoking is associated with reduced sperm count and motility. Deterioration of semen quality is more pronounced in moderate and heavy smokers.

Metabolic Diseases

Corona G et alt: Is late-onset hypogonadotropic hypogonadism a specific age-dependent disease, or merely an epiphenomenon caused by accumulating disease-burden? Focusing on metabolic diseases. Minerva Endocrinol. 2016 Feb 17.

To summarize the available evidence supporting the link between late onset hypogonadism (LOH) and associated common clinical illnesses, focusing on metabolic diseases. The possible benefits or risks related to testosterone replacement therapy (TRT) in these conditions will also be analyzed.

An extensive Medline search was performed. LOH is closely associated with a worse metabolic profile and a higher cardiovascular risk. The relationship between hypogonadism obesity and insulin resistance is complex and bidirectional. Emerging evidence suggests a positive role of TRT in improving body composition and metabolic outcomes in subjects with LOH.

Despite the aforementioned data, it is not completely known whether reduced testosterone levels in elderly males might play a direct pathogenetic role in these conditions or whether low T and associated morbidities are concomitant conditions, both associated with the aging process. Further and longer studies are advisable to confirm the preliminary results.





Have you read? Best of the Best: Basic Research

by Javier Angulo



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Erectile dysfunction – Low intensity shockwave therapy

Low Intensity Extracorporeal Shockwave Therapy (Li-ESWT) Improves Erectile Function in a model of Type II Diabetes Independently of NO/cGMP Pathway

Assaly-Kaddoum R, Giuliano F, Laurin M, Gorny D, Kergoat M, Bernabé J, Vardi Y, Alexandre L, Behr-Roussel D. *J Urol 2016, doi: 10.1016/j. juro.2016.03.147* [Epub ahead of print]

Low intensity extracorporeal shockwave therapy (LiESWT) consists of acoustic waves that are generated outside the body, but when propagated through an adequate medium can be focused to an anatomical area. A technology firstly developed for lithotripsy, it was later used for relieving pain in musculoskeletal diseases and has been finally used to clinically treat erectile dysfunction (ED) with some success. However, the beneficial effects of LiESWT in patients have been demonstrated empirically with a plethora of different intensities and schedules, and little is known on the mechanisms responsible for improving erectile function. The study by Assaly-Kaddoum and collaborators aimed to address this question by using an animal model of ED.

The authors have developed and built a shock-wave device for application to rat penis. The designed setting involves the immersion of the penis in salt water for providing an adequate propagation medium for shockwaves. They evaluated this therapeutic approach in a diabetic model of ED, the Goto-Kakizaki (GK) rat. LiESWT was applied in 2 sessions (300 shocks

at 2 Hz) per week for 3 weeks repeated after a 3-weeks no treatment interval to 7 weeks old GK rats. Shockwaves were generated through a probe calibrated to deliver a controlled flux intensity of 0.09 mJ/mm2. The effects of LiESWT on erectile and cavernosal functions of GK rats were evaluated after a 4-weeks washout period. The investigators found a partial but significant recovery of erectile responses to cavernosal nerve stimulation in GK rats by LiESWT application. This positive effect was enhanced after acute treatment with the PDE5 inhibitor, sildenafil. The combination of LiESWT plus acute sildenafil was significantly superior to the LiESWT alone but displayed only a trend to be superior to the treatment with sildenafil alone. However, the objective demonstration of the improving effects of LiESWT on erectile function in diabetic rats was not related to a recovery of the impairment of endothelium-dependent, -independent or nitrergic relaxations of corpus cavernosum in these animals.

This study, using a methodology carefully adapted to deliver LiESWT in a comparable way to the paradigm of its application in patients, confirms that LiESWT application improves erectile responses in type 2 diabetic rats, similarly to that reported for type 1 diabetic rats. On the other hand, the study cannot confirm a contribution of NO/cGMP pathway enhancement to the pro-erectile effects of LiESWT. In fact, despite the previous evidences suggesting an increase in endothelial nitric oxide synthase (eNOS) and neuronal NOS (nNOS) expression, LiESWT failed to potentiate the impaired NO/ cGMP mediated relaxation of corpus cavernosum in this first functional evaluation of cavernosal responses after LiESWT application. Thus the study prompts to continue in the search of the mechanisms responsible for the improvement of erectile function by LiESWT and reinforces the idea of the necessity to confirm by functional assays the findings observed in molecular biology determinations.

Combination therapy using human adiposederived stem cells on the cavernous nerve and low-energy shockwaves on the corpus cavernosum in a rat model of post-prostatectomy erectile dysfunction

Jeon SH, Shrestha KR, Kim RY, Jung AR, Park YH, Kwon O, Kim GE, Kim SH, Kim KH, Lee JY. *Urology 2016, 88: 226.e1-9.*

This study by Jeon and collaborators focuses on other type of ED, the ED secondary to radical prostatectomy (RP), using a well known rat model of bilateral cavernous nerve injury (BCNI). They aimed to evaluate the effects of LiESWT in this model of ED and to determine the ability of this therapeutic approach to enhance the beneficial effects of stem cell therapy after cavernous nerve injury. For this purpose, they targeted cell therapy with human adipose-derived stem cells (h-ADSC) to the cavernous nerve injury site while LiESWT was directed to the corpus cavernosum. ADSC implantation was made at the time of BCNI while LiESWT application started 3 days after BCNI. LiESWT application was similar to the study by Assaly-Kaddoum and collaborators regarding the nature of the sessions (300 shocks at 2 Hz) and energy density (0.1 mJ/mm2) but the treatment schedules were quite different: in this study 3 sessions per week for 3 weeks were applied with a lapse of only a few (3-4) days from last session to the evaluation of responses.

The authors observed that either individual implantation of h-ADSC in cavernous nerve or individual application of LiESWT to the penis resulted in a moderate but significant improvement of erectile responses in BCNI rats. The improvement of erectile responses after combined treatment with h-ADSC and LiESWT was significantly superior to the individual approaches although did not reach a complete recovery of erectile function in BCNI rats. Histological analyses revealed that the combination therapy was superior in the recovery of the expression of smooth muscle markers as well and in the reduction of apoptosis in the



Have you read? Best of the Best: Basic Research

corpus cavernosum of BCNI rats. With respect to the mechanisms involved, LiESWT (either alone or in combination with ADSC) completely restored VEGF expression in corpus cavernosum of BCNI rats. In addition, LiESWT increased nNOS expression in dorsal nerve and eNOS expression in corpus cavernosum of BCNI rats and the cGMP content in the penises from these animals. The up-regulation of these markers of NO/cGMP pathway was superior after combining h-ADSC implantation and LiESWT than after application of individual therapies.

This study suggests a positive effect of LiESWT in ED caused by cavernous nerve injury and supports the utilization of LiESWT for enhancing the therapeutic effect of combinative approaches such as cell therapy. In addition, and in contrast to the functional evidence provided by Assaly-Kaddoum and collaborators in diabetic ED, the present study suggest an involvement the NO/ cGMP pathway in the improvement and the potentiating effects driven by LiESWT in erectile responses after cavernous nerve injury. However, it should be highlighted that a functional confirmation is lacking in this study. LiESWT application also induced an up-regulation of the angiogenic factor, VEGF suggesting that LiESWT could trigger an angiogenic response.

Considering both studies, it might be speculated that an increase in cavernosal angiogenesis, a process that has been shown to be impaired in diabetes, could account for the beneficial effects of LiESWT on erectile function. On the other hand, we cannot discard an impact of LiESWT in vasodilatory capacity of penile arteries that are vascular structures with a key contribution to the process of erection together with the relaxation of cavernosal tissue. In fact, therapeutic strategies that have been shown to specifically enhance vasodilation of penile arteries improved erectile responses in diabetic rats.

Cavernosal physiology – Potassium channels

Effect of a novel BKCa opener on BKCa currents and contractility of the rabbit corpus cavernosum

Hannigan KI, Large RJ, Bradley E, Hollywood MA, Sergeant GP, McHale NG, Thornbury KD. Am J Physiol Cell Physiol 2016, 310: C284-C292.

There exists substantial evidence supporting the role of potassium channels in the regulation of penile smooth muscle in animals and humans. In fact, the pharmacological activation of potassium channels has been shown to potentiate cavernosal relaxation and penile arteries vasodilation while preliminary attempts for delivering a gene coding for large-conductance calcium-activated potassium channels (BKCa) by intracavernosal injection promised positive effects on erectile function in patients with ED. Indeed, it has been calcium-activated potassium channels (KCa) and, specifically, BKCa, the subtype of potassium channels that has deserved most attention as a therapeutic target for ED. One of the reasons is that a dramatic hypotensive response is not expected after BKCa activation as it happens with other channels such as the ATP-sensitive potassium channels (KATP). However, despite the preclinical evidence suggesting a therapeutic potential of BKCa activation in the treatment of ED, this therapeutic approach has not been moved to the clinical development. This could be due to the lack of potent, really selective and pharmacokinetically adequate drugs.

Hannigan and collaborators describe in this study a novel BKCa activator, GoSlo-SR5-130, that is able to modulate physiological responses of rabbit corpus cavernosum smooth muscle (CCSM) cells. Using electrophysiology methods in patches of CCSM cell membranes, they show that GoSlo-SR5-130 increases the

number of open BKCa and reduced the voltage potential required for BKCa activation. Then, in the presence of GoSlo-SR5-130, BKCa channels were open in the physiological range of membrane potentials. This results in increased spontaneous transient potassium outward currents in myocytes isolated from rabbit CCSM and in hyperpolarization of the membrane. Finally, using organ chamber assays for tension recording, they confirmed that GoSlo-SR5-130 inhibited spontaneous contractions of rabbit corpus cavernosum strips.

The study by Hannigan and collaborators offers a new pharmacological tool for stimulating BKCa activity which modulates cavernosal smooth muscle contractile tone. Activation of BKCa is a potential target in the treatment of ED, mainly in situations where other relaxation pathways of penile smooth muscle such as NO/cGMP pathway are profoundly impaired and the response to conventional therapy for ED based in potentiation of this pathway fails.

It is interesting to note that GoSlo-SR5-130 as well as other BKCa activators have the ability to modulate bladder activity, an effect that could be relevant in the frequent association of ED with lower urinary tract symptoms (LUTS). Further research is needed for establishing advantages of this novel BKCa activator over those previously described BKCa activators. This includes its evaluation in preclinical models of ED and the determination of pharmacokinetic characteristics of the molecule. As a difference from most BKCa activators, GoSlo-SR5-130 requires the participation of regulatory B-subunits of the channel for its stimulating effect. This is interesting from a pharmacological viewpoint but the functional relevance of this characteristic needs to be determined.



Have you read? Best of the Best: Basic Research

Molecular and functional characterization of Kv7 channels in penile arteries and corpus cavernosum of healthy and metabolic syndrome rats

Jepps TA, Olesen SP, Greenwood IA, Dalsgaard T. Br J Pharmacol 2016, doi:10.1111/bph.13444 [Epub ahead of print]

Kv7 are voltage-dependent potassium channels that are present in many tissues including neuronal and muscular excitable cells. This type of potassium channels have been shown to participate in the regulation of vascular tone and in bladder contractility.

Jepps and collaborators have evaluated the effects of Kv7 activation on smooth muscle relaxation of rat penile arteries and corpus cavernosum. They have used a rat model of metabolic syndrome, the spontaneously hypertensive heart failure (SHHF) obese rat for evaluating Kv7 activation in pathological situation. At mRNA level, expressions of Kv7.3, Kv7.4 and

Kv7.5 isoforms were detected in penile arteries and corpus cavernosum while Kv7.1 was only detected in corpus cavernosum. At protein level, Kv7.4 and Kv7.5 were immunolocalized in both structures. The functional relevance of molecular detection of Kv7 was confirmed by tissue-tension experiments. In this sense, Kv7 activators relaxed pre-contracted rat penile arteries and corpus cavernosum strips. These relaxations were independent of NO synthesis or endothelium-derived hyperpolarization. However, blockade of Kv7 attenuated relaxations induced by the NO-donor, sodium nitroprusside, or the PDE5 inhibitor sildenafil in penile arteries and corpus cavernosum. These effects, the relaxation driven by Kv7 activation and the inhibition of NO/ cGMP-mediated relaxations by Kv7 blockade. were reduced in penile arteries and corpus cavernosum from SHHF rats. In fact, transcripts for Kv7.3, Kv7.4, and Kv7.5 were down-regulated and for Kv7.1 up-regulated in corpus cavernosum but not penile arteries from SHHF rats.

In rats at least, this study demonstrates the contribution of the Kv7 family of potassium channels to the control of both penile arterial and trabecular smooth muscle tones. In addition to cause direct relaxation of penile smooth muscle, Kv7 activity contributes to the NO/cGMP-mediated relaxation of penile smooth muscle. Since Kv7 action seems to be compromised under conditions of cardiovascular and ED risk such as metabolic syndrome, this could contribute to the impairment of NO/cGMP-mediated relaxation of penile arteries and corpus cavernosum in this pathological situation. Consideration of Kv7 activation as a potential target in the treatment of ED requires a confirmation of its participation in relaxation of human penile smooth muscle and of its ability to enhance physiological and/or pharmacological relaxation of penile vascular structures and to improve erectile responses in animal models of ED.



SAVE THE DATE!



ONE DAY PRE CONGRESS UPDATE 2017

IN SEXUAL MEDICINE

FROM KNOWLEDGE TO BEDSIDE PRACTICE

1 February 2017 | Nice Acropolis | Nice, France

►► www.essm-update2017.org



Italian Society of Andrology (SIA): 40 years old

by Gaia Polloni



Gaia Polloni Clinical Psychologist, Psychotherapist, Clinical Sexologist, European Certified Psychosexologist, Centro Terapia Cognitiva, Como, Italy

In Florence, on Saturday 9th of April 2016, the Italian Society of Andrology (SIA) celebrated 40 years since its foundation with a congressevent called "Love Match". This was possible thanks to the partnership with the international

In addition to the exciting congress which, during the day, embraced important issues of andrology and sport, in the evening a football

pharmaceutical company Menarini.

match took place with a crowd of 5000 people. The game saw the Italian National Team of Singers playing against a team made up of Italian andrologists, actors and football players. Both teams were wearing t-shirts with the Italian Society of Andrology logo.

This special night started with paratroopers diving from the sky whilst holding the Italian Society of Andrology flag. The stadium was crowded with andrologists coming from all parts of Italy to cheer and support their team.

The media reaction was bewildering and unique. The role of the andrologists and the importance of prevention for men's health was praised and, for an entire week, TV channels, newspapers and radio shows talked about this event.

The captain of the andrologists team, Nicola Mondaini, who is also the creator and coordinator of the event, is now thinking of organizing another match in Europe, following a Champion's league model.

And of course, all of the above was blessed by Pope Francis! (see Photo)







Italian Society of Andrology (SIA): 40 years old



tackles the singer and rapper Moreno

Carlo Bettocchi, treasurer of the ESSM,









Dr. Graham Jackson

† 28th April 2016



I bear tragic and unexpected news, of a great man and legend in his field. Dr. Graham Jackson, sadly, and prematurely, died on the 28th April 2016. He had a debilitating illness which he fought bravely, and without complaint, working and sending messages, right up to the very last minute.

He was a Consultant Cardiologist at London Bridge Hospital, London, and BMI Shirley Oaks Hospital in Croydon, Surrey. Graham's NHS medical base was as a senior cardiologist at Guy's and St Thomas' Hospitals.

His special interest included the detection, management and treatment of sexual dysfunction in cardiac patients. He was the first cardiologist to establish a clinic specifically for patients with sexual dysfunction and cardiovascular disease in the UK.

He was the principal UK investigator in several lipid lowering trials including PROVE-IT and published widely on sex and the heart and on the perils of counterfeit medicines.

He was a member of the International Society for Sexual Medicine Standards Committee and a prominent speaker at the American Heart Association, the American College of Cardiology, and the British/European Society of Cardiology/World Congress of Cardiology meetings, and at many meetings nationally and internationally on sexual problems in cardiac patients.

In 2010 he was appointed president of the World Congress of Men's Health and continued as president in 2011. He was on the board of the International Society of Men's Health.

He has for many years been advocating the need for aggressive cardiac risk reduction in men with erectile dysfunction (ED) and no cardiac symptoms, using ED as a means of reducing subsequent cardiac events. He was editor of the book series Difficult Cardiology and has authored numerous books, including Angina in Practice; Sex, the Heart and Erectile Dysfunction; and The Practical Management of Ischaemic Heart Disease. The fourth edition of his book for patients, Heart Health at your Fingertips, was published in 2009. He has published more than 400 papers on cardiology and general medicine and was a well-respected member of several editorial boards. He was also emeritus editor of the International Journal of Clinical Practice after 22 years as editor-in-chief, and chairman of the Sexual Advice Association (www.sexualadviceassociation.co.uk), a role he loved and really cared about.

His death has shocked and saddened us all and our thoughts are with his family, friends and colleagues who will miss his humour, goodwill, sound advice and caring nature. He is irreplaceable and a great loss to the field of medicine.



Key from Kols: PROPPER Update

by Dr. Gerard Henry



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The PROPPER registry is a large, prospective, multicenter, multinational, IRB-approved, monitored study where the patient is followed for 5 years with independent third party phone calls, 5 validated questionnaires, and recording any adverse events. A desire for a large advocacy study in the field of surgical men's health lead to the creation of Prospective Registry of Outcomes with Penile Prosthesis for Erectile Restoration (PROPPER).

The PROPPER study was initiated in June 2011 with 14 sites initially agreeing to participate. Current patients with BSC/AMS penile prostheses continue to be enrolled at 11 North American sites. Preoperatively the physician investigators recorded baseline patient characteristics such as age, penile measurements and primary etiology, and patients completed the IIEF-5 (International Index of Erectile Function-5)/Sexual Health Inventory for Men, SF-12 Health-Related Quality of Life Questionnaire, Erectile Hardness Questionnaire, AUA-SI (American Urological Association Symptom Index) and UCLA-PCI (Prostate Cancer Index) Questionnaire. Surgical techniques evaluated included drain use, foley use, dressing use, suture use, technique for closing corporotomy, and equipment and technique for corpora dilation. Surgery type included original, revision/ replacement, salvage and replacing into a previously explanted corpora.

At followup, which extends from 1 to 5 years after implant, patients are asked 2 standardized questions to assess device use and satisfaction, including whether they use the device and, if used, with what frequency. This satisfaction question is gauged on a 5-point Likert scale (with responses "very satisfied," "satisfied," "neither

satisfied nor dissatisfied," "dissatisfied" and "very dissatisfied"). The baseline questionnaires are also repeated at followup, and obtained in person, by mail, or via telephone by the authorized study personnel. Complications assessed by the investigator as related to the device and/or procedure are also reported. Data are collected in an online secured database. Study site monitors periodically visit sites (at a yearly minimum) and inspect data for compliance and adverse event reporting. The study sponsor, AMS, is responsible for funding, online database maintenance, monitoring and statistical analysis.

Two articles have been published to date, both in the J of Urology, including "The Who, How and What of Real-World Penile Implantation in 2015: The PROPPER Registry Baseline Data". Thankfully, the article was one of three on the front cover. The article includes data on 1,019 men who were enrolled at 11 sites through April 2, 2015.

Of these subjects the majority (983) underwent implantation with an AMS 700 IPP, of whom 495 received the LGX model. In addition, 26 patients received an AMS Ambicor and 10 underwent placement of an AMS Spectra (Table 1).

The average age of the patients in the study was 63.6 ± 10 years (range 21 to 87). Radical prostatectomy was the predominant etiology in 285 subjects (28%). The other major contributing etiologies included diabetes (220, 21.6%), cardiovascular disease (200, 19.6%) and Peyronie's disease (91, 8.9%). Of those 285 patients treated with RP 280 (98.2%) received an AMS 700. Overall cardiovascular disease was the most common reported condition (31.1%), followed by diabetes (11.8%) and Pevronie's disease (11.7%). Of the patients who received an AMS 700, 53 (18.9%) who had undergone RP had concomitant SUI, while only 8 (1.1%) patients not treated with RP had concomitant SUI (p <0.001) (Table 2).

Table 1 of DRAIN by DRESSING					
Controlling for STATUS=					
	DRAIN(Drain used during surgery)		DRESSING(Surgical dressing used)		
Frequency Percent Row Pct Col Pct		None	Compression/mummy wrap	Non-compressive	Total
Yes		0 0.00	0 0.00 0.00	0 0.00	0.00
No		0 0.00 0.00	1 100.00 100.00 100.00	0 0.00 0.00	1 100.00
Total		0 0.00	1 100.00	0 0.00	1 100.00

		Tab	le 2 of DRAIN by DRESS	ING	
		Controlling for S	STATUS=Admitted/inpatie	nt/>= to 24 hours	
	DRAIN(Drain used during surgery)			DRESSING(Surgical dressing used)	
Frequency Percent Row Pct Col Pct		None	Compression/mummy wrap	Non-compressive	Total
Yes		0 0.00 0.00 0.00	17 30.91 100.00 32.69	0 0.00 0.00 0.00	17 30.91
No		1 1.82 2.63 100.00	35 63.64 92.11 67.31	2 3.64 5.26 100.00	38 69.09
Total		1 1.82	52 94.55	2 3.64	55 100.00



Key from Kols: PROPPER Update

Overall ED duration was 6.9 ± 4.7 years (in 713, 5.0, range 0.1 to 30.0) for all subjects. The most common previous ED treatment was PDE-5i, followed by ICI, VED, previous penile implant, and combination therapy (Table 2). Patient status in terms of hospital length of stay revealed that 523 patients (51.3%) were under 24-hour observation, while 441 (43.3%) underwent same day surgery discharge and 54 (5.3%) were admitted to the hospital for more than 24 hours. Among those patients receiving an AMS 700, those treated with RP and those with diabetes had more outpatient admissions (less than 24 hours, 56.8% and 52.1%) compared to patients with cardiovascular disease and Peyronie's disease (42.0% and 35.6%, p < 0.001). The majority of patients were implanted via a penoscrotal approach (821, 80.6%), as opposed to a infrapubic approach (196, 19.2%). Independent of hospital admission status, a large percentage of patients received a mummy wrap/compression dressing. However, drain presence was strongly correlated with overnight hospital stay, while lack of drain placement was associated with same day discharge (p < 0.001) (Table 3).

Average procedure length was significantly shorter for the patients who received the AMS 700 implant $(47.0 \pm 28.7 \text{ minutes})$ compared

with those who received the Ambicor (71.4 \pm 27.3 minutes) and Spectra (62.2 \pm 21.0 minutes, p <0.001). Statistically significant differences were also observed in procedure length between the patients who received the AMS 700 implant with cardiovascular disease and those who had undergone RP (41.3 \pm 20.7 vs 49.4 \pm 28.0 minutes, p 1/4 0.018). At baseline the UCLA-PCI sexual function score and urinary function score for all patients was 21.6 ± 16.4 and 79.4± 24.6, respectively. There was a statistically significant difference in UCLA-PCI sexual function and urinary function scores observed in different primary etiology groups. Patients treated with RP had the lowest scores (UCLAPCI sexual function 18.0 \pm 14.7, urinary function 69.7 \pm 27.4, p <0.001). Urinary function (total 79.4 \pm 24.6 in 567, 86.8, range 0.0 to 100.0 vs RP 69.7 ± 27.4 in 221, 75.0, range 0.0 to 100.0) for baseline scores was significantly lower than in other patient groups (p < 0.001).

This registry revealed interesting data in contrast to the conventional wisdom about penile prostheses. For example, the traditional belief was that malleable and 2-piece prosthetics are faster to place than an IPP. However, this study revealed a statistically significant shorter OR time when placing an IPP compared with the malle-

able and 2-piece implants. The longer OR time for malleable and 2-piece implants could be due to the typical need for a longer corporotomy, with subsequent longer closure with multiple sutures. However, this could be due to the fact that the majority of the authors have greater experience with 3-piece IPP implantation and less experienced implanters would have a shorter OR time with malleable and 2-piece implants. Another surprising finding was that surgery for patients whose primary etiology was Peyronie's disease was shorter than for their post-RP counterparts. This study also revealed significantly higher rates of SUI and climacturia in the radical prostatectomy group compared with other patient groups. These findings were also seen with lower UCLA-PCI urinary function scores. The RP group had significantly lower UCLA-PCI scores for sexual function, urinary function and urinary bother. This study suggests that the primary etiology group, radical prostatectomy, has multiple factors that need to be addressed after prostate cancer therapy. Ten years ago almost every patient with a penile implant spent at least one night in the hospital with extensive dressings and drains. Now almost half of the patients in the study were discharged home the day of surgery. The complicated, compressive spider web tape dressing and/or placement of a drain

Table 3 of DRAIN by DRESSING						
	Controlling for STATUS=Same day discharge (before midnight)					
	DRAIN(Drain used during surgery)			DRESSING(Surgical dressing used)		
Frequency Percent Row Pct Col Pct		None	Compression/mummy wrap	Non-compressive	Total	
Yes		0 0.00 0.00 0.00	38 7.13 100.00 7.20	0 0.00 0.00 0.00	38 7.13	
No		2 0.38 0.40 100.00	490 91.93 98.99 92.80	3 0.56 0.61 100.00	495 92.87	
Total		2 0.38	528 99.06	3 0.56	533 100.00	



Key from Kols: PROPPER Update

encourages the physician to use an overnight stay in the hospital. However, with insurance reimbursement changes forcing many cases to become truly outpatient (same day) surgeries, a quandary remains for using dressing to prevent hematomas. This predicament inspired the creation of the "mummy wrap," with more than 97% of cases using a compressive, mummy-type wrap that essentially did not exist 10 years ago. The economics of health care can be a driving force in the evolution of care, as evidenced by these changes. Most patients who underwent drain placement also spent at least one night

in the hospital. If health care economics mandate more same day discharge in the future, drain use may decrease at that time. In addition to changes in the type of implant used, surgical techniques have evolved greatly in recent years. This has resulted in decreased operating times, lower infection rates and improved outcomes. However, the study population reveals the traditional 80%/20% split of penoscrotal vs infrapubic approach and an 84%/13%/1% split on primary/revision/salvage procedures. These patients are prospectively followed for 5 years with annual followup and validated question-

naires. We hope to report significant data with which to supplement research on these groups. Additionally, this study collects data on different surgical techniques, which is a much debated but poorly studied topic in prosthetic urology.

We hope to update the published literature as the data mature during this 5-year study. Once the data mature, the findings of this study could change various aspects of our future surgical penile prosthetic practice. The primary goal of the study is patient advocacy to demonstrate why PP should be covered.

Table 4 of DRAIN by DRESSING					
Controlling for STATUS=Outpatient/< 24 hours					
	DRAIN(Drain used during surgery)		DRESSING(Surgical dressing used)		
Frequency Percent Row Pct Col Pct		None	Compression/mummy	Non compressive	Total
Corpet		None	wrap	Non-compressive	Total
Yes		9 1.48 1.81 90.00	485 79.90 97.59 81.65	3 0.49 0.60 100.00	497 81.88
No		1 0.16 0.91 10.00	109 17.96 99.09 18.35	0 0.00 0.00 0.00	110 18.12
Total		10 1.65	594 97.86	3 0.49	607 100.00



Key from Kols: The complex world of Premature Ejaculation: From diagnosis to drug and behavioural management

by Paolo Verze



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Premature ejaculation (PE) is considered the most frequently reported male sexual dysfunction and affects several millions of men worldwide.

It is usually referred as uncontrolled ejaculation either before or shortly after sexual penetration. It happens with minimal sexual stimulation and before the person wishes. It may result in unsatisfactory sex for both partners and this can increase the anxiety that may add to the problem.

One of the major problem with estimating the real epidemiological impact of premature ejaculation had been the lack of univocal and clear definition of the disease. There have previously been two official definitions of PE, neither of which have been universally accepted. The first definition was included in the Diagnostic and Statistical Manual of Mental Disorders IV-Text Revision (DSM-IV-TR), recently updated in the DSM V edition. The second definition was included in the World Health Organization's International Classification of Diseases-10 (ICD-10). To have available the first evidence-based definition of PE we had to wait for the International Society for Sexual Medicine (ISSM) to adopt in 2014 a completely new definition taking into account several parameters: the time to ejaculation, the inability to control or delay ejaculation, and negative consequences (bother/ distress) from PE.

However, the major point of debate is still quantifying the time to ejaculation, which is usually described by Intravaginal Ejaculatory Latency Time (IELT), that is a difficult to measure parameter. IELT has a significant direct effect on perceived control over ejaculation, but not a significant direct effect on ejaculation-related personal distress or satisfaction with sexual intercourse. In addition,

perceived control over ejaculation has a significant direct effect on both ejaculation-related personal distress and satisfaction with sexual intercourse.

The context has been made even more complicated by the recent addition of two new types of PE syndromes (Variable PE and Subjective PE) that may aid patient stratification, diagnosis and treatment, but whose exact role remains to be defined.

Due to the lack of an accurate (validated) definition for PE, highly variable estimated epidemiological rates had been reported across the recent years. The highest prevalence rate of 31% (men aged 18–59 years) was reported in 1999 by the USA National Health and Social Life Survey (NHSLS) study. It is, however, unlikely that the PE prevalence is as high as 20–30% based on the relatively low number of men who present for treatment of PE. More recently significantly lower prevalence rates have been reported in European studies (PEPA study), even if the study methodology was mainly different.

Regardless of the highly variable epidemiological data, it is clearly established that men suffering with PE are more likely to report low satisfaction with their sexual relationship, low satisfaction with sexual intercourse, difficulty relaxing during intercourse, and less frequent intercourse. Furthermore, the negative impact of PE extends beyond sexual dysfunction so that can cause a detrimental effect on self-confidence and the relationship with the partner, and may sometimes cause mental distress, anxiety, embarrassment and depression. On the other side, the female partner's satisfaction with the sexual relationship decreases with increasing severity of the man's condition, with most partners of PE patients reporting feelings of disappointment and scarce interest to sexual activity. Female partners of men with PE report significantly greater sexual problems, with reduced satisfaction, increased distress and interpersonal difficulty, and more orgasmic problems than partners of non-PE men.

Another important aspect in PE management is the fact that female partners of men with PE

have a different reaction compared to those of men suffering with erectile dysfunction (ED). In fact, in the latest case, women dump the blame on themselves (i.e. "What is wrong with me?"), whilst in the case of PE patients, female partners take an accusatory attitude against the patient (i.e. "What is wrong with him?"). The following partner's perceptions of PE are often reported when female partners are queried: "Why can't he control himself?"; "Why does he let me down every time?"; Why doesn't he care for me?".

When treating a man with PE, the partner's participation should be encouraged to enable the physician to fully understand the extent of the problem, and consider other relevant factors, from her perspective. Identifying the best approach for the couple requires consultation with each person individually and together.

Diagnosis of PE is essentially based on the patient's medical and sexual history. The latter is crucial to classify PE as lifelong or acquired and determine whether PE is situational (under specific circumstances or with a specific partner) or consistent. Special attention should be given to the duration time of ejaculation, degree of sexual stimulus, impact on sexual activity and QoL, and drug use or abuse. Furthermore, great attention should be paid to the coexistence of ED and/or prostatitis because, if present, it is important to treat first.

In clinical practice, treatments for PE are likely to include a combination of pharmacological, psychological, sexological, and/or behavioral approaches for both the man and his partner.

Treatment of lifelong PE is challenging and should be mainly based on the use of drug therapy as a first line choice. It is worth to remind that Dapoxetine is the only on-demand pharmacological treatment approved for PE in many countries except for the USA. All other medications used in PE are off-label indications.

I personally consider Dapoxetine as an effective and safe weapon in our hands for managing PE patients, irrespective of their etiology. However,



Key from Kols: The complex world of Premature Ejaculation: From diagnosis to drug and behavioural management

before beginning treatment, it is essential to discuss the patient's expectations thoroughly, in order to maximize the therapeutic goal. I usually spend most of the time of the consultation in trying to let the patient to realize the relevance of his disease and the positive impact that he could achieve from treating it. At the same time I consider worth to stress the point that it is not only a matter of time to increase, but mainly a matter of overall sexual satisfaction to achieve, more importantly, not for himself but for the couple.

For the same reason I personally limit the use of off-label drugs, that, even if efficacious in delaying ejaculation stimuli, have no proven effect on sexual satisfaction. Furthermore, the patient is exposed to the counterproductive effect of using an off-label

compound, rather than being at higher risk of recurrence after treatment cessation.

When looking at major guidelines, behavioural techniques are not recommended for immediate use in lifelong PE, whilst there is an indication for the use of psychological/behavioural therapies in combination with pharmacological treatment in the management of acquired premature ejaculation.

However, a very recent publication by our research group had showed that the combination of Dapoxetine and behavioural treatment provides better results than Dapoxetine alone in the management of patients with lifelong premature ejaculation. Based on our findings, we can confidently assume that, providing Dapoxetine can act positively on

the dominant organic/neurobiological aetiology of lifelong PE, sex-behavioural treatment can impact the physical and psychological control of sexual performance, thus providing better results than Dapoxetine alone.

Overall, although PE is a common male sexual dysfunction, it is poorly understood. Patients are often unwilling to discuss their symptoms and, to my opinion, also because they do not trust their physicians who do not know about effective treatments. As a result, patients are often misdiagnosed or mistreated. For this reason we, as urologists dedicated to managing sexual dysfunctions, should field the best energies to increase the awareness about the disease and improve the therapeutic strategy we can offer.



The ESSM School of Sexual Medicine 2016

14–23 October 2016 | Budapest, Hungary





MEETINGS AND EVENTS CALENDAR 2016



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

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July

Androforum. UROup 2016

July 1, 2016

Location: Hospital Universitario Puerta de

Hierro Majadahonda, Madrid, Spain.

Website: http://www.androforum2016.com/

ESHRE 2016 Annual Meeting

July 3 - 6,2016

Location: Helsinki, Finland

Website: https://www.eshre2016.eu/

49th Annual Meeting of the Society for the Study of Reproduction

July 16 - 20, 2016

Location: Sheraton San Diego Hotel & Marina,

San Diego, California, USA

Website: http://www.ssr.org/16Meeting

August 2016

The Annual Scientific Meeting of the Endocrine Society of Australia and the Society for Reproductive Biology

August 21 - 24, 2016

Location: Gold Coast Convention & Exhibition

center, Broadbeach, Queensland,

Australia

Website: http://esa-srb.org.au/

September 2016

CBRA 2016. 20º Congresso Brasileiro de Reprodução Assistida

September 14 – 17, 2016 Location: Belo Horizonte, Brazil Website: http://cbra2016.com.br/

22nd IFFS World Congress on fertility and sterility

September 21 - 25, 2016 Location: New Delhi, India

Website: http://www.iffs-reproduction.

org/?page=IFFSCongress

9th European Congress of Andrology (ECA2016)

September 21 – 23, 2016

Location: Rotterdam, The Netherlands
Website: http://www.ecacongress2016.com/

62nd Annual meeting of the Canadian Fertility and Andrology Society (CFAS)

September 22 - 24, 2016Location: Toronto, Canada

Website: http://www.cfas.ca/index.php

The 20th World Meeting on Sexual Medicine, Global Chinese Andrology and Sexual Medicine Congress

September 22 – 25, 2016 Location: Beijing, China

Website: http://www.wmsm.org/

October 2016

72nd Annual Meeting of the ASRM

October 15 – 19, 2016 Location: Salt Lake City, USA

Webiste: http://www.asrmannualmeeting.org/

ASHG 2016

October 18 - 22, 2016Location: Vancouver, Canada

Website: http://www.ashg.org/2016meeting/



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Announcement for the next Congress

19th Congress of the European Society for Sexual Medicine

2 - 4 February 2017 | Nice, France



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