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ESSM NEWSLETTER

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Welcome Address

This is not goodbye, just “until we meet again!”

I am delighted to welcome you to this 2017 issue of the ESSM newsletter and my last as Editor-In-Chief.

First of all, I would like to thank all ESSM staff and my editorial team (Drs. Angulo, Mondaini and Vozmediano) for their outstanding job and interest during these years: Without them it would not have been possible.

Since the 2009 ESSM meeting in Lyon we took over this responsibility and it was always our goal to improve the usefulness and quality of this newsletter for all our members. Personally, I was feeling very fortunate to have the chance to serve our great Society and its community members. Along these many years, the response we have received from all invited authors, people interviewed, case reports, congress highlights and reviews, was always very enthusiastic and professional. My thanks to all of them as well.

I am sure that my successor, Dr. Fusco, and his new team will continue improving the newsletter's value and take it to the next level. That would indeed be a very good sign of the good health of our Society.

In this issue, we have included an interesting interview with our ESSM President, Prof. Giuliano, a world-wide known expert in Sexual Medicine. Among other subjects, we have covered many Key from Kols collaborations, regarding infertility, penile prosthesis, Peyronie's Disease, basic science, digitalized medicine among others along with our classic sections by my associate editors (Dr. Mondaini & Angulo). We hope you will enjoy reading it.

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

My very best
Juan I. Martínez-Salamanca



Interview with Dr. François Giuliano

Seven questions

by Juan I. Martinez-Salamanca (JIMS)



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significant progress made by psychologists, I believe that it is nowadays to consider sexual medicine for both women and men despite the fact that there is still a lot of ignorance and that we must significantly improve our therapeutic armamentarium for a variety of male and female conditions which still represent unmet medical needs. Men's health includes cardio-vascular diseases, metabolic syndrome and many other conditions which are of crucial importance but for which I am not qualified. I have learned a lot from cardiologists, from endocrinologists and so on but they are different specialists with different qualifications.

JIMS: What do you think the role of the urologist should be in the management of Erectile Dysfunction? And what are our major challenges in the near future?

I still believe that urologists are by training the natural experts for male sexual dysfunctions including ED at least from organic origin. Indeed they have the knowledge about the anatomy and the physiology. Nevertheless there is definitely a role for health care providers with a robust training in psycho-sexology in the management of these patients. General practitioners have also a crucial role in the management of ED because in ageing males ED is most often the consequences or the early sign of chronic conditions GPs are dealing with every day including cardiovascular diseases, diabetes, depression ...

The need for a disease modifying non-surgical treatment for ED does represent the challenge in the future. Indeed all the available pharmacological treatments, either oral or local are symptomatic. Will this Holy Grail be therapy with stem cells, with extracorporeal shock waves, with intracavernosal delivery of long acting compounds or any combination thereof. We don't know. But I am very optimistic about next future advances.

Dr. Giuliano is an internationally known figure and world-class leader in the field of Sexual Medicine. 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 tract. 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.

Dr. Giuliano's major research interests include pathophysiology, diagnosis and management of sexual dysfunctions and of benign prostatic hyperplasia and urinary incontinence and comorbidities 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 also served as President of our Society.

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

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

I am a urologist by training. I have been trained in different academic urology departments across France including Dijon and Auxerre in Burgundy and finally in Paris in the urology department chaired by Pr Alain Jardin in Bicêtre hospital in the south suburb. Between the end of my residency and the beginning of an as-

sistant professorship, I have spent 2 years to learn experimental research mainly focusing at that time on the physiology and the pathophysiology of erectile dysfunction. After 4 years as an assistant professor in urology I have got a position for 7 years at the Medical University of Paris South of associate professor in therapeutics which is close to clinical pharmacology. By that time I was practicing general urology with a special interest in sexual medicine. Then I moved to the R. Poincaré hospital in Garches located in the West suburb of Paris. This hospital is dedicated to neurologic patients. I have got full professor position and since 12 years now I have a specialized practice in neuro-urology and andrology. In parallel with my clinical practice I am leading a research group with approximately twenty researches and technicians with currently three main activities: The experimental pharmacology of sexual functions both male and female, the neurophysiology of ejaculation and a gene therapy program for neurogenic bladder.

JIMS: During your career, which has led to the passage from "Andrology" to "Sexual Medicine", and what do you prefer "Sexual Medicine" or "Men's Health"?

This is because we have made significant progress in the understanding of the male sexuality, the pathophysiology of male sexual dysfunctions and their management that the scientific and medical community has been able to start to address the physiology of female sexual response and at least at the experimental level to explore its pharmacology. Thanks also to

Interview with Dr. François Giuliano – Seven questions

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

I must say, based on my daily practice, that when you provide the opportunity to a young adult severely disabled, and we know how much sex is important for them, to regain the ability to enjoy with his partner a satisfactory sexual intercourse, the reward is great. It is even greater when you provide them with ability to ejaculate even if most often they are unable to experience orgasm. This is not unusual for them to cry tears of joy. When you have accomplished that, no question that the reward is there.

JIMS: Dr. Giuliano, regarding the latest controversy about the relation between Lower Urinary Tract Symptoms and Sexual Health, what is your personal opinion about that?

I still believe there is a link between LUTS and male sexual dysfunctions. In addition to ED for which the epidemiological are robust, I would like to emphasize based on the surveys which have been conducted but also on my daily practice that male LUTS are very often associated with ejaculatory disorders especially decrease in the semen volume and/or decrease in the forcefulness of semen expulsion. Patients, in my experience, are more and more complaining about these changes and we are totally helpless. Your

question is also an opportunity to re-emphasize about the potential harmful effects on sexual functions especially ejaculation of the pharmacological and surgical treatments for LUTS even when they are claimed to be minimally invasive.

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

There is no question that practicing medicine is a fascinating activity. The diversity is a treasure. Always be curious and never stop studying and working. I believe we are the beginning of a revolution because of the nanobiotechnologies. It will be extremely important for young physicians to develop strong and productive relationships with all these new professions. Medicine cannot become computer driven but there is a need for more innovative technologies in future practice. It will probably end up there anyway. Accordingly working with Google, Amazon, Facebook, Apple and Microsoft will become an obligation.

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?

There is a long list of challenges for sexual medicine which is still in its infancy. The physiology of ejaculation is actually much better understood

but we do not have any pharmacological treatment neither for delayed ejaculation nor for an-ejaculation. There are pharmacological targets which have been identified, this is now a matter of collaboration between chemists, central nervous system pharmacologists and interest from pharmaceutical companies. The physiology of both male and female orgasm remains almost completely unexplored. I see a huge opportunity for central pharmacology to target low sexual desire disorder both in women and men. Again there are several targets available from experimental research. It is also of outmost importance to attempt to standardize and to assess the psycho-sexological practices.

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.

The logo for ESSMToday, with 'ESSM' in a bold, white, sans-serif font and 'Today' in a black, italicized, sans-serif font, set against a background of colorful, abstract watercolor-like shapes.

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Key from Kols: Combination of α_{1A} -adrenergic blockade and PDE5 inhibition as a strategy for the treatment of ED after radical prostatectomy by Juan I. Martínez-Salamanca, Javier Angulo



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specific increase in apoptosis or fibrosis [14] in opposite to that observed by ourselves in the rat model of cavernous nerve injury [24]. However, this rat model shared key cavernosal functional alterations with penile tissue from men with ED-RP, displaying preserved endothelial and smooth muscle relaxations, deeply impaired nitrgic relaxation and enhanced neurogenic contraction, being these both alterations of cavernosal function correlated with erectile function in vivo [24].

These evidences led us to propose that strategies directed to reverse neurogenic imbalance by recovering/preserving nitrgic responses and avoiding adrenergic enhancement could be of relevance in the management of ED after RP rather than those targeted to preserve endothelial and smooth muscle function.

Interactions between adrenergic system and NO/cGMP pathway

Loss of nitrgic function could be responsible for the enhancement of neurogenic contractions in cavernosal tissues from ED-RP since NO/cGMP pathway modulates EFS-induced noradrenergic contractions in human corpus cavernosum [25]. In fact, NO inhibition causes a stronger potentiation of adrenergic contractions in sham operated rats than in rats with induced cavernous nerve injury, reinforcing the concept that a potential inhibitory effect driven by nitrgic system on such responses is blunted after cavernous nerve injury [26].

Adrenergic system antagonizes neurovascular processes leading to erection [25]. Penile smooth muscle contraction in response to NE involves α_1 - and α_2 -adrenergic receptor subtypes, although functional studies suggest that α_1 predominate over α_2 subtype in human erectile tissue [27]. Although the presence of pre-synaptic α_2 -adrenoceptors has not been confirmed in nitrgic terminals of human corpus cavernosum, it has been proposed that these pre-synaptic receptors cause inhibition of nitrgic responses

Post-prostatectomy erectile dysfunction

Erectile dysfunction after radical prostatectomy (ED-RP) represents an outstanding challenge the Sexual Medicine professionals have to face. RP remains the reference treatment for organ-confined prostate cancer in patients with a life expectancy of 10 years or more [1], but despite the advent of nerve sparing techniques it often causes sustained ED [2,3]. Disparity exists in the literature regarding postoperative rates of erectile function recovery, ranging from 20 to 80% of patients [4-8]. In addition, ED-RP patients display a poor response to oral treatment with type 5 phosphodiesterase (PDE5) inhibitors [9]. Although early and continuous administration of these compounds has been shown to produce a positive effect on erectile function in ED-RP, the recovery of erectile function is obtained in a limited percentage of patients [10-13]. Post-prostatectomy erectile dysfunction (ED-RP) typically results from injury to the cavernous nerves that course along the posterolateral aspects of the prostate and provide most of the autonomic input to the erectile tissue.

Key functional alteration after cavernous nerve damage: Imbalance of neurogenic control

Recently, we have performed functional evaluation of human erectile tissue obtained from patients with ED-RP in comparison to healthy specimens and to those from patients with vasculogenic ED (ED-VASC). The outstanding feature that specifically characterizes functional alterations induced by RP in human cavernosal tissue

is a profound impairment of nitrgic relaxation. Corpus cavernosum from ED-RP displayed severely reduced nitrgic relaxations that were not only reduced with respect to healthy tissue but also were significantly decreased with respect to ED-VASC, who manifested a milder reduction [14]. In contrast, neurogenic (adrenergic) contractions were enhanced with respect to healthy tissue to the same extent as that observed in ED-VASC, suggesting that severe impairment of nitrgic responses is not related to a generalized neurogenic derangement.

Results obtained in rat models of cavernous nerve injury [15-17] and a very limited number of histological/immunohistological studies in human cavernosal tissue [18,19], have suggested that neurapraxia/damage of cavernous nerves causes cavernosal inflammation and hypoxia leading to cavernosal fibrosis. When this process is completed, a potential nerve restoration could find an unresponsive erectile tissue that would impede erectile function recovery even when nerve sparing techniques are applied [20,21]. This view of ED-RP pathophysiology mainly based in animal studies does not agree with the functional evidence that we have obtained in human penile tissue. Functional evaluation revealed preserved endothelial and smooth muscle relaxations in penile tissue from ED-RP which even conserved relaxation to sildenafil [14], in contrast to ED-VASC that displayed a clear impairment as previously reported [22,23]. These functional evidences were consistent with the histological analysis of showing that penile tissue from men with ED-RP did not exhibit a

Key from Kols: Combination of α_{1A} -adrenergic blockade and PDE5 inhibition as a strategy for the treatment of ED after radical prostatectomy

[28,29] At the functional level, the α_1 - and α_2 -adrenoceptor antagonist, phentolamine, has shown an improving effect on erectile function in patients with ED [30] besides increasing the efficacy of other vasodilators to relax rabbit [31] and human corpus cavernosum [32]. Although the three subtypes of α_1 adrenoceptors, α_{1A} , α_{1B} and α_{1D} have been detected in human [33,34] and rat [35] corpus cavernosum, α_{1A} and α_{1D} seem to predominate.

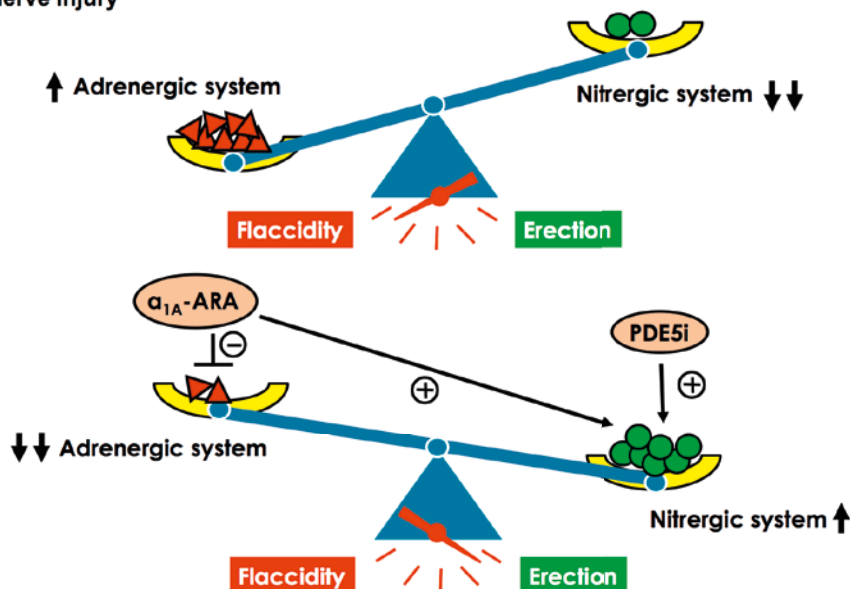
Improvement of erectile and cavernosal functions after cavernous nerve injury

Thus, based on the observation of a potentiated adrenergic input after cavernous nerve injury we proceeded to evaluate the ability of inhibiting α -adrenergic receptors (α -AR) to improve erectile responses in rats after cavernous nerve injury. Chronic antagonism of α -AR with either an unspecific α -blocker such as phentolamine or a specific α_{1A} -adrenergic receptor (α_{1A} -AR) antagonist such as silodosin partially preserved

erectile responses in rats after cavernous nerve injury. This protective effect was superior with specific α_{1A} -AR blockade, resulting in greater improvement of erectile responses after treatment with silodosin. Analysis of cavernosal responses revealed that chronic treatment with silodosin but not phentolamine reversed the potentiation of neurogenic contractions associated with cavernous nerve injury while the impairment of nitrgic relaxation secondary to nerve damage was partially prevented by treatment with α -blockers, mainly with the α_{1A} -AR antagonist [26]. Thus, the efficacy of chronic administration of α -AR antagonists to preserve erectile responses after cavernous nerve injury was probably related to its ability to relieve the imbalance of neurogenic control of cavernosal tone caused by cavernous nerve injury that favours adrenergic contractions over nitrgic relaxations. Specific α_{1A} -AR antagonist displayed higher efficacy than an unspecific α -AR antagonist that would potentially act on α_{1A} -AR too. We cannot provide a definitive explanation for this finding but could be related to the fact that pre-synaptic

α_2 -AR modulate sympathetic outflow by inhibiting norepinephrine release from adrenergic neurons causing vasodilatory effects [36]. However, the interaction of adrenergic system with NO-mediated responses could be produced at smooth muscle level. On the other hand, long-term administration of silodosin prevented, at least in part, nitrgic derangement induced by cavernous nerve injury in rat corpus cavernosum, as indicated by the higher cavernosal neuronal NO synthase (nNOS) expression remaining in the cavernosal tissue from injured rats treated with silodosin [26]. Preservation of nNOS expressing nerve terminals in corpus cavernosum would probably account for the improving effect driven by silodosin on nitrgic function making possible the recovery of neurogenic control balance. Nevertheless, this is not the only mechanism responsible for silodosin-induced effects since acute administration of silodosin was able to improve erectile responses in vivo as well as to increase nitrgic relaxation and to reduce neurogenic contractions of corpus cavernosum ex vivo in rats with damaged cavernous nerve [26].

Combined α_{1A} -adrenergic receptor antagonism (α_{1A} -ARA) and PDE5i on neurogenic control balance of penile smooth muscle after cavernous nerve injury



Recovery of response to PDE5 inhibition

In addition, chronic antagonism of α -AR could enhance the efficacy of PDE5 inhibitors in the treatment of ED after cavernous nerve injury, since treatment with α -blockers allow for the manifestation of a potentiating effect by acute tadalafil in rats after nerve damage [26]. This concept has potential clinical relevance in the management of this type of ED. Furthermore, synergy between PDE5 inhibition and α -AR antagonism was manifested in human penile tissue. In this sense, in addition to exert a significant potentiating effect in corpus cavernosum from ED-VASC patients or from those with ED secondary to radical prostatectomy (ED-RP), silodosin was able to recover the ability of PDE5 inhibition to enhance neurogenic relaxation which was lost in ED-RP patients. In fact, after adding silodosin and tadalafil in combination a notable potentiation

Key from Kols: Combination of α_{1A} -adrenergic blockade and PDE5 inhibition as a strategy for the treatment of ED after radical prostatectomy

of neurogenic relaxations was obtained in corpus cavernosum from ED-RP patients while tadalafil alone failed to influence neurogenic relaxations in these tissues and silodosin alone caused a mild potentiation, suggesting that these pharmacologic strategies could act synergistically. In fact, a synergistic interaction between the α -adrenergic blockade and the potentiation of the NO/cGMP pathway to increase neurogenic relaxation of corpus cavernosum from healthy rabbits [31] while additive effects of combinations of α -blocker with PDE5 inhibitor to relax human corpus cavernosum have been demonstrated [37,38]. This is consistent with the idea that NO has to override the constrictive effect of tonic α -adrenergic stimulation to drive an erection [39]. This concept fits with our findings that point to a cavernosal contraction/relaxation, adrenergic/nitroergic imbalance as the key functional impairment in ED after cavernous nerve injury [14,24,26]. Thus, dual strategy targeting both adrenergic enhancement and nitroergic derangement could produce an important functional improvement (Figure). Accordingly, silodosin was effective in enhancing the therapeutic effect of the PDE5 inhibitor, tadalafil, on neurogenic relaxations of corpus cavernosum from ED-RP patients and on erectile responses in rats after cavernous nerve injury, suggesting that a therapeutic strategy combining α_{1A} -AR blockade and PDE5 inhibition could be reasonable for the management of ED secondary to RP.

Future perspectives

Preclinical evidences above described strongly suggest a therapeutic potential of the combination of an α_{1A} -AR antagonist and a PDE5 inhibitor in the treatment of patients with ED-RP. However, this possibility can only be confirmed by the clinical evaluation of this therapeutic strategy. Feasibility to take this step is supported by the availability of and familiarity with both classes of drugs by urologists. However, the design of a putative clinical trial is key for its outcome and should be deeply meditated. In this sense, the paucity of administrations could condition the success.

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Key from Kols:

Sexual health in digitalized medicine: Future perspectives

by Eduardo Garcia Cruz



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Sexual health is one of the health cornerstones, and the WHO perceives the achievement of the highest attainable standard of sexual health as part of human rights fulfillment. Due to cultural constructs of masculinity, men tend to be more reluctant than women to consult their healthcare provider: In the particular case of sexual health disorders, shame and the lack of privacy commonly act as barriers to seeking professional help. The result of this is low consultation rate and patients taking parallel paths towards solution, specially in erectile dysfunction, premature ejaculation, Peyronie's disease, and symptoms associated with hypogonadism. The revolution of digital technologies offers now a scenario of privacy in which men can easily access to a vast amount of information about almost every single health issue. It is not surprising, then, that digital initiatives and resources related to men's sexual health flourish day by day.

Our personal experience with digital medicine entails social media, blogging and apps. Three years ago we set up a blog and a web began to post on the most requested topics in sexual

medicine, following a strategy called content marketing, in which a SEO-optimized content (a post that has been optimized so as Google search algorithm gives it the best rating and provides optimal positioning) was backed by social media (Twitter, LinkedIn, Flickr, SlideShare, Instagram, YouTube). The first year we reached 50,000 readers. Three years later we hit 1,5 millions single users.

In the meantime we have developed two apps (Men's Sexual Medicine and Men's Sexual Medicine PRO) reaching more than 56,000 downloads. These two apps provide a comprehensive algorithm that allows the user to reach an orientative diagnose and treatment, aiming to be the first step towards physician office "analogic" consultation. Moreover, every time an app is downloaded a query must be fulfilled to unblock it, we harvest plenty of data about real world patients far from office consultation. All this data permits us to handle huge amount of data and opens a door towards new strategies in data recruitment and publication. This amount of information can only be handled using automated machine systems such as exploratory data analysis and massive data analysis, allowing us to generate new hypothesis.

The digital revolution has changed the way we communicate, the way we generate and access to knowledge: In other words, the way we live our lives. The healthcare field is not immune to this change, and it is being transformed in a

revolutionary manner by internet, social media, apps, wearable devices, and an endless list of digital strategies which make the healthcare system evolving towards unknown scenarios. Overall, the potential contribution of digital resources in healthcare and medical research is beyond doubt.

The particular field of sexual healthcare is strongly influenced by two important factors not affecting other medical areas:

1. the psychological barrier – arising from cultural constructs of masculinity –, which prevents many patients from seeking help, and
2. the lack of education in sexual field among general healthcare professionals, which often leads to disregard treatable sexual dysfunctions.

Digital resources overcome these limitations by providing patients with anonymity and disseminating knowledge worldwide, regardless of the characteristics of the healthcare system and the educational interventions implemented in each country.

In conclusion, the digital is changing the world. Based upon the singularities of our area of knowledge, we as professionals and our scientific societies should move towards the possibilities that this new resources offers, such as big data, augmented and mixed reality and artificial intelligence.

Key from Kols: Is there a role for DNA fragmentation in patients with male infertility today?

by Saturnino Luján



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Sperm DNA fragmentation (SDF), is more common in infertile patients than in fertile counterparts. Several conditions can produce an increase of SDF, for example, infections, varicocele, environment toxins (pollutants, cigarette smoking), increase of paternal age, or systematic diseases. SDF has an important role in infertility because an elevated SDF may affect fertility by impeding fertilization, early embryo development, implantation, and pregnancy (1). Even though these implications for male infertility, currently, there seems to be insufficient evidence to support the routine use of SDF in male factor evaluation (2). Despite this lack of general evidence, it is necessary to identify certain cases where obtaining SDF would be of significant value.

SDF testing has been proposed as complementary to the information provided by routine semen analysis. Various methods exist to test sperm DNA fragmentation such as the sperm chromatin dispersion (SCD) test, the sperm chromatin structure assay (SCSA), the single cell gel electrophoresis (Comet) assay and the terminal deoxynucleotidyl transferase mediated deoxyuridine triphosphate nick end labelling (TUNEL) assay. The most commonly used tests are TUNEL, SCD and SCSA. It is considered that an SDF higher than 30% is abnormal.

DNA damage is produced by reactive oxygen species (ROS) and is manifested as increased of SDF. This damaged occurs when the spermatozoa are transported through the epididymis. Different strategies have been identified to decrease SDF in patients with male infertility such as varicocelectomy, stops smoking or oral antioxidant.

Nowadays there is a greater number of studies that promote the use of testicular rather than ejaculated sperm for ICSI in cases of high SDF, oligospermia or recurrent in vitro fertilization failure, because has been reported a better pregnancy outcome (3).

Therefore, and evaluating the value of the SDF we could propose several clinical scenarios where this biomarker could be useful.

- ▶ Varicocele and infertility: There is a significant association between SDF and varicocele. Varicocelectomy improves the percentage of SDF resulting in an improved pregnancy rate. Current evidence suggests SDF is recommended in patients with grade 2/3 varicocele with normal semen parameters and infertility and in patients with grade 1 varicocele with borderline or abnormal semen parameter results (4).
- ▶ Recurrent pregnancy loss or recurrent IVF failures: High SDF is found in men with normal semen analysis and is associated with greater incidence of abortion after natural conception or IVF-ICSI procedures. SDF testing in patients with recurrent ART failure is indicated as it can provide useful prognostic information on future ART cycles (4). On the other hand, several studies have shown benefit in using testicular (TESE, testicular Sperm Extraction) rather than ejaculated sperm if the patient has severe oligospermia, high SDF (>30%) and recurrent assisted reproductive techniques failure (3).

However, we have to take into account that the potential risk of testicular biopsy as postoperative pain, hematoma, and testicular atrophy.

In conclusion, and the evidence currently available, SDF is not for all patients with male infertility as a diagnostic tool. By my point of view, SDF should be justified and reserved for selected men for known (varicocele) and unknown causes of SDF and before of surgical procedure (varicocelectomy or testicular sperm extraction). This biomarker could give us information in order to make a surgical decision.

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Key from Kols: Novel use of collagen fleece graft combined with plaque incision and penile prosthesis implantation in Peyronie's Disease surgery by Esaú Fernández-Pascual & Juan I. Martínez-Salamanca



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tunica defect and no need for sewing the graft into the tunica defect. Therefore, this technique is less time consuming compared with other grafting techniques. In addition, a hemostatic effect is provided by the fleece.

We have used this type of grafts in conjunction with penile prosthesis implantation (malleable or inflatable) in patients with or without erectile dysfunction and Peyronie's disease.

We operated 7 patients using this technique, three by implantation of a malleable prosthesis and the other four with inflatable. Four of them kept proper erectile function and one had significant shortening of the penis without curvature. Two of them had been previously operated: One inflatable prosthesis plus modeling; and other with sequelae after simple plication. Surgery was performed in the case of malleable through a single incision (with penile degloving) while IPP was performed either by 2 incisions (scrotal + penile degloving) or through a single incision (Kulkarni approach). Curvature correction was made by partial plaque incision with an H modified technique in the area of maximum curvature (or corporeal relaxing incisions) and placing a patch without suturing, covering prosthetic material.

No patients had significant hematoma that requires surgery, glans ischemia or any infectious complications. All patients showed good ability of penetration and correction of the penile curvature (<10° of residual curvature in the seven patients) 3 months after surgery. Six patients had glans hypoesthesia at this time, while after the first 3 months, only 3 of them remains symptomatic. The overall satisfaction rate was of 90%.

In our experience, plaque incision and collagen fleece grafting during penile prosthesis implantation seems to be a safe and reproducible technique that yields higher satisfaction rates and greater penile lengthening than prosthesis implantation alone. Also this technique could be considered in the management of sequelae after PD surgery.

Peyronie's disease (PD) is an acquired, localized fibrotic disorder of the tunica albuginea. The initial, or acute, phase can present with penile pain upon erection and intercourse in 15–30% of cases, as well as progressive penile curvature. The chronic, or quiescent, phase denotes the end of inflammation and stabilization of the penile curvature or abnormality and usually occurs within 12–18 months following onset. Other associated features may include palpable penile plaques, hourglass defects, penile hinging, and penile shortening. Furthermore, association between PD and erectile dysfunction (ED) is seen in 20% to 54% of cases.

Careful assessment of this associated condition is a key to correctly determine the need for surgery and to ensure the success rate of reconstruction procedures.

Surgical management should be implemented for patients who have reached the chronic phase, with a plaque that has been stable for at least 3–6 months with resolution of pain. Furthermore, surgery is indicated if medical management has failed, the deformity prevents optimal sexual intercourse, the penile plaque is extensive, or if a patient with stable disease desires rapid results. The goals of surgical treatment are to correct the penile curvature or deformity, preserve or restore erectile function, and prevent loss of penile length and girth. The current surgical arsenal available to physicians includes tunical shortening procedures such as the Nesbitt and modified plications, tunical lengthening procedures (plaque incision or partial excision and grafting), and penile prosthesis (PP) implantation formen with concurrent ED.

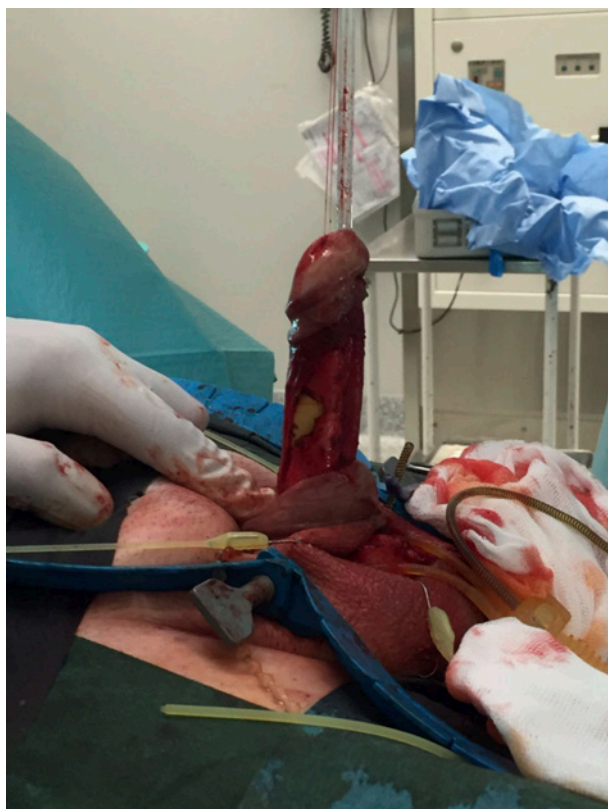
PP implantation is recommended for patients with PD and medication-refractory ED. One of the major factors for success in PP implantation is the intraoperative management of residual curvature. While successful curvature correction can be achieved with PP cylinder placement alone, there may be a need for further intraoperative straightening procedures in up to 61% of cases.

When IPP insertion alone does not sufficiently correct penile curvature, manual modeling is the next step to reduce residual curvature. While modeling is highly successful in adjusting residual curvature after IPP insertion, many authors have reported significant residual curvature in 20–30% of patients that required additional surgery. When post-modeling residual curvature exceeds 30°, most algorithms recommend a plaque-releasing incision or plication to further reduce the curvature.

Penile plication has been shown to be an effective means of curvature reduction, but with the obvious disadvantage of a loss of penile length. Plaque-releasing incisions can result in defects, often necessitating tunical grafting. Although no standard exists, it is recommended that an incisional defect >2 cm be corrected with a graft to prevent scarring contracture or herniation of the prosthesis. Traditionally, synthetic grafting material has been used, but biografts are currently the standard of care. Recently the use of other bioabsorbable materials has been described in substitution of the previously described materials. A new technique using self-adhesive collagen fleece has been described for grafting after plaque excision in Peyronie's disease.

The advantages of this new technique include no need for exact adjustment of the graft to the

Key from Kols: Novel use of collagen fleece graft combined with plaque incision and penile prosthesis implantation in Peyronie's Disease surgery



Key from Kols: Penile prosthesis revision surgery: State of the art by Josep Torremade Barreda



Inflatable Penile Prosthesis (IPP) is a high efficient therapy in the treatment of refractory erectile dysfunction. Since its introduction in 2013 by F. Brantley Scott (1), IPP treatment has become more and more popular.

But the beginnings were not easy. The first devices had rates of mechanical failure as high as 70% in less than 10 years (2). Manufacturers have made several changes in the IPP mainly intended to improve mechanical survival and to reduce the rate of infection. Regarding the first, we can highlight the use of parylene coating, kink-resistant tubing, polyurethane material and safer connections (3). As regards the second, these improvements are attributed to the use IPP with mynocyline and rifampicin coating (InhibiZone®) (4) or hydrophilic coating that binds antibiotics (5). These advances in technology over the past 40 years have turned the IPP into one of the most reliable devices in prosthetic surgery with a satisfaction rate of around 90% (6).

Despite the overall device survival of these new devices reported after 5 years is superior to the 90%, this decreases to the 60% at 15 years follow up (7). For this reason a large number of patients will request a replacement of its IPP in the coming years. In our hospital, revision surgery for mechanical failure represents 20–30% of IPP surgeries.

This review aims to illustrate the technical aspects to take into account in this type of surgery.

Preoperative care

The same recommendations that have shown effective to decrease the risk of infection in virgin IPP must be applied in the revision surgery by its greater risk of infection. As a reminder, these are:

- 1) parenteral antibiotics starting one hour prior to the incision,
- 2) hair removal at the operative site prior to surgery,
- 3) thorough skin scrub,
- 4) closed suction drainage or mummy wrap (8).

Complete or partial removal of the IPP

The cause of the mechanical failure can be different depending on the type of virgin IPP. With the use of last generation IPP, the cause of mechanical failure is mainly tubing fracture (67.5%), being less frequent other alterations as the cylinder aneurism, reservoir hernia and pump malfunction (10.4%) (9). In other series, with older devices, the main cause of mechanical failure is the cylinder leak (45%) followed by the tubing leak/break (13%) or the fluid loss not otherwise specified (20%) (10). But in any case, the final diagnosis will be based on the intraoperative findings.



Fig 1. Mechanical malfunction due to bilateral cylinder aneurism

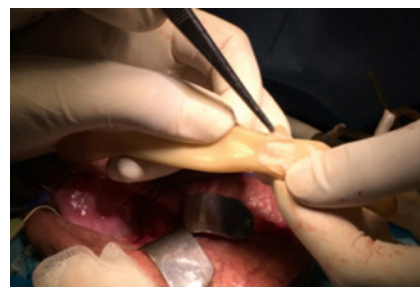


Fig 2. Mechanical malfunction due to cylinder fracture

In case of mechanical failure, the most prudent action is to replace both cylinder and pump. But in case of early dysfunctions of the pump, some authors have proposed changing only the damaged pump by a new one, avoiding the manipulation of those cylinders.

There is also discussion on what to do with the old IPP reservoir. Rajpurkar reports it is safe to leave the old reservoir and place the new one in the contra-lateral side (11). Even though, the retained reservoir and suboptimal washout of the space may increase the risk of infection. For that reason, it remains at the discretion of the surgeon as to decide whether the existing reservoir should be removed at the time of surgery review for a non-infected device (12).

Washout as strategy to decrease infection rates

It has been observed an increased risk of infection (13-18%) when IPP require surgical revision due to mechanical failure (13,14). It is attempted to explain this phenomenon with the implant of bacteria and the subsequent formation of a biofilm during the first surgery. These bacteria will remain protected by a biofilm until reactivated at the time of surgery revision.

Washout of the implant space has been described after component removal as a strategy to disrupt biofilm, to diminish the bacterial load and to facilitate the activity of antibiotics (15). However, there is not a consensus on which is the best system or which solutions to use. A multicentric study with more than 200 revision surgeries demonstrated a significant difference in the rate of infection in those patients who received washout with solution containing different antibiotic solutions versus those who did not receive washout (16). Abouassaly simplifies the washout method to a washing method of 1 L with 50000 units of bacitracin reporting an infection rate of 1.8% for a 32 months follow-up (9). Other authors observed no differences in the

Key from Kols: Penile prosthesis revision surgery: State of the art

rate of infection when comparing 2 groups of patients with washout versus the standard sterile technique, but they do observe an increase in the operating time of around 20 minutes (17). Another possibility is to use high pressure washing systems, as described in the salvage procedure of Brant and Mulcahy for penile implant infection (18). With these systems of high pressure we obtain an energetic irrigation from both corpus cavernosum and reduce greatly the surgical time of the irrigation. It is reasonable to hypothesize that the mechanical disruption of the biofilm by vigorous lavage with the chosen solution may be more important than the content of the solution itself (8).

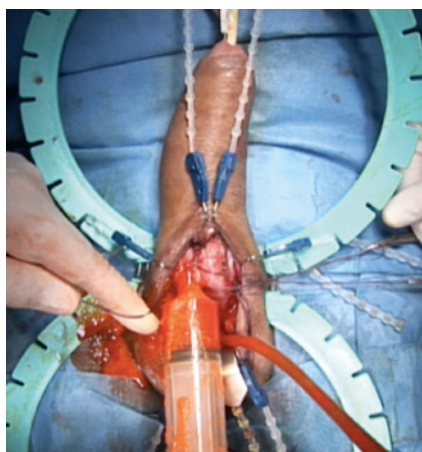


Fig 3. a) Antibiotic washout



b) High pressure saline washout

New device and upsizing

It is widely recognized that antibiotic coated IPP diminish the rates of infection in primary implants (19,20). Nerha shows in its series a greater over-life of antibiotic impregnated IPP independent of the revision cause and a smaller rate of infection in impregnated IPP (3.3%) when comparing it with non impregnated IPP (7.6%) (21). Since many groups use antibiotic coated IPP in virgin cases, it seems mandatory to use them also in cases of revision for the aim of diminishing the number of infections (8).

There is no data published in literature regarding if revision surgery would allow for a larger corporal cylinder to be placed. Some authors have proposed that presence of a working IPP prior to revision can contribute in a progressive corporal expansion after the surgery (22). AMS Ultrex and AMS 700 LGX were introduced to minimize penile shortening following prosthetic surgery (23). Recent data have reported significant differences in penile length between baseline and 6-12 months using these devices (24). This would allow us to make further cylinders upsizing in case of mechanical malfunction. By all previously exposed, when facing a case of revision surgery we will not replace the prosthesis by another one with the same dimensions and we will make new measurements. In many cases we will be able to make an up-sizing from 1 to 2 cm.

Conclusions

Re-operative penile prosthetic cases are always more complex and have a higher infection rate than first-time implantation. More studies are needed in order to prove which is the best strategy. However, those points where there is a greater consensus are focused on the use of antibiotic coated or soaked IPP, preoperative antibiotics, not touch techniques and performing washout procedures. Complete removal of IPP is not always needed and leaving reservoirs in situ does not seem to associate to an increase of the complications.

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Have you read? Best of the Best: Basic Research

by Javier Angulo



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Diabetic erectile dysfunction – Enhancing cell therapy

Cell therapy still represents an important focus in translational research in the field of Sexual Medicine. Since preclinical research evidence has shown a beneficial effect of cell therapy in different animal models of ED but these effects are not complete, important efforts in preclinical research are targeted to create conditions that could enhance the therapeutic potential of stem cells. In this sense, two articles have been recently published in the Asian Journal of Andrology aiming to evaluate two different strategies for increasing the therapeutic capacity of adipose tissue-derived stem cells (ADSCs) to recover erectile function in a rat model of diabetic ED. The relative resistance of diabetic ED to conventional therapy makes this type of ED an objective for the search of alternative more effective therapeutic approaches.

Superparamagnetic iron oxide nanoparticle targeting of adipose tissue-derived stem cells in diabetes-associated erectile dysfunction

Zhu LL, Zhang Z, Jiang HS, Chen H, Chen Y, Dai YT. Asian J Androl 2016, doi: 10.4103/1008-682X.179532 [Epub ahead of print]

In this study as well as in the following one, the two groups selected ADSCs as the tool for cell therapy application. This type of progenitor cells appear as the most feasible source for cell therapy due to the easy way of obtaining and the low immunogenicity that even allows for allogenic use. In fact, positive effects of intracavernosal injection of ADSCs have been reported in rat models of type 1 and type 2 diabetes.

The strategy evaluated by Zhu and collaborators for enhancing therapeutic potential of ADSCs consisted of the magnetization of the cells for targeting its permanence in corpus cavernosum by applying a magnetic field. For this purpose they used superparamagnetic iron oxide nanoparticles (SPIONs) which are conventional magnetic resonance imaging contrast agents. They evaluated the effects of ADSCs containing SPIONs on improving erectile function in rats with streptozotocin-induced (type 1) diabetes when using an external magnetic field.

ADSCs obtained from rat paratesticular fat were cultured in medium containing SPIONs that were internalized by the cells as confirmed by Prussian blue staining. SPION containing ADSCs were intracavernosally injected to 8-weeks diabetic rats. A magnet was placed or not (controls) under the injection site for 30 min to expose the labeled ADSC to a magnetic field.

In vitro assays demonstrated the ability of ADSCs to internalize SPIONs and the capacity of attraction to a magnetic field. Nevertheless, SPION-ADSCs behaved similarly to ADSCs without labeling with respect to their viability and proliferative capacity. Animal studies demonstrated that magnet application increased the number of labeled ADSCs in corpus cavernosum 4 weeks after injection, although differentiation of these cells into smooth muscle or endothelial cells was not produced. However, functional recovery of erectile responses was superior after magnet application. This functional advantage was associated with greater augmentation of endothelial and smooth muscle content and increased VEGF expression in corpus cavernosum of diabetic rats.

These results suggest that magnetic field application to injected SPION-ADSCs allowed for more effectively remaining in the corpus cavernosum and then increasing their ability to influence cavernosal structure and function.

Therapeutic effects of adipose-derived stem cells-based microtissues on erectile dysfunction in streptozotocin-induced diabetic rats

Zhou F, Hui Y, Xin H, Xu YD, Lei HE, Yang BC, Guan RL, Li M, Hou JQ, Xin ZC.

Asian J Androl 2016, doi: 10.4103/1008-682X.182817 [Epub ahead of print]

The study by Zhou and collaborators used the same rat model of type 1 diabetes, including diabetes duration before treatment administration (8-weeks) and period of evaluation (4-weeks). Moreover, they also utilized ADSCs isolated from paratesticular fat as the cell therapy effectors. The difference lies in the strategy for improving ADSC efficacy in reversing diabetic ED. They compared the ability of intracavernosal injection of ADSC-based microtissues (MT) to improve erectile function in diabetic rats to that of intracavernosal injected ADSCs. This approach is based in previous reports showing enhanced therapeutic potential of stem cells cultured as spheroids and improved erectile function in rats undergoing cavernous nerve injury.

MTs were obtained by culturing ADSCs in hanging drops. Cells growing in hanging drops aggregate and forms spheroid MTs that decrease in size and gain in regular shape along time (up to 120 h). These MTs maintain the in vitro potential for multipotency as the ADSCs while displaying increased production of several growth factors (VEGF, NGF, TSG-6) and reduced expression of the inflammatory factor NF- κ B. After intracavernosal injection to diabetic rats, MT remain in corpus cavernosum for a longer time than ADSCs and produce a superior recovery of erectile responses 4-weeks after injection in diabetic rats when compared to ADSCs. This functional improvement was accompanied by increased expression of endothelial and smooth muscle, and nitrergic nerve markers in corpus cavernosum of diabetic rats as well as augmented expression of VEGF and NGF. In contrast, MTs caused a greater reduction than ADSCs in cavernosal expression of NF- κ B.

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These two articles evaluated different strategies for augmenting the efficacy of cell therapy for recovering erectile function in diabetic ED, both displaying advantageous effects of their respective approaches. Despite their differences, both methods coincide in producing an increase in the time the stem cells remain in the corpus cavernosum. This would allow the injected cells to exert a more efficacious paracrine effect on cavernosal tissue that enhances functional recovery. In fact, both studies reinforce the hypothesis that differentiation of stem cells into target tissues (endothelium/smooth muscle) little accounts for the restorative effects of cell therapy, suggesting that promotion of growth factors production and anti-inflammatory actions by stem cells are the key mechanisms driving therapeutic effects.

Cavernosal physiology – Hydrogen sulfide and NO

Hydrogen sulfide compensates nitric oxide deficiency in murine corpus cavernosum

Yetik-Anacak G, Dikmen A, Coletta C, Mitidieri E, Dereli M, Donnarumma E, d'Emmanuele di Villa Bianca R. Pharmacol Res 2016, 113: 38-43.

In the last years, accumulating evidence points to hydrogen sulfide (H₂S) not only as a pharmacological target for erectile dysfunction but also as a possible regulator of cavernosal physiology. In this sense, H₂S is endogenously synthesized through the activity of the enzymes cystathionine γ -lyase (CSE), cystathionine β -synthase (CBS) and 3-mercaptopyruvate sulphurtransferase (3-MPST) using L-cysteine as the main substrate for H₂S

production. Either exogenous addition of H₂S donor (NaHS) or stimulation of endogenous production with L-cysteine causes corpus cavernosum relaxation. Although the view of L-cysteine/H₂S pathway as exactly analogous to L-arginine/NO pathway is probably incorrect, the existence of a cross-talk between both pathways has been proposed based on several evidences. However, these evidences are focused on the influence of H₂S on NO pathway. In contrast, the aim of the study by Yetik-Anacak and collaborators was to analyze the influence of NO pathway modulation on L-cysteine/H₂S pathway, hypothesizing that this last signaling pathway could compensate NO deficiency.

They evaluated the effects of NO deficiency on L-cysteine/H₂S-mediated relaxation, H₂S



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generation and H₂S-synthesizing enzymes expression in mouse corpus cavernosum. NO deficiency was pharmacologically induced with the exposure to the NO synthase (NOS) inhibitor N ω -Nitro-L-arginine (L-NNA) or genetically induced by evaluating mice with deletion of the gene for endothelial NOS (eNOS).

Although the inhibition of NO production with L-NAME did not modify relaxations caused by exogenous addition of the H₂S donor, NaHS, NOS inhibition produced a significant enhancement of L-cysteine-induced relaxations in mouse corpus cavernosum. This suggests that under NO deficiency L-cysteine/H₂S-mediated relaxations are facilitated. In this sense, knockdown of eNOS gene results in increased generation of H₂S in corpus cavernosum tissue in response to L-cysteine addition. This increased H₂S production is also driven by NOS inhibition in wild type mice. The enhancement of H₂S generation by NOS inhibition is lost in cavernosal tissue from mice lacking CSE gene, suggesting that this H₂S synthesizing enzyme is essential for the potentiation of L-cysteine/H₂S pathway caused by NO deficiency. In fact, NOS inhibition in CSE knockout mice results in reduced H₂S production. eNOS deletion in mice was also associated to increased expression of H₂S synthesizing enzymes CSE and 3-MPST in corpus cavernosum while the expression of the other H₂S producing enzyme, CBS, decreased.

The study by Yetik-Anacak and collaborators shows that NO deficiency augments endogenous H₂S generation in murine cavernosal tissue probably by increasing CSE and 3-MPT expression in this tissue. In this sense, increased expression of these H₂S synthesizing enzymes in different tissues has been detected in situations associated with reduced NO availability such as acute oxidative stress, diabetes,

and atherosclerosis. Thus, the authors propose that L-cysteine/H₂S pathway compensates impaired relaxation of cavernosal tissue in the absence of NO. This phenomenon is related to increased endogenous H₂S formation through up-regulation of H₂S synthesizing enzymes CSE and 3-MPST.

Although this sense in the cross-talk between NO and H₂S pathways should be confirmed in vivo and in human tissue, these results together with accumulating evidence delineate a complex interaction between the different gasotransmitters regulating vascular and cavernosal tone. The lack of evaluation of downstream inhibitors of NO pathway did not allow the confirmation of a protein kinase G-dependent phosphorylation of CSE that causes its inactivation as an additional mechanism for the reported effects of NO deficiency on H₂S pathway, as reported for H₂S-mediated oxygen sensing. In any case, this study represents an additional evidence proposing the H₂S pathway as a potential therapeutic target for ED management.

Female Sexual Dysfunction – eNOS and PDE5.

Expressions of vaginal endothelial nitric oxide synthase and phosphodiesterase 5 in female sexual dysfunction: A pilot study
Cho KJ, Lee KS, Choo MS, Seo JT, Kim JH, Choi JB, Oh SJ, Kim JC. Int Urogynecol J 2016, [Epub ahead of print].

Expressions of endothelial NO synthase (eNOS) and phosphodiesterase type 5 (PDE5) as well as of other elements of the NO/cGMP pathway have been reported in human vagina some time ago. However, the influence of sexual function status on the expression of these enzymes is unknown. Cho and collaborators compared expression of eNOS and PDE5 in

vaginas from women with preserved sexual function to that observed in vaginas from women manifesting sexual dysfunction.

Vaginas were obtained from women scheduled to undergo surgery for stress urinary incontinence. Subjects were sexually active premenopausal women with 40 or more years of age. Female sexual dysfunction was defined as having a score in the Female Sexual Function Index (FSFI) below 18 and less than 3 in arousal domain (n=10). Controls had FSFI scores ≥ 26 and individual domain scores ≥ 3 (n=10). Immunofluorescence and Western blot methodologies were used for analyzing eNOS and PDE5 expressions in vaginal tissues.

PDE5 and eNOS were immunolocalized in vaginal epithelium. Quantification of expression assays revealed significantly decreased expression of both enzymes in vaginal tissues from women with sexual dysfunction. Based on these results, authors claim a pathophysiological role for eNOS and PDE5 in female sexual dysfunction. It should be considered that this article reports just an associative relationship between eNOS and PDE5 expression and sexual dysfunction in a limited number of women. Although these results are in agreement with reported association of low vaginal eNOS expression with the presence of type 2 diabetes in women, the assumption of a causal relationship requires more evidence. In this sense, modulation of NO/cGMP pathway with PDE5 inhibitors has generated contradictory clinical results. On the other hand, it should be noted that eNOS and PDE5 would play antagonistic roles in NO/cGMP pathway. However, a marked reduction in PDE5 expression in genital structures could partly explain a lack of positive effects by PDE5 inhibition, further evidence is required for establishing this pathophysiological scenario.

Have you read? Best of the Best: Clinical

by Nicola Mondaini



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Erectile Function

Lindau ST, Sexual activity and function in the year after an acute myocardial infarction among younger women and men in the United States and Spain. JAMA Cardiol. 2016 Oct 1;1(7):754-764.

Most younger adults who experience an acute myocardial infarction (AMI) are sexually active before the AMI, but little is known about sexual activity or sexual function after the event. To describe patterns of sexual activity and function and identify indicators of the probability of loss of sexual activity in the year after AMI. Data from the prospective, multicenter, longitudinal variation in recovery: Role of gender on outcomes of young AMI patients study (conducted from August 21, 2008, to January 5, 2012) were assessed at baseline, 1 month, and 1 year. Participants were from US (n = 103) and Spanish (n = 24) hospitals and completed baseline and all follow-up interviews. Data analysis for the present study was conducted from October 15, 2014, to June 6, 2016. Characteristics associated with loss of sexual activity were assessed using multinomial logistic regression analyses. **MAIN OUTCOMES AND MEASURES:** Loss of sexual activity after AMI.

Of the 2802 patients included in the analysis, 1889 were women (67.4%); median (25th-75th percentile) age was 49 (44-52) years (range, 18-55 years). At all time points, 637 (40.4%) of women and 437 (54.9%) of men were sexually active. Among people who were active at baseline, men were more likely than women to have resumed sexual activity by 1 month (448 [63.9%] vs 661 [54.5%]; $P < .001$) and by 1 year

(662 [94.4%] vs 1107 [91.3%]; $P = .01$) after AMI. Among people who were sexually active before and after AMI, women were less likely than men to report no sexual function problems in the year after the event (466 [40.3%] vs 382 [54.8%]; $P < .01$). In addition, more women than men (211 [41.9%] vs 107 [30.5%]; $P < .01$) with no baseline sexual problems developed one or more incident problems in the year after the AMI. At one year, the most prevalent sexual problems were lack of interest (487 [39.6%]) and trouble lubricating (273 [22.3%]) among women and erectile difficulties (156 [21.7%]) and lack of interest (137 [18.8%]) among men. Those who had not communicated with a physician about sex in the first month after AMI were more likely to delay resuming sex (adjusted odds ratio [AOR], 1.51; 95% CI, 1.11-2.05; $P = .008$). Higher stress levels (AOR, 1.36; 95% CI, 1.01-1.83) and having diabetes (AOR, 1.90; 95% CI, 1.15-3.13) were significant indicators of the probability of loss of sexual activity in the year after the AMI. Impaired sexual activity and incident sexual function problems were prevalent and more common among young women than men in the year after AMI. Attention to modifiable risk factors and physician counseling may improve outcomes.

El NAA MM et al: Sildenafil potentiates the antitumor activity of cisplatin by induction of apoptosis and inhibition of proliferation and angiogenesis. Drug Des Devel Ther. 2016 Nov 16;10:3661-3672.

Sildenafil is the first phosphodiesterase-5 inhibitor used for the treatment of erectile dysfunction. However, recent studies have been suggesting an antitumor effect of sildenafil. The current study assessed the aforementioned activity of sildenafil in vivo and in vitro in solid-tumor-bearing mice and in a human cell line MCF-7, respectively. Moreover, we investigated the impact of sildenafil on cisplatin antitumor activity. The solid tumor was induced by inoculation of Ehrlich ascites car-

cinoma cells in female mice. The tumor-bearing mice were assigned randomly to control (saline), sildenafil (sildenafil 5 mg/kg/d, PO daily for 15 days), cisplatin (cisplatin 7.5 mg/kg, IP once on the 12th day of Ehrlich ascites carcinoma inoculation), and combination therapy (cisplatin and sildenafil) groups. The tumor volume was measured at the end of the treatment period along with the following parameters: Angiogenin, vascular endothelial growth factor, tumor necrosis factor- α , Ki-67, caspase-3, DNA-flow cytometry analysis, and histopathological examination. The study results showed that sildenafil has significantly decreased the tumor volume by 30.4%, angiogenin and tumor necrosis factor- α contents, as well as vascular endothelial growth factor expression. Additionally, caspase-3 level significantly increased with sildenafil treatment, whereas Ki-67 expression failed to show any significant changes. Furthermore, the cell cycle analysis revealed that sildenafil was capable of improving the category of tumor activity from moderate to low proliferative. Sildenafil induced necrosis in the tumor. Moreover, the drug of interest showed cytotoxic activity against MCF-7 in vitro as well as potentiated cisplatin antitumor activity in vivo and in vitro. These findings shed light on the antitumor activity of sildenafil and its possible impact on potentiating the antitumor effect of conventional chemotherapeutic agents such as cisplatin. These effects might be related to antiangiogenic, antiproliferative, and apoptotic activities of sildenafil.

Penile Surgery

Pescatori E.: INSIST-ED: Italian Society of Andrology registry on penile prosthesis surgery. First data analysis. Arch Ital Urol Androl. 2016 Jul 4;88(2):122-7.

The Italian Society of Andrology, i.e. "Società Italiana di Andrologia" (S.I.A.), launched on December 2014 a prospective, multicenter, monitored and internal review board approved registry for penile implants, the "INSIST-ED"

Have you read? Best of the Best: Clinical

(Italian Nationwide Systematic Inventarisation of Surgical Treatment for ED) Registry. Purpose of this first report is to present a baseline data analysis of the characteristics of penile implant surgery in Italy.

The INSIST-ED Registry is open to all surgeons implanting penile prostheses (all brands, all models) in Italy, providing anonymous patient, device, surgical procedure, outcome, follow-up data, for both first and revision surgeries. A Registry project Board overviews all the steps of the project, and a Registry Monitor interacts with the Registry implanting surgeons.

As by April 8, 2016, 31 implanting surgeons actively joined the Registry, entering 367 surgical procedures in its database, that comprise: 310 first implants, 43 prosthesis substitutions, 14 device explants without substitution. Implanted devices account for: 288 three-component devices (81,3%), 20 two-component devices (5,4%), 45 non-hydraulic devices (12,3%). Leading primary ED etiologies in first implant surgeries resulted: Former radical pelvic surgery in 111 cases (35,8%), Peyronie's disease in 66 cases (21,3%), diabetes in 39 cases (12,6%). Two intraoperative complications have been recorded. Main reasons for 57 revision surgeries were: device failure (52,6%), erosion (19,3%), infection (12,3%), patient dissatisfaction (10,5%). Surgical settings for patients undergoing a first penile implant were: Public hospitals in 251 cases (81%), private environments in 59 cases (19%).

The INSIST-ED Registry represents the first European experience of penile prosthesis Registry. This baseline data analysis shows that: Three-pieces inflatable prosthesis is the most implanted device, leading etiology of erectile dysfunction (ED) in patient receiving a prosthesis is former radical pelvic surgery, primary reason for revision surgery is device failure, primary settings for first penile implant surgery are public hospitals. Evaluation of penile implant impact on recipients quality of life is presently ongoing.

Fertility

Kordzadeh A: Male infertility following inguinal hernia repair: A systematic review and pooled analysis. *Hernia*. 2016 Dec 3.

The aim of this systematic review is to establish the clinical impact of open (mesh and/or without mesh) and laparoscopic hernia repair (transabdominal pre-peritoneal (TAP) and/or totally extra-peritoneal (TEP)) on male fertility. The incidence of male infertility following various types of inguinal hernia repair is currently unknown. The lack of high-quality evidence has led to various speculations, suggestions and reliance on anecdotal experience in the clinical practice.

An electronic search of the literature in Medline, Scopus, Embase and Cochrane library from 1966 to October 2015 according to PRISMA checklist was conducted. Quality assessment of articles was conducted using the Oxford Critical Appraisal Skills Programme (CASP) and their recommendation for practice was examined through National Institute for Health and Care Excellence (NICE). This resulted in ten studies ($n = 10$), comprising 35,740 patients. Sperm motility could be affected following any type and/or technique of inguinal hernia repair but this is limited to the immediate postoperative period (≤ 48 h). Obstructive azoospermia was noted in 0.03% of open and 2.5% of bilateral laparoscopic (TAP) hernia repair with mesh. Male infertility was detected in 0.8% of the open hernia repair (mesh) with no correlation to the type of mesh (lightweight vs. heavyweight).

Inguinal hernia repair without mesh has no impact on male fertility and obstructive azoospermia. However, the use of mesh in bilateral open and/or laparoscopic repair may require the inclusion of male infertility as the part of informed consent in individuals that have not completed their family or currently under investigations.

Female Sexual Dysfunction

Barbara G: When love hurts. A systematic review on the effects of endometriosis surgical and pharmacological treatments on female sexual functioning. *Acta Obstet Gynecol Scand*. 2016 Sep 30.

Endometriosis is associated with an increased risk of dyspareunia, therefore this chronic gynaecologic disease should be considered as a major cause of sexual dysfunctions. The aims of this study were to review the literature on the effects of endometriosis surgical and pharmacological treatments on female sexual functioning, and to provide suggestions for future treatment strategies. We followed the PRISMA guidelines to conduct this systematic review, which involved an electronic database search of studies on the association between endometriosis and sexuality published between 2000 and 2016. As a result of the screening process, 22 studies were included in this systematic review. The 22 studies included were divided in 2 categories: 1) surgical intervention studies ($n = 17$), examining postoperative sexual outcomes of surgery for endometriosis; 2) pharmacological intervention studies ($n = 5$), evaluating the effects of pharmacological endometriosis treatments on sexual functioning. The studies considered showed that overall surgical and pharmacological interventions for endometriosis can lead to medium-/long-term improvement, but not necessarily to a definitive resolution of female sexual dysfunctions due to endometriosis. Sexual functioning is a multidimensional phenomenon and the ideal treatment for endometriosis related sexual dysfunctions should be conducted by a multidisciplinary team that involves not only gynaecologists, but also sexologists and psychologists/psychotherapists. Improving global sexual functioning, and not just reducing pain at intercourse, should be considered as a major clinical goal of endometriosis treatment.

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Education Corner

by Pedro Vendeira



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Education is one of the main purposes of ESSM. The main objective of the Education Committee is to promote research and exchange of knowledge about the clinical entity of sexual dysfunction throughout Europe, to establish and support the highest standards of ethics in clinical practice, education, and research in the field of sexual dysfunction and to provide education to clinicians who had limited or no experience in the field, as well as continuing education to those involved in the management of sexual dysfunctions.

EFS & ESSM Certified Psycho-Sexologist (ECPS) and Fellow of the European Board of Sexual Medicine (FECSM)

In cooperation with the European Federation of Sexology (EFS) and the Multidisciplinary Joint Committee on Sexual Medicine (MJCSM), ESSM provides two qualification examinations on a regular basis. The FECSM – Fellow of the European Board of Sexual Medicine – and the according exam to be passed is under the auspices of the Multidisciplinary Joint Committee on Sexual Medicine (MJCSM) by UEMS since 2012. Since 2014 also the European Certification Exam

for Psychologists in collaboration with EFS has taken place. Prior to both exams, three-days' Preparation Courses were given by well-known specialists in the field. Last year at the time of our Annual Congress in Madrid we had another examination and we are proud to announce that we are now 484 successful FECSM since 2012 and 79 successful ECPS since 2014.

SAVE THE DATE!

The next examination will take place in Lisbon, Portugal, prior to the ISSM/ESSM meeting **end of February 2018**. Go to www.essm.org for further information. As a rule the recommended consulting books are the **ESSM Manual of Sexual Medicine and The EFS and ESSM Syllabus of Clinical Sexology** written by the Educational Committee of the ESSM and the EFS and available for all members.

2016 ESSM School of Medicine

As in previous years, the 2016 edition of the ESSM School was held in Budapest. Participants entered this "hard" 10 days residential course, that covered a wide range of Sexual Medicine and Clinical Sexology topics and provides the essential background learning from which clinical experience and research can be developed. All sessions during the program were conducted in English language and participative learning techniques for skill development as well as didactic teaching were used. Last year we had 47 participants from

30 different countries in all 5 continents, and the evaluation results do show that quality rules in this program. We thank the Faculty for their effort and we are now thinking on the 2017 edition having in mind that we already have people waiting... that couldn't find a spot in 2016. We'll work on that enthusiastically!!!

Stay Tune: The One Day Pre Congress ESSM UPDATE 2017

For the first time ESSM proudly announces the ESSM UPDATE 2017. This event is intended to support some gaps in the field of Sexual Medicine Education, namely what is not written in the books. That's why we call it "From Knowledge to Bedside Practice". This is the right place where you might be able to find what you always wanted to learn, but didn't know where to look for...

For further information go to
www.essm-update2017.org

And don't forget to take the step and move into our pearls of knowledge – The ESSM Annual Congress Workshops – organized by the Educational Committee at the time of the Annual Congress, with a full description on program and Congress APP and providing hands-out on the Website (protected).

See you in Nice...

Pedro Vendeira

Chairman ESSM Educational Committee

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Education Corner

High flow priapism secondary to arteriocavernosal fistula caused by penile prosthesis implantation mimicking autoinflation.

Fes Ascanio EA, Garaffa G, Ralph DJ

Institute of Urology, University College London Hospitals

Introduction and Objectives

To report a case of high flow priapism secondary to arteriocavernosal fistula caused by inflatable penile prosthesis implantation. The tumescence caused by priapism was simulating autoinflation.

Patients and Methods

A 55 year old gentleman underwent implantation of inflatable penile prosthesis for the management of end stage erectile dysfunction secondary to non-nerve-sparing radical robotic prostatectomy in March 2013. Surgery was uneventful, with easy dilatation of the corpora, and the patient was discharged in postoperative day one, once the implant had been completely deflated.

At 3 weeks postoperative follow-up, a persistent tender tumescence of the corpora was present. All attempts of resolving the tumescence by trying to fully deflate the device were unsuccessful due to pain and therefore the patient was offered revision and exchange of the implant after 3 months.

Intraoperatively, although the device was found to be functioning properly, all the component of the implant were removed. Surgery was complicated by profuse bleeding from the right crura, which became apparent after the removal of the right cylinder. Therefore, implantation of a 3-pieces-inflatable device was abandoned in favour of a malleable one, in order to provide a better haemostasis.

Results

► A Doppler ultrasound of the penis, to investigate the nature of the bleeding, identified the presence of an A-V fistula and high peak systolic velocity in keeping with high-flow priapism.

- Selective angiogram with superselective embolization of the left pudendal artery was successfully performed, with complete closure of the fistula.
- The patient has therefore undergone a successful elective exchange to a 3-pieces inflatable prosthesis.

Conclusions

This case shows that, although rare, high-flow priapism should be excluded in patients with persistent penile tumescence following penile prosthesis implantation.

If high-flow priapism is suspected, this has to be confirmed by Doppler ultrasound and pudendal angiogram before offering the patient superselective embolization of the A-V fistula.

Infertility and erectile dysfunction as clinical signs of an undiagnosed 30-year old Klinefelter patient

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Intro: A 30 years old male, was referred to our Unit suffering from infertility, for at least 18 months, due to azoospermia. Patient reported normal libido but complained about moderate Erectile Dysfunction (ED), which started only after the initiation of the effort to conceive a child. He had no prior medical history of cryptorchidism, viral infection or surgery. He was a non smoker, non drug user and without any professional risks. No family history of recurrent spontaneous abortions, malformations or mental retardation was reported.

Clinical Presentation: Patient's secondary sex characteristics were almost in the normal except from the chest hair distribution and abdominal fat distribution. Sperm and urine cultures were sterile. Patient's hormone profile revealed low serum testosterone 148 ng/dl, SHBG 35 nmol/L, high FSH (18.1 mIU/ml) and LH (15.3 mIU/ml), slightly decreased inhibin-b level and normal PRL and TSH.

A Doppler ultrasound of the scrotum revealed bilateral low testicular volume and high RI. Afterwards a karyotype blood exam was performed in order to exclude genetic causes of azoospermia. Patient proved to be an undiagnosed 47 XXY with Klinefelter mosaicism. For the evaluation of ED, a penile color Doppler ultrasound revealed DSV 95 cm/sec and RI 0.9 while an IIEF-5 questionnaire resulted in 19 score. Cardiological and endocrinological evaluation was performed along with psychological profile assessment.

Treatment: After an assiduous briefing, patient underwent a bilateral microTESE which was successful and resulted in retrieval of viable spermatozoa in order the couple to proceed with an ICSI. Since arteriogenic compound was ruled out according to PCDU, ED was attributed to underlying hypogonadism along with psychological factors (considering the acute onset and normal night erections). Daily Tadalafil 5 mg was prescribed to the patient along with sessions with a sex therapist. Cardiological diagnostic work out showed no further pathology. In accordance with endocrinologists, testosterone replacement treatment was not offered until fertility issues have been addressed, while lifestyle modifications have been suggested due to signs of metabolic syndrome (increased LDL, abdominal fat distribution).

Discussion: Klinefelter's syndrome is the most common sex chromosome abnormality. Approximately 60–75% remain undiagnosed and only 10–25% of the cases are diagnosed in childhood or adolescence. The phenotype varies and testosterone levels may be normal or low. Germ cell presence and sperm production are variable and spermatozoa can be recovered in about 30% of the cases via a micro-TESE. Due to the significant increase of sex chromosomal and autosomal abnormalities in the embryos of Klinefelter's patients, PGD or amniocentesis analysis should be considered. Androgen replacement therapy should be started only after fertility issues have been addressed and when testosterone level is in the range of hypoandro-

genism. Testosterone replacement therapy may present several benefits regarding body composition, bone mineralization, metabolic control, psychological and sexual parameters bearing in mind that infertility (or active desire to have children) represents a contradiction against TRT. Finally, weight reduction, lifestyle modification and good treatment of comorbidities are quite important apart from just TRT.

Conclusion: Infertility, along with ED, may represent the only clinical signs of undiagnosed patients suffering from Klinefelter's syndrome.

Integrated therapy of erectile and ejaculatory dysfunction in a patient with multiple sclerosis

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Clinical Presentation

- ▶ 26-year old male self-referred for the treatment of erectile and orgasmic/ejaculatory difficulties
- ▶ Stable relationship since 6 years, married, live together. No relevant relationship concerns
- ▶ Previously consulted by urologist, treated since 1 year with sildenafil citrate 50–100mg prn – can achieve 3rd grade erection with successful vaginal penetration but unable to reach orgasm/ejaculation
- ▶ Both patient and his wife desire pregnancy

Medical History

- ▶ Appendectomy in early childhood
- ▶ Multiple sclerosis diagnosed 7 years ago – optic neuritis, dizziness
- ▶ Treated with interferone β -1b (250mcg s.c. EOD) since 6 years with no relapses
- ▶ MRI scan – old MS plaques within spinal cord (especially sacro-lumbar part), brainstem and cerebellum
- ▶ Ultrasound of prostate and testicles – no pathology

Sexual History

- ▶ Heterosexual
- ▶ No sexual education at home, poor emotional communication
- ▶ Masturbation: As teenager, infrequently, with guilt feelings (religious inhibitions) but no erectile or ejaculatory dysfunction
- ▶ First partnered sexual experience after the onset of MS, penetration impossible due to ED
- ▶ Wife is his second partner
- ▶ He could achieve 2nd grade erections during manual stimulation
- ▶ After 5 years of unsuccessful penetration attempts decided to visit urologist → partial improvement with sildenafil treatment, full penetration became possible but no orgasm/ejaculation, reported only occasional, slight (ejaculate?) leakage during sexual stimulation

Clinical Interview/Examination

- ▶ Body appearance normal, no abnormalities in general and genital examination
- ▶ EDSS=2 (cerebellar)

- ▶ No depressive symptoms but generally upset about the situation, performance anxiety
- ▶ Ashamed, poor sexual terminology/communication
- ▶ Perceives wife as very attractive, feels spontaneous desire, thoughts, fantasies
- ▶ Good non-sexual relationship
- ▶ Wife: Supporting and patient, no sexual dysfunction
- ▶ **Diagnosis:** Erectile dysfunction, orgasmic disorder/retarded/absent ejaculation

Laboratory Testing

- ▶ Blood tests
- ▶ No abnormalities in morphology, biochemistry (lipid profile, AST, ALT, fasting glucose, creatinine, albumin), tPSA 0.428 ng/ml
- ▶ Hormonal levels within normal range
- ▶ Total testosterone 4.66-5.83 ng/ml, estradiol 10.35-52.04 pg/ml, LH 5.28 mIU/ml, prolactin 245.1 uIU/ml, TSH 1.95 mIU/L, SHBG 25.33 nmol/l
- ▶ Neurophysiological testing
- ▶ Bulbocavernous reflex unattainable with maximal stimulation (rectangular 100mA, 0.2msec to n.dorsalis, annular electrode)

Treatment and Outcome

- ▶ Tadalafil 5 mg q.d. → 4th grade erections were achieved but no success with climax
- ▶ Psychosexual therapy (9 sessions)
- ▶ 1–2: Education, relaxation techniques, mindfulness, sensate focus (non-genital)
- ▶ 3–4: Continuation, sensate focus (genital, non-intercourse) → less performance anxiety

World Meeting on Sexual Medicine



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European Society for Sexual Medicine



21st World Meeting of the
International Society for Sexual Medicine

February 28 - March 3, 2018
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Education Corner

- ▶ 5–7: Sensate focus (full intercourse) → orgasm/ejaculation in half of attempts, increased satisfaction
- ▶ 8–9: Continuation, inclusion of sexual fantasies and scenarios → orgasm/ejaculation in nearly all attempts
- ▶ 2 months later pregnancy was achieved
- ▶ Tadalafil discontinuation failed (ED), but reduction to 2.5 mg q.d. successful (full-erection maintained)

Discussion

This case study shows a common interplay of somatic (here: neurological) and psychological factors. The latter could easily be overlooked especially when neurophysiological testing suggested severe abnormalities supported by the localization of spinal cord lesions. Previous treatment based solely on PDE-5 inhibitor was only partially effective in restoring erection. Change to continuous tadalafil administration was superior. However, the implementation of psychosexual therapy was the pivotal decision as it resulted in a complete outcome including orgasm/ejaculation, further improvement of erectile function (PDE-5 inhibitor dose was finally reduced) and most importantly increase of sexual satisfaction of both partners and successful natural fertilization. The most important aspects of psychosexual therapy included reduction of performance anxiety and task-orientation, focus on pleasure, body mapping and erogenous zones stimulation intensification.

Conclusion

Clinicians should not overlook psychosexual issues even when organic pathology seems evident. Psychosexual therapy should be routinely considered, especially when pharmacotherapy fails or is not fully effective.

45 year-old woman referred due to low sexual desire and altered orgasms at the background of dyspareunia, which has gained ground for the last 2 years

Romashchenko O, Kyiv, Ukraine

Patient information

She has been working as a head of the department in a bank and is satisfied with her work. She has been in a second marriage for 15 years. She has been smoking for 30 years, but lately has limited the consumption of cigarettes to 3–4 per day. She goes to gym 5 days per week with one session lasting 40–45 minutes long, and has a tendency to put on weight.

Clinical Presentation

Psychological health and previous treatment: No previous treatment. She describes herself as emotionally stable, loving wife and mother.

General medical health: Menopause – 2.5 years after stress (mother's death). IMT – 25.2 kg/m². For the last year the increase of arterial pressure to 130/90 mm have been marked (she was previously inclined to hypotension), with hot flushes up to 5–7 times per day, superficial sleep.

Obstetric history and subjective complaints:

Multipara, normal pregnancies and vaginal birth. In 3 years after childbirth she went through artificial abortion, complicated with intensification of chronic inflammatory disease of organs of small pelvis. An anti-inflammatory therapy was carried out.

Sexual debut: At the age of 18. Previous sexual experience: No sexual assaults/abuse, heterosex, previously stable sexual relationships with few partners prior to the first marriage (during 2 years) and to the second marriage.

Sexual complaints: Before the early menopause there were no sexual complaints. Since the menopause the patient has not been able to achieve the same level of orgasm as pre-op. She has experienced low desire situationally. Her partner complained about the patient's inability of achieving the same level of orgasm as prior to the menopause. She has complained of slight and deep dyspareunia (by the principle of 'vicious circle').

Pelvic examination and diagnostics: No abnormalities, besides hypertonic pelvic muscles. The vaginal tissue looks atrophic. Reduction of estrogen level in blood (E_2 – 40 pg/ml). Colposcopy: Thinning of mucous membrane of vagina, petechial hemorrhage, translucent capillaries. pH of vaginal contents – 6.8. Reduction of blood flow level in clitoris vessels before and after sexual stimulation when assessing the blood flow speed with the Doppler method. Rise of susceptibility threshold of first-order erogenous zones when assessing their tactile reaction with the vibro test.

Treatment

Sexual counseling/psychotherapy. Step-by-step introduction to sensate focus exercises with and without partner. Masturbation techniques with and without partner. System hormonal replacement therapy and topical estrogen.

Discussion

As the complaints the patient has addressed with have become stable for the last years, treatment has to be complex and take into account the general state and age changes of a woman, and psychological problems of spouses in a single context.

2 months after treatment: Improvement of the general state: sleep has normalized, lost 2 kg, normal weight/BMI. Lubrication restored, dyspareunia removed, sexual desire improved with the achievement of orgasm in most cases and couple's sexual comfort.

MEETINGS AND EVENTS CALENDAR 2017



Dr. Raul Vozmediano-Chicarro
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January

10th Joint conference of the UK Fertility Societies

Date: 5 – 7 January 2017
Location: Edinburgh International Conference Centre, Edinburgh, UK
Website: <http://www.fertilityconference.org/>

February

One Day Pre-Congress UPDATE 2017 in Sexual Medicine

Date: 1 February 2017
Location: Nice Acropolis, Nice, France
Website: www.essm-update2017.org

19th European Congress on Sexual Medicine

Date: 2 – 4 February 2017
Location: Nice, France
Website: <http://www.essm-congress.org/>

The Best of ASRM and ESHRE

Date: 23 – 25 February 2017
Location: Paris, France
Website: http://www.asrm.org/2017_Best_of_ASRM_ESHRE/

March

64th Annual Scientific Meeting Society for Reproductive Investigation

Date: 15 – 18 March 2017
Location: Orlando, Florida, USA
Website: <http://www.sri-online.org/>

65th Annual Meeting of the Pacific Coast Reproductive Society March

Date: 22 – 26 March 2017
Location: Indian Wells, California, USA
Website: <http://www.pcrsonline.org/EventReg>

PGDIS Congress Preimplantation Genetic Diagnosis International Society

Date: 26 – 29 March 2017
Location: Valencia, Spain
Website: <http://www.pgdis.org/>

Subfertility and Reproductive Endocrinology Course

Date: 27 – 30 March 2017
Location: RCOG, London, UK
Website: https://britishfertilitysociety.org.uk/?post_type=meeting&p=23167

April

ENDO 2017. The Endocrine Society

Date: 1 – 4 April 2017
Location: Orlando, Florida, USA
Website: <http://www.endocrine.org>

The XXIV North American Testis Workshop

Date: 19 – 22 April 2017
Location: Miami, Florida, USA
Website: <http://andrologysociety.org/meetings/asa-annual-meeting/future-meetings/event-details.aspx?id=ASA1704TW>

ASA 42nd Annual Conference

Date: 19 – 25 April 2017
Location: Miami, Florida, USA
Website: <http://andrologysociety.org>

May 2017

AACE 26th Annual Scientific and Clinical Congress

Date: 3 – 7 May 2017
Location: JW Marriott and the Austin Convention Center, Austin, Texas, USA
Website: <http://am.aace.com/>

11th International Congress of Andrology

Date: 6 – 9 May 2017
Location: Copenhagen, Denmark
Website: <http://www.ica2017.dk/>

Annual AUA Meeting 2017 (American Urological Association)

Date: 12 – 16 May 2017
Location: Boston, Massachusetts, USA
Website: <https://www.auanet.org/>

23rd Congress of the World Association for Sexual Health

Date: 14 – 18 May 2017
Location: Prague, Czech Republic
Website: <http://www.was2017.org/sd>

18 Congreso nacional de Andrología, medicina sexual y reproductiva (ASESA)

Date: 18 – 20 May 2017
Location: Cartagena, Murcia, Spain
Website: <http://www.asesacartagena2017.com/>

ECE2017 European Society of Endocrinology

Date: 20 – 23 May 2017
Location: Lisbon, Portugal
Website: <http://www.eese-hormones.org>

PAYMENT OF THE ESSM MEMBERSHIP FEE 2017

To be sent back to:

ESSM Secretariat
Via Ripamonti 129 – 20141 Milano, Italy
www.essm.org

Phone: +39 02–56601 625
Fax: +39 02–70048 577
email: admin@essm.org

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from January to December

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First Specialty: _____	Second Specialty: _____	

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- ☐ Full Member
☐ Associate Member

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2. _____

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2. _____

- ☐ Herewith confirms the payment of EUR 50,00 for the **ESSM membership** cost for the year 2017 by:
☐ Herewith confirms the payment of EUR 25,00 for the **ESSM membership FOR RESIDENTS IN TRAINING*** cost for the year 2017
☐ Herewith confirms the payment of EUR 160,00 for the **ESSM and ISSM membership** cost for the year 2017

* A letter of the Chairman of the Department is necessary.

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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.

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AIM Congress Srl – AIM Group – Via Ripamonti 129, 20141 Milano – C.a. Ms. Daniela Pajola

For your consent on data processing and communication as described in the above report:

Date _____	Signature _____
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For more information please visit www.essm.org



www.essm.org

Announcement for the next Congress

World Meeting on Sexual Medicine



20th Congress of the
European Society for Sexual Medicine



21st World Meeting of the
International Society for Sexual Medicine

February 28 - March 3, 2018
Lisbon, Portugal

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THE
DATE

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