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HIGHLIGHTS FROM THE EDITION

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Welcome Address

With the next 2018 ISSM/ESSM meeting just a few weeks away, sexual medicine is becoming increasingly of interest throughout Europe. The European Society of Sexual Medicine is very happy to welcome to Lisbon the greatest worldwide experts on sexual and reproductive functioning and we look forward to giving a voice to the hundreds of speakers who will disclose their latest research results!

In this issue of ESSM TODAY, we touch on just a few of the several topics in our discipline, but this is enough to further open our eyes and reawaken our thirst for knowledge, expanding our vision of what is today defined as sexual medicine and will be tomorrow or far into the future.

“Old” solved and unresolved questions are now accompanied by new ones: Is testosterone treatment advisable and safe? Will we ever be able to perform penile transplantations on a regular basis? What is the effect of PDE5 inhibitors on male fertility? Can we use the Platelet Rich Plasma of a given patient to heal his cavernous nerve injuries and restore erectile function?

In Lisbon many more physicians and psycho-sexologists will become FECSM and ECPS fellows. Starting now I would like to tell them that they are more than welcome as we at the European Society of Sexual Medicine need their brains and their brawn to win old therapeutic battles and challenge new ones.

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Dear ESSM members,

As you may already know, a novel society has been recently founded with the name of "Androgen Society". You may have been already contacted by the founders of this society to become members or to take part of the forthcoming congress in Lisbon. The Executive Committee of ESSM has discussed about this issue and I would like to illustrate you some of the major points, which prompted us to take an official position against this initiative:

1) the topic of this society largely overlaps with the area of interest of ESSM with a consequent fragmentation of the field of Sexual Medicine.

2) "Androgens" are already an important part of the program of our meetings and ESSM annual meetings represent one the best-qualified scientific event for this topic. The major experts of this field in Europe are ESSM members.

3) the "Androgen Society" raises also ethical issues about its relationship with pharmaceutical industry and consequently raises questions about its transparency.

After having taken into consideration the above points, we consider the role of "founding member" or "members at large" or "officers" of the new society incompatible with ESSM officers position. Moreover, I strongly recommend not taking active part as "speaker" or "chairperson" of the forthcoming congresses of this Society.

I am confident that all ESSM members will share our decision, because we can only confront the attempts to fragment our field if we act in unison.

On behalf of the EC

François Giuliano
ESSM President

Testosterone replacement treatment in USA: A short interview with Joseph Alukal

by Ferdinando Fusco (FF)

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ESSM TODAY briefly interviewed Joe Alukal about the current attitude of urologists in USA to prescribe testosterone replacement treatment in USA.

FF: Professor Alukal, what kind of cardiovascular test, if any, you consider important for a patient before starting a testosterone replacement therapy?
A cardiac risk assessment (exercise tolerance, prior cardiac history including stents, history of chest pain) can be taken easily by a urologist or an andrologist. Certainly a cardiologist can be involved if any of these questions are answered "yes". If the patient already has a cardiologist, simply discuss the decision to start testosterone with the cardiologist in question. Reassure them that this is not inherently dangerous from a cardiac standpoint; the patient simply needs to be monitored.

FF: In a large number of men, serum testosterone progressively declines with the age, inducing sexual dysfunction and other symptoms of hypogonadism. What is the current approach in USA for this "late-onset hypogonadism?"
There is real controversy regarding this condition; the FDA no longer considers "late onset hypogonadism" as an indication for testosterone replacement. Many patients continue this treatment regardless. It is important therefore to discuss risks with these patients.

FF: Prostate cancer is a contraindication to testosterone treatment. However, many hypogonadal men who should receive testosterone, although not affected with prostate cancer, might develop it during the treatment and testosterone therapy might be accused to have increased the risk. What is your opinion about the role of testosterone therapy on the risk of prostate cancer?
Both myself and many other urologists in our department and around the country do not believe that testosterone replacement in the hypogonadal male increases his risk of developing prostate cancer. That being said, a prospective study proving this would be ideal. This study does not yet exist, and will be difficult to perform because of the necessary patients and length of follow up required to determine this effect.

FF: Testosterone is available in many different formulations. Is there a best formulation in general or, at least, can we use objective criteria in selecting the best formulation for the single patient?
I do not believe any one formulation is better; there is simply a need to tailor treatment options to particular patients. For example, gel formulations are not ideal in men who have small children or are worried about transfer to their spouses. Cost is certainly a factor in the united states as well.

FF: How do you suggest to follow-up hypogonadal men after testosterone prescription?
Men should be monitored with a yearly digital rectal examination and physical exam, biannual PSA testing, and q3–4 month testosterone levels as well as complete blood count testing.

See application form on page 19.

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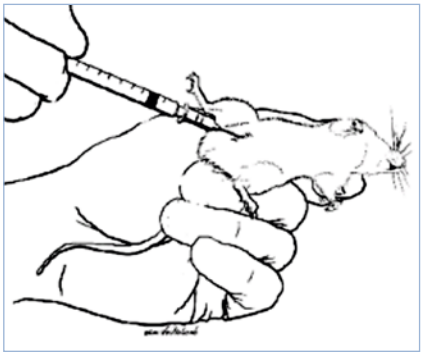
Platelet Rich Plasma (PRP) is prepared by centrifugation of the patient's own blood to remove red blood cells [1]. The plasma obtained is rich in platelets that contain various growth factors, such as platelet-derived growth factor (PDGF), transforming growth factor (TGF)-b, IGF-I and VEGF. When platelets are activated, they release those factors, which play important biological roles in various conditions [2]. During the last 15 years PRP has been used to encourage a brisk healing response across several specialties, in particular dentistry, orthopedics and dermatology. Basically, patient's blood is collected and centrifuged at varying speeds until it separates into 3 layers: Platelet Poor Plasma (PPP), PRP, and red blood cells. Usually 2 spins are used. The first spin ("Hard spin") separates the Platelet Poor Plasma (PPP) from the red fraction and platelet rich plasma (PRP). The second spin ("Soft spin") separates the red fraction from the PRP. The material with the highest specific gravity (PRP) will be deposited at the bottom of the tube. Immediately prior to application, a platelet activator/agonist (topical bovine thrombin and 10% calcium chloride) is added to activate the clotting cascade, producing a platelet gel. The whole process takes approximately 12 minutes and produces a platelet concentration of 3–5 x that of native plasma [3].

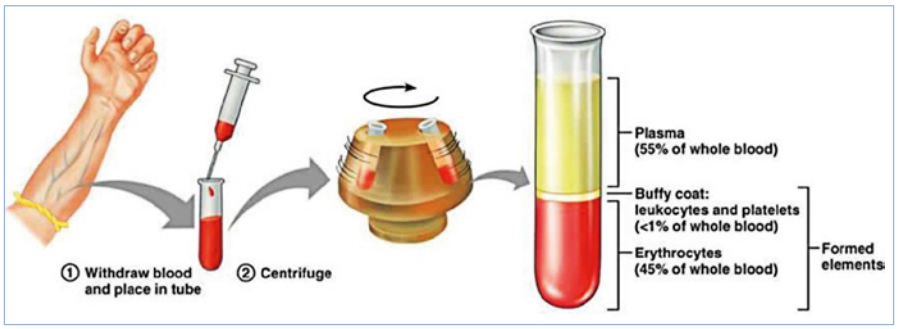
Growth factors are involved in key stages of wound healing and regenerative processes including chemotaxis, proliferation, differentiation, and angiogenesis [4]. An advantage of PRP over the use of single recombinant human growth factor delivery is the release of multiple growth factors and differentiation factors upon platelet activation [5]. The morphologic and molecular configuration of PRP was reported, it showed PRP is a fibrin framework over platelets that has the potential to support regenerative matrix [6]. In humans, PRP has been evaluated and used as a injective "drug" for several types of medical treatments, including chronic tendinitis,[7] osteoarthritis,[8] for bone repair and regeneration,[9] in oral surgery,[10] and in plastic surgery,[11]. Accumulating evidence indicates that neuroimmunophilin ligand and many growth factors, such as insulin growth factor-1 (IGF-1), brain-derived growth factor (BDNF) and vascular endothelial growth factor (VEGF) play a significant role in neural regeneration and up-regulation of neuronal nitric oxide synthase (nNOS), as well as in the recovery of erectile function after CN injury [12].

This evidence is the starter point for a speculative research in Uro-andrological field evaluating the use of PRP by corpus cavernosus (CC) injection in "patients" (rat models) undergone anatomic nerve-sparing Radical Prostatectomy which often cause incomplete or delayed recovery of erectile function. In many instances, the cavernous nerves (CNs) may have been inadvertently damaged by manipulation during nerve-sparing prostatectomy.



The recovery of erectile function may depend on re-growth of nerves from the remaining neural tissue [12]. In two different studies Ding X-G et al. [12] and Wu YN et al. [13] evaluated different preparation of PRP in recovery of erectile function after bilateral cavernous nerve injury in a rat model. Despite differences of methods and quality of PRP (different production methods), both studies demonstrated that the injection into the corpus cavernosum facilitated recovery of erectile function.
Although the interesting premises, real RCTs are lacking and even in the sports medicine literature was not demonstrating any benefit. A Cochrane review that reviewed PRP therapy studies in musculoskeletal injuries, demonstrated no significant difference in treatments groups versus controls [14]. Another note that contribute to conceal a possible effectiveness of PRP is that there are no listings on www.clinicaltrials.gov for PRP and ED.

Things changes when we put the key words "PRP, erectile dysfunction" on Google. A research performed in October 2017 showed 133.000 results (147,000 for "Platelet Rich Plasma, erectile dysfunction"). The results were all about the effectiveness and safety of the procedure. A similar research on Google was performed by Lawrence

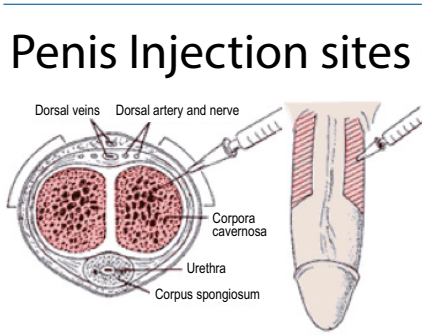


PRP (Platelet Enriched Plasma) and erectile dysfunction: How far along we are?

C. et al in 2015; they found that among the claims of websites marketing this treatment are included "bigger erections, improved sex life, improvement in climax/orgasm, increased sensitivity, increased libido" and "improved sensation even years after prostatectomy." Approximately 228 available providers are listed in the directory for the Priapus shot®, which is a trademark for the PRP injection process [15].

Nowadays, the rational data can't support the use of PRP, but the "real-life.andrology" provides this treatment as "decisively efficacious".

From the internet research was also found that physicians, propose to patients PRP injection procedures at cost between $1,500 and $3,000 cash per injection [15].



It is obvious that trials for the approval of PRP for the indication of ED treatment will take several years to complete, and thus, such treatment for ED in humans would not be submitted for FDA review for at least another 5 years. In the meantime, we wait with great anticipation the results of these studies. We as clinicians and scientists along with our international society and our regional affiliate societies must insist on the conduct of clinical trials and regulatory agency approval but, based on the apparent lack of toxicity in all the fields where PRP was applied, this treatment could, perhaps, be offered to selected patients, as long as the patients were widely informed with a specific informed consent that underline the lack of demonstrated efficacy and safety data in ED.

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Effects of PDE5 inhibitors on the male reproductive potential: A dinner conversation

by Fotios Dimitriadis, Athanasios Zachariou, Nikolaos Sofikitis

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AZ: Gentlemen, the restaurant is great, please relax, and let's have a nice dinner.

NS: Fotios, I see that your face looks skeptical and confused. Why? You do not like the wine?

FD: I have just finished the outpatient clinic. One of my idiopathic infertile patients asked me a difficult question which I receive several times every week: Are there any effective pharmaceutical agents for the therapeutical alleviation of oligoasthenoteratozoospermia?

NS: To the best of my knowledge there are fewer than five randomized, placebo-controlled trials evaluating the effects of pharmaceutical agents on the reproductive potential of infertile men.

FD: After 2009, the number of publications on the effects of PDE5 inhibitors on quantitative and qualitative sperm parameters has been dramatically increasing, isn't it interesting?

AZ: It is interesting but not unexplainable. Let us remember that several members of the families of phosphodiesterases are present both in the testis and in the epididymis.

FD: Do you mean that specific cellular subpopulations within either the testis or the epididymis are positive for distinct members of the phosphodiesterases' families?

NS: To the best of my knowledge, peritubular myoid cells are positive for PDE5 expression. Leidyg cells are positive for PDE11A, PDE4B, PDE5, PDE8A and PDE11. Sertoli cells are known to be positive for PDE1, PDE3 and PDE4 expression. Human epididymis is known to be positive for PDE3 and PDE5 expression. Vascular monocytes within the testis are positive for PDE11 and PDE5. Vas deferens is positive for PDE5. Prostate is positive for PDE5a, PDE11A4 and PDE11A1. It is logical to hypothesize that administration of inhibitors of PDE5 may affect testicular endocrine and exocrine function, epididymal function, prostatic secretory function and prostatic physiology. However it should be emphasized that PDE5 inhibitors may additionally inhibit to a smaller degree other phosphodiesterase families within the testis. For instance, PDE5 inhibitors additionally inhibit to a smaller degree PDE11, PDE4, PDE8, and PDE3. Therefore administration of PDE5 inhibitors may affect several cellular subpopulations within the male reproductive tract.

AZ: What about the subpopulations of haploid male gametes?

FD: Spermatids are positive for PDDE11, PDE4A, PDE4D, PDE1A, and PDE1C. Spermatozoa are positive for PDE1A, PDE3A, PDE4, PDE5, PDE6, and PDE10A.

AZ: And what about the subpopulations of diploid male gamete?

FD: Spermatogonia are positive for PDE11A, PDE1, and PDE2. Primary spermatocytes are positive for PDE11, PDE3, PDE4, and PDE1C.

NS: The above localization of selected PDE5-families explains the enhanced Leydig cellular secretory function and the increased Sertoli cellular secretory function after administration of either sildenafil or vardenafil. In fact, the increased Leydig cellular secretory function post-sildenafil administration has been proven by the increased INSL3 production by human Leydig cells after sildenafil administration. On the other hand, the increased Sertoli cellular secretory function post-vardenafil administration has been proven by the increased androgen-binding activity/content produced by human Sertoli cells after vardenafil administration. Increased peripheral serum testosterone concentration has been demonstrated post-avanafil administration, as well.

AZ: Do the above alterations in the secretory function of Leydig or Sertoli cells affect any of the standard parameters of the semen analysis?

FD: The enhanced Leydig or Sertoli cell secretory function after sildenafil or vardenafil administration may result in increased intraepididymal lumen concentrations of testosterone or androgen binding protein allowing optimal epididymal sperm maturation process. The final result may be an increase in sperm motility after administration of either sildenafil or vardenafil. An alternative mechanism to explain the beneficial effects of sildenafil on sperm motility may be the enhanced prostatic secretory function established after administration of sildenafil. In fact post-sildenafil administration increased concentrations of markers of prostatic secretory function have been demonstrated. Therefore a second

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attractive hypothesis may be that administration of sildenafil, acting on prostatic PDE5, increases prostatic secretory function with an overall result a positive effect on sperm motility. Such a positive effect of sildenafil, vardenafil, or avanafil on sperm motility has been demonstrated very vividly in our laboratory and in other independent laboratories. In a previous study the beneficial effects of avanafil on sperm motility were attributed to the longer length of sperm midpiece post-avanafil administration. It is well known that the sperm midpiece is the "battery" of the spermatozoon and therefore positive effects of avanafil on the sperm cytoskeleton affecting the sperm motility have been demonstrated in the above study. On the other hand, other groups did not demonstrate a positive effect of sildenafil on the standard parameters of semen analysis.

AZ: What kind of patient subpopulations were employed in the above studies?

FD: In all of the above studies, one at least of the standard parameters of the semen analysis was abnormal (sperm concentration, or sperm motility, or sperm morphology) in all the participants. One meta-analysis and systematic review in 2017 has demonstrated that oral PDE5 inhibitor treatment could modestly increase the sperm motility and morphology in infertile men.

AZ.: I understand that sildenafil or vardenafil have been proven in several studies effective to improve sperm motility in oligoasthenospermic infertile men. Do the above substances affect reproductive hormones?

FD: It appears that the above pharmaceutical agents do not affect serum reproductive hormonal levels. On the other hand, a recent report has indicated that avanafil administration increases the peripheral serum testosterone levels.

AZ: What about the effects of tadalafil on sperm qualitative and quantitative parameters?

NS: Tadalafil is known to inhibit to a certain degree the PDE11. PDE11 is highly expressed in the testis, prostate, and developing spermatozoa. PDE11 knockout mice display reduced sperm concentration, rate of forward progression, and percentage of live spermatozoa. Pre- ejaculated sperm from the above mice display increased premature/spontaneous capacitance. In the above study from UK the authors emphasize that agents, like tadalafil, that inhibit PDE11 may have the potential to disrupt regulation of spermatozoa cAMP, and as a result may have detrimental effects on sperm physiology. A study from Andria, Italy, has demonstrated that once-a-day tadalafil administration improves the spermogram parameters in fertile patients. However the above study has been criticized because the respective results refer to fertile patients. It would be a more clinically significant study, a clinical trial evaluating the effects of tadalafil on the reproductive potential of infertile patients since a small impairment in sperm qualitative and quantitative parameters may not be clinically important in fertile patients, however, an impairment in sperm qualitative and quantitative parameters may have more serious consequences in infertile patients (especially if they do not want to participate in assisted reproductive technology programs). In another communication from New Orleans, LA, USA, it has been proven that there are not deleterious effects of nine months of daily tadalafil 20 mg on spermatogenesis or hormones related to testicular function in men elder than 45 years old. In a similar fashion, the above study cannot be unequivocally interpreted as a clinical trial establishing a safety profile for tadalafil due to the barrier that the latter study has employed men with relatively high (or normal) sperm concentration, normal sperm motility, and normal sperm morphology. In another different study from New Orleans, LA, USA, it has been demonstrated that chronic daily administration of tadalafil at doses of 10 and 20 mg for six months has no adverse effects on spermatogenesis on reproductive hormones in men older than 45 years. However, for subjects to be enrolled in the latter study, semen samples had to have certain minimum normal values based on WHO criteria. Thus the latter study has similar, as above stated, limitations due to the fact that men with male factor infertility and at least one abnormal parameter of the semen analysis had not been included. In an in vitro study from Cairo, Egypt, it has been shown that semen samples recovered from asthenozoospermic men and subsequently treated with tadalafil concentration equal to 1 mg/ml demonstrate significant increase in sperm progressive motility, whereas, specimens treated with 4 mg/ml tadalafil concentration demonstrate a significant decrease in sperm motility. Scientists suggested that the effect of tadalafil on sperm motility in vitro can be explained by a stimulation of the cAMP-protein kinase A pathway, whereas the inhibitory effect of this substance on PDE11 may also contribute to the effect of tadalafil on sperm motility. All the above studies should be coupled with the reports that tadalafil has been shown to inhibit human recombinant PDE11A1 activity at therapeutic concentrations, which is highly expressed in the testis and prostate, and its important function in spermatogenesis has been documented. On the other hand, several studies have indicated that sildenafil and vardenafil are one-two orders of magnitude more selective for PDE5 than PDE11 compared with tadalafil. The later studies offer a safety profile for sildenafil and vardenafil for sperm physiology, in contrast to the existing concerns on the influence of tadalafil on sperm parameters in men with abnormal values in semen parameters.

AZ: Dear friends, what about azoospermic men? Is it safe to recommend the administration of any PDE5 inhibitor in non-obstructed azoospermic men prior to the performance of testicular biopsy?

DF: The international literature supports that administration of vardenafil in men with non-obstructive azoospermia does not alter the sperm

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recovery rate after testicular biopsy procedures. Thus non-obstructed azoospermic men with erectile dysfunction may use vardenafil without any consideration for the outcome of a subsequent testicular biopsy procedure.

AZ: Gentlemen, let me remind you that the positive effects of PDE5 inhibitors on erectile function may assist a subpopulation of men who attempt to produce a semen sample at the day of oocyte pick-up (in assisted reproductive trials), to reduce their stress and produce a semen sample of better quality. In these cases the production of a semen sample with higher quantitative or qualitative sperm parameters may be due to the reduction of the stress during the ejaculation process and the subsequent achievement of higher sexual satisfaction. Several studies from Yonago, Japan, have indicated that the higher the sexual satisfaction is, the higher the semen quality is. In addition, in the above studies, it has been shown that semen samples selected via sexual intercourse are of higher quality than semen samples collected via masturbation. Thus administration of vardenafil, or sildenafil, or avanafil may be indicated in men attempting to produce a semen sample during the day of the female partner-oocyte pick-up.

FD: What about the effects of udenafil on male reproductive capacity?

AZ: No adverse reproductive effects of udenafil have been observed in experimental animals in dose under 70 mg/kg.

FD: Dear friends, let me remind you that PDE5 is present in the vas deferens. Are there any effects of PDE-5 inhibitors on the vas deferens?

AZ: It has been shown that in patients with premature ejaculation, sildenafil plus paroxetine has a significantly higher therapeutic success rate that paroxetine alone. The inhibitory effect of sildenafil on PDE5 increases the level of cGMP in the vas deferens muscular fibers achieving the relaxation of the smooth muscle cells in vas deferens. This may prolong the time necessary for the achievement of ejaculation. Furthermore sildenafil may induce reduction in adrenergic neurotransmission in the smooth muscular fibers of the vas deferens and subsequently may reduce its pattern of contraction.

FD: Let me add that PDE5 is additionally expressed in epididymis. It has been demonstrated that no alterations occur in the epididymal secretory function by administering vardenafil. Additionally, it has been observed that in oligozoospermic infertile men treated with sildenafil, no increase in semen levels of α-glucosidase (a marker of epididymal function) is found. Furthermore, the effect of sildenafil on epididymal semen parameters has been evaluated in Sprague-Dawley rats. It has been demonstrated a significant increase in epididymal sperm motility and concentration compared to the control group.

NS: Since you are speaking for the male accessory genital glands, let us remember that PDE5 is expressed in the seminal vesicles, as well. The outcome of different studies of PDE5 inhibitors on the seminal vesicular physiology is controversial. The effect of sildenafil on the seminal vesicles in oligozoospermic men has been evaluated. Comparing semen samples before and after sildenafil treatment, no significant difference in seminal fructose levels, which is a marker of seminal vesicular function, has been observed. In an interesting study, the ultrasound alterations of seminal vesicle in infertile diabetic patients treated with tadalafil for three months have been studied. Compared to placebo, a significant reduction in seminal fundus/body ratio, a

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higher pre- and post-ejaculation anteroposterior diameter, and a significant increase in seminal ejection have been observed.

AZ: We have discussed a lot for the effects of PDE5 inhibitors on sperm motility. Furthermore, some studies tend to suggest that vardenafil or sildenafil increase the total sperm count and the sperm morphology. However, are there any studies evaluating the effects of PDE5 inhibitors on sperm functional assays? It is well known that the standard parameters of semen analysis cannot predict accurately the male reproductive potential. Thus we need to employ sperm functional assays in order to appreciate the effects of PDE5 inhibitors on the male reproductive potential.

FD: The potential effect of sildenafil on spermatozoal ability to undergo capacitation process has been investigated. The investigators demonstrated that several concentrations of sildenafil may activate the capacitation process of washed spermatozoa. In another study, the impact of sildenafil on sperm acrosomal reaction has been evaluated. Spermatozoa were exposed to different doses of sildenafil. The investigators demonstrated that sildenafil affected the sperm acrosomal reaction with enhanced percentage of acrosomally reacted spermatozoa in comparison with the control specimens. It has been demonstrated that cGMP directly opens cyclic nucleotide-gated channels for calcium entry into the spermatozoa initiating the acrosome reaction.

FD: Let us go to the DNA structure. Do PDE5 inhibitors affect the spermatozoa DNA integrity?

AZ: There is a study that has been awarded a Ph.D. title from Greece indicating that spermatozoa treated with tadalafil in vitro demonstrated an increased DNA fragmentation. In that study it has been hypothesized that elevation of the second messenger cGMP level due to inhibition of PDE5 by tadalafil activates a nuclear cGMP-dependent protein kinase PKG with an overall detrimental effect on sperm chromatin structure. In addition tadalafil upregulating spermatozoal NOS expression subsequently increases intracellular sperm nitric oxide profiles which may diffuse in the sperm nucleus. Thus the intranuclear NO increased levels may exert their effect on nuclear transcriptional factors and chromatin remodeling enzymes. Alternatively it may hypothesized that the effect of tadalafil on sperm DNA is due to the formation of hydrogen bonds between the C=O groups of the molecule of tadalafil and the NH2 group in the guanine moiety of the DNA. The latter hypothesis is strongly supported by previous research efforts indicating a similar mechanism responsible for the interaction between sildenafil with salmon sperm DNA.

FD: So, which is the conclusion of our previous discussion? Is it appropriate to recommend the usage of PDE5 inhibitors as an adjunct tool for the therapeutic management of male infertility?

NS: We may suggest that administration of sildenafil, vardenafil, or avanafil may be recommended for semen production during assisted reproductive technology trials when the stress of the male is a great barrier for the production of a semen sample. Considering that randomized controlled trials provide positive results for the influence of sildenafil, or vardenafil, or avanafil on sperm motility, it may be suggested that the above pharmaceutical agents may have a beneficial role in the alleviation of asthenospermia in idiopathic infertile men. Definitely, additional research efforts are justified to further investigate the influence of PDE5 inhibitors on sperm qualitative, quantitative, and functional parameters and on semen physiology. Furthermore it appears to be of great clinical importance to further investigate the role of PDE11 in spermatogenesis process, epididymal sperm maturation process, and the overall sperm fertilizing capacity taking into serious consideration a) that PDE11 is highly expressed in spermatogonia, spermatocytes and spermatids in addition to its expression in Leydig cells, and b) that studies from Kent, U.K., have suggested that agents that inhibit PDE11 level have the potential to disrupt regulation of spermatozoal cAMP, and as a final result may have detrimental effects on sperm physiology and may lead to a reduced fertilization ability according to the investigators opinion.

AZ: The steaks and the hamburgers have just arrived, the red wine smells and tastes good, and let us enjoy our dinner.

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Penile transplantation in men: Past, present and future

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Penile transplantation is a novel treatment strategy for severe penile disfigurement. In reconstructive surgery, replacing like tissues with like tissues is the goal. Given the penis' complex architecture required for its functions of fluid transportation and penetrative intercourse, no other tissues in the body are similar. Phalloplasty using soft tissues from the arm, leg, or other areas achieve satisfactory cosmetic results. However, neophalluses have no erectile capability without implanting a penile prosthesis, which is delayed from the time of transplantation by approximately one year to allow the development of protective sensation and is fraught with complication rates approaching 40% [1]. The South African experience suggests that even when a neophallus is successfully implanted, it cannot withstand the physical demands of frequent sexual intercourse. Neophallus fluid transport capabilities are also less than ideal with complications including fistulas and strictures at rates of 42% to 65% [2]. With the increasing experience and success in vascularized composite allotransplantation (VCA) such as face and arm transplantation, penile transplantation has become a reality.

To date, there have been 4 attempts at human penile transplantation, 3 of which were successful. The first documented case was performed in 2006 in China on a 44-year-old man who lost his entire pendulous penis in a traumatic accident 8 months prior. Although there were no signs of rejection and the patient was able to spontaneously void on post-operative day 10, the transplanted penis was removed on post-operative day 14 due to "a severe psychological problem of the recipient and his wife"[3]. The second attempt and first successful human penile transplantation was performed in December 2014 at the Tygerberg Academic Hospital in South Africa.[4] The 21-year-old man lost his pendulous penis due to infectious complications of a ritual circumcision performed 3 years earlier. This case has the longest documented follow-up of 24 months with encouraging results. By 24 months, the patient did not experience an episode of rejection, was having unaided erections with normal orgasm and ejaculation that was sufficient enough to impregnate his girlfriend. Most importantly, the patient has fully accepted his transplanted penis and his quality of life is significantly improved. His immunosuppresion regimen consists of prednisone, tacrolimus, and azathioprine and complications thereof include acne and hypertension, which resolved with dose adjustment, and a successfully treated episode of a supra-patellar bursa fungal infection. The same group has recently performed their second penile transplantation (4th penile transplant overall) April 2017, of which the results and follow-up have not been published [4].

The second successful penile transplant was performed at the Massachusetts General Hospital in May 2016 after the 64 year-old recipient had a penectomy for penile cancer 4 years prior. [5] After 7 months of follow-up the patient has had 2 acute rejection episodes, has partial penile sensation and erectile function, and is voiding spontaneously. In both reported successful penile transplantations, recipients required several additional procedures for complications including hematoma evacuation, eschar debridement, and urethralcutaneous fistula closures.

Given that penile transplantation is life-enhancing and not life-saving, thorough discussions with the patient regarding the risks and benefits of the procedure are paramount. In both documented cases, patients underwent extensive psychological evaluation with assessment of motivation and treatment adherence. Treatment teams emphasized discussions regarding possible psychological rejection of the graft, unmet expectations of treatment outcomes, graft failure, and social stigmatization. Patients were also counseled on the need of life-long immunosuppression and the associated risks including infection and malignancy. Psychological counseling and support is continued following the procedure. Informing society and organ donors of the benefit of this procedure to facilitate the donation of this very intimate organ is also important. To this end, the South African team created a neophallus for the donor, which was critical for the consent of the donor's family [4].

To date, penile transplantation has been performed for complete loss of penile tissues either due to trauma or iatrogenesis. Likely, this will be the largest population of patients who will benefit from penile transplantation. Complications of ritual circumcision result in varying degrees of penile tissue loss in 250 young-men per year [4]. The protracted military conflicts in the Middle East with the extensive use of buried improvised explosive devices and improved survival in battlefield trauma has resulted in large amounts of young soldiers with disfiguring genital trauma. Other indications include congenital penile disfigurement in the setting of bladder exstrophy and disorders of sexual development. There is no rigorous data as of yet to determine whether penile transplantation will be desired for gender reassignment in the transgender population. Thus, one of the most important factors for the indication of penile transplantation will be the patient's wishes and desires for their genital reconstruction. If only cosmesis is desired, then a reconstructive neophallus may be sufficient. If the patient desires include frequent sexual intercourse and/or robust urinary transport then replacing like tissue with like tissue using penile transplantation may be the best option.

One of the greatest impedances to widely adopting this treatment modality is the significant risk associated with life-long immunosuppression. These include hypertension, renal failure, neuropathy, infection, and increased risk for developing a malignancy. Exciting immunosuppression research seeking to achieve immune tolerance

of the recipient's immune system to the transplanted organ by using novel small molecules and stem cell infusions may lead to therapies that minimize the current risks of immunosuppression. This would greatly alter the risk-benefit ratio of penile transplantation and likely greatly increase its acceptance.

Another obstacle to broad implementation, as with most other forms of VCA, are the highly skilled multidisciplinary teams including specialists such as psychiatrists, counselors, organ procurement coordinators, urologists, and plastic surgeons. They are required for patient identification, assessment, counseling, transplantation coordination, and performing the technically challenging procedures of penile harvest and implantation. Unlike kidneys transplantations, which on average require 3 anastomoses – one artery, one vein, and a urinary anastomosis, the penis may require up to 10 small to micro-anastomoses depending on the anatomy and surgical approach – 2 dorsal arteries, 2 cavernosal arteries, 2 external pudendal arteries, deep dorsal vein, 2 dorsal nerves, and the urethra, not including joining the tunica albuginea and skin. None of the successful cases have employed all of these anastomoses but variations thereof due to recipient anatomy and technical feasibility.

As with all novel clinical endeavors, research is required to better understand the challenges that lie ahead. Given the uniqueness of penile architecture, function, and certain tissues, it is unclear based on prior VCA or solid organ transplantation how penile tissues may undergo rejection and how this will affect its function. Skin is commonly considered one of the most immunogenic tissues in VCA and often monitored for early signs of rejection. Our preliminary research (not yet published) suggests that the urethra may also elicit a rejection response. Given the sensitivity of penile microvasculature, early rejection may be detected by new onset loss in erectile function. Penile transplantation basic science and translational science is complicated by the poor recapitulation of penile transplantation in rodent models and the ethical challenges in using larger species such as canines and monkeys. There are many exciting opportunities and discoveries to be made to better understand and optimize penile transplantation.

Penile transplantation is an ethically and technically challenging treatment for the devastating loss of penile tissue and function. It includes the significant risks of life-long immunosuppression, surgery, and psychological stress. However, it may provide natural erectile function and more robust fluid transport function than current phalloplasty procedures can offer. Advances in research of immunosuppression and penile transplantation will hopefully improve the success of this operation, minimize its side effects, and offer an effective management for the very difficult to treat condition of sever penile disfigurement.

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Urethroplasty and erectile dysfunction

by Salvatore Sansalone and Guido Barbagli

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Urethral stricture disease affects the quality of life of the patient and his partner. Treatment of urethral stricture is always a great challenge for urologists, although a paradigm shift in managing this disease has occurred within the past decades. In addition to attaining meaningful improvement in voiding efficiency and alleviating symptoms, satisfaction with remaining erectile function after surgery is also an important criterion of ideal postoperative outcome for urethroplasty because no one technique is appropriate for all stricture diseases. The urologist must be familiar with various open surgical techniques. Some urologists accept that erectile dysfunction (ED) usually occurs after open urethral surgery and that ED rate is dramatically different due to the variety of procedures.

The outcomes of urethral reconstructive surgery have traditionally focused on parameters such as urinary flow rate, lower urinary tract symptom (LUTS) score, or recurrent urethral stricture requiring further treatment. Mundy [1] was the first urologist to report the incidence of ED after urethroplasty in 1993 reporting a permanent ED rate of 5% after anastomotic repairs and a rate of 0.9% after graft urethroplasty. In studies assessing postoperative erectile function at more than one time point, ED was found to be transient, resolving between 6 to 12 months in 86% of cases. Up to date, there has been a scarcity of systematic studies specifically evaluating the effect of different types of urethroplasty on erectile function. The difficulty of evaluating the specific incidence of ED after open reconstructive surgery may lead to further misguidance in providing treatment for these patients. The incidence of de novo ED after urethroplasty is largely underreported. Erectile dysfunction can be caused by altered blood flow through arteries, defective venous engorgement or absent neural transmission. As described by Lue et al. [2] cavernosal nerves mostly traverse about 3 mm outside cavernosa and only few traverse through it. So anatomically, there seems to be minimal risk to erectile neural mechanism after urethroplasty. Various literatures have shown varying results of ED following urethroplasty depending on site, size and operative techniques. During PPU for PFUI (pelvic fracture urethral injury), dissection is carried out more posteriorly to excise scar tissue and to gain adequate length for tension-free anastomosis. To achieve tension free anastomosis, corporeal separation or inferior pubectomy may be needed, increasing the chances of injury to neurovascular structures and thereby increasing the likelihood that ED will develop.

Surgical treatment of urethral strictures includes numerous open techniques, such as graft urethroplasty, urethral anastomosis, urethral realignment, and so on. Although these procedures have become increasingly popular and effective, the relationship between open urethroplasty and ED is still controversial. So far, only few comparative studies have carefully assessed patient erectile function after various kinds of open urethroplasty. Therefore, a metaanalysis of this problem is necessary so that the morbidity of ED after different open urethroplasty can be evaluated objectively. Based on these results, urologists can choose the best strategy for treating these patients in order to avoid the occurrence of ED as much as possible. We have conducted according to the PRISMA Statement a meta-analysis review [3]. A total of 790 studies were identified in our database and bibliographic probe. Seventy of these studies (8.86%) were identified as relevant, but 47 of these (67.14%) were excluded because they did not meet the inclusion criteria or because they contained data that were undeducible for statistical analyses. In conclusion, 23 studies (2.91%) were germane to the predetermined inclusion criteria. In aggregate, these 23 studies included 1,729 patients, and ED was reported in 560 (32.39%) cases.

Comparison I

Before urethroplasty vs. after urethroplasty – overall assessment

Five studies eligible for the meta-analysis reported patient erectile function before and after various anterior open urethroplasty. No statistical difference was found in the incidence of ED pre- and postoperation (OR = 0.85; 95% CI: 0.52–1.40; P = 0.53). Meanwhile, erectile status before and after various posterior open urethroplasty were evaluated in six studies. The analysis revealed that the incidence of ED before the operation was significantly higher than that after the operation (40.96% vs. 25.63%; OR = 2.21; 95% CI: 1.23–3.27; P < 0.001) but with unacceptable statistical heterogeneity (I2 = 61%).

Comparison II

Comparison of a different anterior urethroplasty site

According to the location of the urethral stricture, we further classified the anterior urethroplasty into penile and bulbar urethroplasty. The single study eligible for comparing ED before and after penile graft urethroplasty was from Erickson et al. [4] The rate of ED before urethroplasty was similar to that after urethroplasty (23.53% vs. 35.29%). There was no statistically significant difference between the two groups (P = 0.45). Furthermore, we compared the ED incidence be-

tween penile graft and bulbar graft urethroplasty. There are two studies that discussed this issue. Finally, the data analysis did not demonstrate statistical significance (penile graft urethroplasty 23.81% vs. bulbar urethral anastomosis group 16.67%; OR 1.62; 95% CI: 0.51–5.81;P = 0.41). In these reports on bulbar urethroplasty, less ED occurred in those patients who underwent bulbar graft urethroplasty (16.67%) than in those who underwent bulbar anastomosis (36.54%), and the results were statistically significant (OR = 0.32; 95% CI: 0.11–0.93;P = 0.04). Only one study reported the ED occurrence ratio both before and after the bulbar anastomosis. There was again no statistically significant difference between the two groups (24.14% vs. 27.59%; P = 0.76).

Comparison III

Comparison of various types of posterior urethroplasty

A single study by Lumen et al. compared ED incidence after posterior open urethroplasty between patients with a history of previous posterior open urethral surgery and those without a previous history. No statistical difference was found among these groups (33.33% vs. 32.5% P = 0.95)

In five cohort studies, the data analysis revealed that the ED incidence in patients who underwent immediate posterior urethra repair was no different from those who underwent the delayed anastomosis procedure (19.75% vs. 21.24%; OR 0.93; 95% CI: 0.45–1.90; P = 0.84).

A total of seven cohort investigations compared the incidence of ED between an open realignment group and a delayed anastomosis group and showed no significant difference. Two studies contributed to the meta-analysis of ED incidence in patients who underwent open realignment and immediate repair. It seemed that a higher incidence of ED appeared in the open realignment group than that in the immediate group, whereas the difference was not statistically significant (21.53% vs. 12.5%; OR 0.69; 95% CI: 0.51–7.38; P = 0.34)

In conclusion, confirming our clinical experience, this meta-analysis showed that urethroplasty itself has no obvious effect on ED. On the contrary, there is an overall decrease in the ED incidence after the posterior urethral surgery. For anterior open urethroplasty, only bulbar urethral anastomosis may lead to a higher incidence of ED compared with the other kinds of procedures we investigated.

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Have you read? Best of the best: Clinical research

by Nicola Mondaini

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INDURATIO PENIS PLASTICA

Seveso M, Melegari S, De Francesco O, Macchi A, Romero Otero J, Taverna G, Bozzini G: **Surgical correction of Peyronie's disease via tunica albuginea plication: Long-term follow-up.** Andrology. 2017 Dec.

Peyronie's disease (PD) is an acquired connective tissue disorder of the tunica albuginea with fibrosis and inflammation that lead to palpable plaques formation, penile curvature, and pain during erection. Patients report negative effects on main domains such as physical appearance and self-image, sexual function, and performance. The aim of this study was to evaluate plication of the albuginea outcomes after a long-term follow-up period. Between 1998 and 2006, a total of 204 patients with PD underwent surgical correction with albuginea plication technique. We obtained complete long-term follow-up data in 187 cases. The follow-up data included evaluation of curvature correction, penile shortening, sexual function, complications, and patient satisfaction. After a mean follow-up of 141 months, the most common postoperative complications were: loss of length (150 patients had a minimal penile shortening ≤1.5 cm, 37 patient between 1.5, and 3 cm, none >3 cm), recurrent or residual penile curvature (15 patients, without impairing sexual intercourse), erectile dysfunction (15 patients had IIEF-5 < 10 at 5 years of follow-up vs. 28 patients at 10 years), change in penile sensation (37 patients experienced paresthesia of the glans 1 year after surgery, 28 at 5 years, and 15 at 10 years); painful or palpable suture knots (in 20 cases) spontaneously healed in 3 months. Overall, 77% of the patients and partners were completely satisfied, 14% partially satisfied, and 9% unsatisfied. Plication procedure is safe and simple to be performed compared with the classical Nesbit's procedure. It has a shorter surgical time, lower costs, and could be successfully performed by less experienced surgeons too. It has a minimal risk of de novo erectile dysfunction, injury to the dorsal neurovascular bundle. Results are good in terms of patient satisfaction according to anatomical outcome and functional correction.

ERECTILE DYSFUNCTION

Capece M, Gillo A, Cocci A, Garaffa G, Timpano M, Falcone M: **Management of refractory ischemic priapism: Current perspectives.** Res Rep Urol. 2017 Aug 29;9:175-179.

The aim of the present manuscript is to review the current literature on priapism, focusing on the state-of-the-art knowledge of both the diagnosis and the treatment of the refractory ischemic priapism (IP).

Pubmed and EMBASE search engines were used to search for words "priapism", "refractory priapism", "penile prosthesis", "diagnosis priapism", "priapism treatment", "penile fibrosis", "priapism therapy". All the studies were carefully examined by the authors and then included in the review. First-line treatment involves ejaculation, physical exercise and cold shower followed by corporal blood aspiration and injection of α-adrenoceptor agonists. Subsequently, a distal or proximal shunt may be considered. If none of the treatment is effective or the priapism episode lasts >48 hours penile prosthesis implantation could be the only option to solve the priapism and treat the ongoing erectile dysfunction. The management of IP is to achieve detumescence of persistent penile erection and to preserve erectile function after resolution of the priapic episode. On the other hand, penile fibrosis and following shortening should be prevented. Early penile prosthesis implantation in patients with refractory IP is able to solve both the priapic episode and prevent the otherwise certain penile shortening. Penile prosthesis implantation is the actual gold standard of care in cases of refractory IP.

Loeb S, Ventimiglia E, Salonia A, Folkvaljon Y, Stattin P: **Meta-analysis of the association between phosphodiesterase inhibitors (PDE5Is) and risk of melanoma.** J Natl Cancer Inst. 2017 Aug 1

The US Food and Drug Administration recently announced the need to evaluate the association between PDE5is and melanoma. We performed a meta-analysis on the association between PDE5i and melanoma using random effects models and examined whether it met Hill's criteria for causality. A systematic search of Medline, EMBASE, and the Cochrane Library from 1998 to 2016 identified three case-control studies and two cohort studies, including a total of 866 049 men, of whom 41 874 were diagnosed with melanoma. We found a summary estimate indicating an increased risk of melanoma in PDE5i users (relative risk = 1.11, 95% confidence interval = 1.02 to 1.22). However, the association was only statistically significant among men with low PDE5i exposure (not high exposure) and with low-stage melanoma (not high stage), indicating a lack of dose response and biological gradient. PDE5i use was also associated with basal cell cancer, suggesting a lack of specificity and likely confounding by ultraviolet exposure. Thus, although this meta-analysis found a statistically significant association between PDE5i and melanoma, it did not satisfy Hill's criteria for causality.

Have you read? Best of the best: Clinical research

FEMALE SEXUAL DYSFUNCTION

Kurtulus FO, Salman MY, Fazlioglu A, Fazlioglu B: **Effects of renal transplantation on female sexual dysfunction: Comparative study with hemodialysis and a control group.** Transplant Proc. 2017 Nov;49(9):2099-2104.

Sexual dysfunction occurs commonly in individuals with end-stage renal disease. Chronic renal failure as well as the treatments used for it generally has a negative impact on sexual function with a subsequent increase in the risk of depression. There is scarcity of published data on female sexual dysfunction and the degree of improvement in patients on hemodialysis (HD) and transplant (Tx) recipients. The aim of this study was to compare the sexual function and degree of depression in HD and Tx patients with control group. For this purpose, we used the validated Female Sexual Function Index (FSFI) and Beck Depression Inventory (BDI).

A total of 23 renal Tx, 29 HD, and 30 control patients were enrolled in the study. HD patients were required to be undergoing HD for ≥6 months, and for renal Tx recipients, the Tx had to be performed ≥6 months before study entry. All women underwent a general and urogynecologic examination. Demographic and clinical variables were documented. FSFI and BDI scale scores were compared among groups.

The rates of female sexual dysfunction were 56.7%, 89.7%, and 73.9% in the control, HD, and Tx, patients respectively. Total FSFI scores in HD group were significantly lower than those in Tx and control patients ($P < .05$). FSFI scores improved significantly in the Tx group. BDI scores in HD and control subjects were 23.24 and 14.17, respectively, with a significant difference between the 2 groups ($P < .005$). BDI score in the Tx group was 16.65 and the difference was statistically insignificant.

This preliminary study documented that successful Tx may positively affect sexual life in women with chronic renal failure. A diagnosis of female sexual dysfunction should be made routinely in patients with chronic renal failure.

SEXUAL PROBLEMS

Acquati C, Zebrack BJ, Faul AC, Embry L, Aguilar C, Block R, Hayes-Lattin B, Freyer DR, Cole S: **Sexual functioning among young adult cancer patients: A 2-year longitudinal study.** Cancer. 2017 Nov 17.

Cancer-related sexual dysfunction has been reported among adolescents and young adults (AYAs); however, its prevalence over time has not been examined. This longitudinal study investigated sexual dysfunction in AYAs over the course of 2 years after the initial diagnosis.

Young adult patients (18-39 years old) completed the Medical Outcomes Study Sexual Functioning Scale within the first 4 months of their diagnosis (n = 123) and again 6 (n = 107) and 24 months later (n = 95). An ordered multinomial response model analyzed changes in the probability of reporting sexual dysfunction over time and the independent effects of demographic, clinical, and psychosocial variables.

More than half of the participants reported sexual functioning to be problematic at each assessment. The probability of reporting sexual dysfunction increased over time ($P < .01$) and was greater for cancer patients who were female ($P < .001$), older ($P < .01$), married or in a committed relationship ($P < .001$), treated with chemotherapy ($P < .05$), and reporting comorbid psychological distress ($P < .001$) and lower social support ($P < .05$). For women, being in a relationship increased the likelihood of reporting sexual problems over time; for men, the likelihood of reporting sexual problems increased regardless of their relationship status.

A substantial proportion of young adults report ongoing problems with sexual functioning in the first 2 years after their cancer diagnosis. These findings justify the need to evaluate and monitor sexual functioning throughout a continuum of care. Cancer 2017.

MEETINGS AND EVENTS CALENDAR 2018

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February

2nd Global Men's Health Summit 2018
February 5 – 9, 2018
Location: Panama City, Panama
Web: gmhsummit.org

ISSWSH Annual Meeting 2018
February 8 – 11, 2018
Location: San Diego, CA, USA
Web: www.isswshmeeting.org

ESSM Preparation Courses 2018
February 25 – 27, 2018
Location: Lisbon, Portugal
Web: www.essm.org/education-certifications/certfications/pre-course/

World Meeting on Sexual Medicine
February 28, 2018 – Mar 3, 2018
Location: Lisbon, Portugal
Web: www.issmessm2018.org

March

26th European Congress of the European Board & College of Obsterics and Gynaecology (EBCCG)
March, 8 – 10, 2018
Location: Paris, France
Web: www.ebccg.2018.org

33rd Annual EAU Congress – EAU18
March 16 – 20, 2018
Location: Copenhagen, Denmark
Web: eau18.uroweb.org/eau18/registration

May

14th Congress of the European Federation of Sexology
May 9 – 12, 2018
Location: Albufeira, Portugal
Web: http://web.aimgroupinternational.com/2018/efs/

AUA 2018 Annual Meeting
May 18 – 22, 2018
Location: San Francisco, CA, USA
Web: www.auanet.org

June

ESAU Oporto Meeting: Joint Meeting ESAU – Portuguese Society of Andrology
June 2, 2018
Location: Porto, Portugal
Web: http://uroweb.org/section/esau/upcoming-events-news/oporto–portugal

PAYMENT OF THE ESSM MEMBERSHIP FEE 2018

To be sent back to:
ESSM Secretariat
Via Ripamonti 129 – 20141 Milan, Italy
www.essm.org

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

Membership goes
from January to December
❑ New Member
❑ Member since: _____

Title:

Name: Surname:

Date of Birth: Nationality:

Position held:

Institution:

Postal address: ❑ home ❑ work

City: Zip code: Country:

Telephone: Fax:

Email:

First Specialty: Second Specialty:

Membership category

❑ Full Member
❑ Associate Member

Membership type

❑ Simple ESSM EUR 50,00
❑ Combined ESSM + ISSM EUR 160,00

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

1.

2.

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

1.

2.

❑ Herewith confirms the payment of EUR 50,00 for the **ESSM membership** cost for the year 2018 by:
❑ Herewith confirms the payment of EUR 25,00 for the **ESSM membership FOR RESIDENTS IN TRAINING*** cost for the year 2018
❑ Herewith confirms the payment of EUR 160,00 for the **ESSM and ISSM membership** cost for the year 2018

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

❑ Bank transfer to AIM Congress srl

Bank: Banca Popolare di Milano – Ag. 24 – Milano, Italy
Bank codes: IBAN IT81K0558401624000000024845
SWIFT/ BIC BPMIITMMXXX

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

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

Credit Card number:

Expiration date: CVC Number:

Holder:

Holder's Signature

Privacy and treatment of personal data

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

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

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

Date Signature

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

www.issmessm2018.org