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ESSM NEWSLETTER

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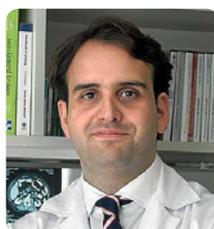
Welcome Address

My dear colleagues,

I am delighted to welcome you to this 2012 first issue of the ESSM newsletter. We have in our society great things coming soon. The ESSM Congress will be held in Amsterdam (6–8 December) with an outstanding scientific program. During last two years members from Educational Committee were working hard to create the Multidisciplinary Joint Committee on Sexual Medicine (MJCSM). The MJCSM determine the standards for training and assessment in Sexual medicine. Successful candidates will be awarded on behalf of the MJCSM the title of "Fellow of the European Board of Sexual Medicine" (FEBSM). This year the first qualification examination of the MJCSM will take place on 5th December 2012 in Amsterdam. Please **save the date! Don't miss this great opportunity to be FEBSM!**

It is a great pleasure to introduce first 2012 issue of the ESSM Today. In this issue, we have included great contributions from world-wide known experts regarding Tadalafil & LUTS, Female Sexual Dysfunction, Endothelial Disease, Peyronie's disease surgery along with our classic sections by my Associate Editors. I had the pleasure and honor of interview Prof. Ronald Virag a truly pioneer and life-long expert in our field, and I hope that you will appreciate his comments and opinions regarding hot topics in Sexual Medicine. In addition we have changes in our website done by our new editors Arik Shechter and Pedro Vendeira. Please use this as an educational resource and to communicate with colleagues. I would encourage you all to submit any articles you feel of relevance to us here. If you would also like to disseminate information regarding meetings related to sexual medicine, we would also be happy to do this for you. Finally, I would like to thank you all for your continued support of our society and I look forward to seeing you in Amsterdam in December.

Very Truly Yours
Juan I. Martínez-Salamanca
Editor-in-Chief



Key from Kols: Use of Tadalafil in treating LUTS/BPH and ED in the United States by Nelson Bennett



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Monotherapy with Tadalafil or Tamsulosin Similarly Improved Lower Urinary Tract Symptoms Suggestive of Benign Prostatic Hyperplasia in an International, Randomised, Parallel, Placebo-Controlled Clinical Trial (1)

Matthias Oelke, Francois Giuliano, Vincenzo Mirone, Lei Xu, David Cox, Lars Viktrup

Background

Recently, the Food and Drug Administration (FDA) in the United States approved the use of Tadalafil for lower urinary tract symptoms (LUTS) in men with benign prostatic hypertrophy (BPH). Physicians in the United States have been slow to adopt this medication for this indication because of the lack of multicenter, randomized, placebo-controlled trials that includes convincing urodynamic data.

Methods

In this double-blind, placebo- and active-controlled, parallel-design trial conducted at 44 international urology sites, 510 men were randomized (1:1:1 ratio) to once-daily tadalafil 5 mg, tamsulosin 0.4 mg, or placebo for 12 weeks. Prior to randomization, screening, a 4 weeks washout, and 4 week single-blind placebo lead-in period commenced.

These eligible men, who were at least 45 years of age and had LUTS/BPH for more than 6 months, were evaluated with IPSS, BPH Impact Index (BII), and International Index of Erectile Function-Erectile Function Domain (IIEF-EF). Additionally,

uroflowmetry was performed using standard calibrated devices at the screening, baseline, and end point visits. The Patient and Clinician Global Impression of Improvement (PGI-I and CGI-I, respectively) instruments and the subject-rated Treatment Satisfaction Scale-BPH (TSS-BPH) were administered at end point.

Results

Demographic and clinical characteristics were similar in all groups. A total of 510 men (mean age 64 years) were randomized into the study. The change in IPSS from baseline to end of study relative to placebo in total IPSS was statistically significant for both tadalafil and tamsulosin. Additionally, measurement of IPSS QoL Index revealed significant improvements compared with placebo at 12 weeks were reported with tadalafil but not tamsulosin. Improvements in urinary flow-rate (Qmax) were significantly greater with tadalafil and tamsulosin versus placebo, however the difference in Qmax from tadalafil to tamsulosin was unremarkable and insignificant.

Differences from placebo in BII were statistically significant for both tadalafil and tamsulosin. Differences from placebo in BII were also significant at 4 weeks for both tadalafil and tamsulosin. For TSS-BPH, overall satisfaction was significantly higher in the tadalafil group compared with placebo. There was no significant difference between tamsulosin and placebo in TSS-BPH overall satisfaction. In global measures of improvement (PGI-I and CGI-I), tadalafil was significantly better than placebo. In men with ED, tadalafil improved erections, where as tamsulosin did not.

Discussion

The coexistence of LUTS suggestive of BPH and erectile dysfunction in the aging population have prompted pharmaceutical companies to explore new uses for old medications. Several

proof-of-concept studies have confirmed that significant symptomatic improvement in LUTS suggestive of BPH occurs with the administration of tadalafil (2 – 4).

The above study is one of the only double-blind, placebo- and active-controlled, parallel-designed, multicenter trials that examine the true relationship of tadalafil and tamsulosin in the treatment of LUTS/BPH and ED (1). The study showed significant improvement in LUTS/BPH after 1 week and a significant increase in Qmax at 12 weeks. This most interesting, and possible controversial, finding is that tadalafil, not tamsulosin significantly improved LUTS/BPH quality of life, global impressions of BPH symptom impact, and BPH treatment satisfaction. Tadalafil also showed expected improvement in erectile function for those men who also reported ED.

Some urologists in the United States are reluctant to utilize tadalafil for LUTS suggestive of BPH because convincing urodynamic data is lacking. In the manuscript from 2010 in *The Journal of Urology*, Dmochowski et al. assessed the impact of daily tadalafil versus placebo on urodynamic measures in men with LUTS suggestive of BPH with urodynamic studies (5). The authors revealed that the urodynamic measures remained largely unchanged during the study with no statistically significant or clinically adverse difference between tadalafil and placebo.

Lastly, American medical insurance companies are increasingly denying coverage for PDE5 inhibitors. For instance, in Massachusetts, most insurance plans will pay for 4 tablets of a PDE5 inhibitor per month regardless of the diagnosis or medical need. Medical coverage, in addition to lack of convincing urodynamic changes with tadalafil have lead to a reluctance of US urologists to use PDE5 inhibitors as a sole therapy for LUTS suggestive of BPH in the setting of ED.

Key from Kols: Use of Tadalafil in treating LUTS/BPH and ED in the United States

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Key from Kols: Use of Tadalafil in Treating LUTS/BPH and ED in the United States by Hartmut Porst



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In their first paragraph the authors claim “Physicians in the United States have been slow to adopt this medication for this indication because of the lack of multicenter, randomized, placebo-controlled trials that includes convincing urodynamic data”. and they reiterate this statement twice in the discussion by saying “ Some urologists in the United States are reluctant to utilize tadalafil for LUTS suggestive of BPH because convincing urodynamic data is lacking” and “in addition to lack of convincing urodynamic changes with tadalafil have lead to a reluctance of US urologists to use PDE5 inhibitors as a sole therapy for LUTS suggestive of BPH in the setting of ED.”

Unfortunately these statements of the authors are purely speculative because they are not backed by the currently quite promising sales rates of Tadalafil 5 mg OAD for LUTS/BPH since its approval and in addition are bare of any evidence from the scientific literature. In this context the authors reference to the urodynamic study of Dmochowsky R et al (1) which “revealed that the urodynamic measures remained largely unchanged during the study with no statistically significant or clinically adverse difference between tadalafil and placebo. This trial, published by Dmochowski et al, was performed on request of the FDA to provide evidence that tadalafil has not any negative impact on bladder wall function and pressure and therefore was part of the filed safety package of tadalafil for the approval in the indication LUTS/BPH. Fortunately the authors were able to show that tadalafil as compared with placebo did not show any significant urodynamic changes (1), a finding, which applies to all PDE 5 inhibitors investigated in the indication LUTS/BPH (2).

With regard to the effects of tamsulosin on urodynamic parameters a systematic review of the literature showed that “the weighted mean difference in the mean change from baseline in peak urine flow was 1.1 (95 % CI 0.59 to 1.51) and 1.1 ml. per second (95 % CI 0.65 to 1.48) for 0.4 and 0.8 mg., respectively” (3): Although these minimal changes of only 1,1 ml/sec. (!) in the mean maximum uroflow were statistically significant as compared with placebo every urologist in the world would argue that this minimal change is both subjectively perceived by the patients and clinically meaningful to them. In addition, in their analysis of the database of a large placebo-controlled, randomized, double-blind study with the alpha-blocker tamsulosin the authors concluded “These data do question the hypothesis that alpha-blockers largely improve lower urinary tract symptoms by reducing bladder outlet obstruction and suggest that they may also act independent of prostatic smooth muscle tone” (4.) Regarding this unanimous data from the literature the authors have to be asked on which “convincing urodynamic data” the urologists in the States are relying when prescribing tamsulosin?

There is no question that both for patients and physicians, regardless of their specialization, the improvement of LUTS secondary to BPH counts. This relief of LUTS has been investigated and proven by the IPSS world-wide in many prospective drug trials with alpha blockers such as tamsulosin, alfuzosin, prazosin, terazosin and silodosin, or with 5-alpha reductase inhibitors such as finasteride and dutasteride or more recently with PDE 5 inhibitors such as tadalafil, sildenafil, vardenafil or udenafil. The trial in question the authors are addressing here was not powered as a direct comparator trial (5). Nevertheless this well-designed randomized prospective trial with a representative number of patients was able to show that both tamsulosin 0,4 mg and tadalafil 5 mg improved LUTS/BPH and reduced the impact of these symptoms on life quality significantly, as assessed by the B II, and significantly increased QMax with tadalafil being ahead (5). In addition it has been shown

that only tadalafil but not tamsulosin was able to significantly improve erectile function and overall sexual satisfaction in men with LUTS/BPH (5) In two recently published review papers with a meta-analysis of the literature the authors point to the fact that in more than two thirds of all men LUTS/BPH and ED are associated conditions and that the majority of the currently available LUTS/BPH medications have a negative impact on erectile and/or ejaculatory function (6). Using the IPSS, which has served as the primary efficacy endpoint in nearly all LUTS/BPH trials, PDE 5 inhibitors such as tadalafil were able to improve the symptoms to the same extent as has been shown with either alpha blocker or 5-alpha reductase inhibitor mono-therapy, but without worsening sexual functions (6,7). In their last review paper the authors concluded that “ PDE5-Is have demonstrated significant improvements in both LUTS and ED in men with BPH; combination therapy with PDE5-Is and 1-adrenergic blockers seems superior to PDE5-I mono-therapy.” (7). This observation is in so far of major clinical relevance as more than 70 % of all LUTS/BPH patients, undergoing specific therapy for LUTS/BPH are both sexually interested and sexually active (6) That tadalafil is able to improve significantly both ED and LUTS/BPH in the same patient has recently been shown in a large multicenter and multinational trial (8). In conclusion : The PDE 5 inhibitor Tadalafil has shown in several large randomized placebo-controlled and double blind trials the same extent of efficacy, assessed by the IPSS, as has previously been reported with either alpha blocker- or 5 alpha reductase inhibitor mono-therapy. In contrast to the previously used alpha blockers and 5 alpha reductase inhibitors tadalafil also improved significantly erectile dysfunction which is present in between 70 and 80 % of all LUTS/BPH patients. Considering the fact that the overwhelming majority of LUTS/BPH patients are on the one hand sexually interested and active but on the other hand suffering from ED there is no question that the recent introduction and official approval of tadalafil for LUTS/BPH is an enrichment of our armamentarium and welcome by both our patients and their physicians.

Key from Kols: Use of Tadalafil in Treating LUTS/BPH and ED in the United States

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Key from Kols: Diabetes and female sexual dysfunction

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Diabetes Mellitus (DM) is an increasing health concern throughout the world and is estimated to affect around 246 million people worldwide, with especially a significant increase in type 2 DM (DM-2) during the last decade.

In men, both Type 1 DM (DM-1) and DM-2 have long been recognized as a major risk factors for impaired sexual function, primarily erectile dysfunction (ED), but also ejaculatory and orgasmic problems as well as low desire have been reported in men with DM. In men, comorbid factors including aging, cardiovascular diseases, obesity, hypercholesterolemia, smoking and medication in combination with DM-specific factors, such as durations and severity of DM and diabetic complications (neuropathy, nephropathy, retinopathy and vascular damages) strongly correlate with ED. The proposed mechanisms for ED in men with DM are endothelial dysfunction, dysfunction of the nitric oxide (NO) pathways, dysfunction of other signal transduction pathways, corporal smooth muscle degeneration and tissue remodeling.

Despite the fact that more women suffer from DM than men, that women share similar risk for diabetic complications with men and the sexual phase in women are the same (desire, arousal and orgasm), less attention has been given to sexual function in women with DM. This may be due to the fact that the prevalence of Female Sexual Dysfunction (FSD) and its risk factors are less clear in women than in men. This may be explained by the fact that women's sexuality is multifaceted and rooted in biological, psychological and social factors, and these are interacting with each other and consequently make the influence of the biological factors less clear than

in men. However, during the last years more information on the effect of DM on women's sexual function has been published.

Mechanisms behind FSD in women with DM

The mechanisms behind FSD in women with DM can be explained by:

- ▶ Hyperglycemia that may reduce the hydration of mucous membranes in the vagina, leading to decreased lubrications and consequently dyspareunia
- ▶ Increased risk of vaginal infections increases the risk of vaginal discomfort and dyspareunia
- ▶ Vascular damage and neuropathy may result in decreased genital blood flow, leading to impaired arousal genital blood flow, leading to impaired genital arousal response
- ▶ Psychosocial factors such as adjustment to the diagnosis, the burden of living with a chronic disease and depression can all result in FSD, particularly affecting sexual desire

Preclinical studies

Inspired by studies on male erectile tissue and animal models of erectile function, animal studies have also investigated the effect of DM on the female physiological response. It has been shown that experimentally induced DM-1 impairs the contractile and relaxant capacity of vaginal musculature and induces a significant decrease in nerve-stimulated clitoral and vaginal blood flow. Furthermore animal studies have shown that DM-1 induces structural changes of vaginal and clitoral structures. Preclinical studies on women with DM-1 showed a significant impaired arousal response, measured as vaginal blood flow in women with DM-1, but no difference in subjective arousal response compared to non-DM controls. These findings

are in agreement with other studies showing that, compared to men, the peripheral feedback from genital arousal seems to be a relatively unimportant determinant of subjective sexual arousal in women.

Clinical Studies

Overall clinical studies show that the effect of DM on women's sexual function is variable within the different domains of sexual dysfunctions (desire, arousal, orgasm and dyspareunia) as well as between women with DM-1 and DM-2. Remarkably, a evident lack in the majority of studies addressing sexual function in women with DM, is that most of the studies report sexual complaints/problems rather than dysfunctions as most studies miss data on sexual distress in the women investigated, and distress is a crucial part of the definition of FSD. Several studies do mix women with DM-1 and DM-2 despite these are two conditions with regard to pathophysiology, age of presentation and treatment.

Desire

Several studies have shown a significantly decreased level of sexual desire in women with DM compared to controls, with rates from 20 % to as high as 78 % of the investigated women. Nevertheless, several studies have also shown no effect of DM on sexual desire. The high prevalence of low sexual desire is primarily seen in women with DM-2 or in studies with mixed DM-1 and DM-2 populations, suggesting that desire problem are primarily related to DM-2.

Arousal

Although sexual arousal has been assessed in most studies, it has been described variably from study to study. Some authors distinguish between genital, subjective or general arousal, whereas others make no clear specifications. It appears that arousal problems vary in women with DM-1 and DM-2, with some studies reporting no effect and others finding prevalences of 14 % – 76 %.

Orgasm

Most studies have reported an increase in orgasmic problems in women with DM, ranging from

Key from Kols: Diabetes and female sexual dysfunction

10% to 84%, but again several studies have failed to show any effect of DM on orgasmic capacity. Furthermore most of the studies rarely differentiated between orgasmic capacity during sexual intercourse versus masturbation.

Dyspareunia

Several studies have shown no increased risk of dyspareunia from DM, whereas others have shown a significant higher occurrence of dyspareunia in women with DM ranging from 3% – 43%. The high prevalence is seen in studies sampling women with DM-1 or mixed groups, indicating that the problem is most predominant in women with DM-2.

Interactions and risk factors associated with FSD and DM

Despite the inconsistent results, the overall picture is that women with DM are at higher risk of FSD in the domains of desire, arousal, orgasm and dyspareunia compared to women without DM. As almost none of the studies include distress as a measure it is more reports on sexual complaints/problems than dysfunctions as defined by the current definitions. Furthermore none of the studies have addressed whether the described sexual complaints are lifelong or secondary to other dysfunctions – for example, whether the woman has got pain due to diabetes related vaginal infections, then has developed arousal problems and finally desire problems.

Although women with DM are at increased risk of having sexual problems, specific associated risk factors including those related specifically to DM are difficult to identify. For example, in contrast to findings in men with DM, most studies in women have shown a low or no correlation

between sexual problems and age, duration of DM, obesity, diabetic complications, medication, glycemic control and hormonal treatment. Only a few studies have shown a correlation between sexual problems and DM-related neuropathy and duration of DM in women. The most well-established risk factor for FSD in women with DM is depression. This relationship was most elegantly demonstrated by Enzlin and colleagues in a comparative study of men and women with DM-1. They established a correlation between sexual dysfunction and diabetic complications and poor diabetes control in men, in contrast to a correlation between sexual dysfunction between depression and psychosocial adjustment in women with DM-1. Furthermore it is known that women with DM are at high risk of developing depression. These studies underline the importance of evaluating depression and sexual problems in women with DM. Other factors apart from depression have shown to be related to sexual impaired sexual function in women with DM. For example several studies have shown that DM-associated factors including fear of dependency, fatigue and impairment of body image may negatively influence sexual function in women with DM.

Conclusion and clinical implications

In conclusion, women with DM are at increased risk of developing sexual problems in the phases of desire, arousal, orgasm and dyspareunia. Larger-scale studies that include distress as a criterion for FSD are needed. Several studies have demonstrated that DM-2 has a greater impact on women's sexuality than DM-1 – an effect that may be related to the late debut of the disease, age, menopausal status, comorbid factors and relationship factors, which need to be parsed out in future

research. Depression is the most important risk factor for sexual problems in women with DM. In the clinical situation women with DM should be asked about their sexual function and possible problems and always be screened for depression. Good regulation of the DM and good psychological health including coping strategies of the disease may prevent sexual problems linked to DM in women.

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Key from Kols: Treatment of congenital penile curvature by corpora cavernosa rotation. Modifications of Shaeer's technique. A new surgical approach with minimal penile shortening by Natalio Cruz Navarro



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Congenital penile curvature is caused by an asymmetric embryonic development of the corpora cavernosa. It's a quite frequent condition, affecting 4–10% of males (1). Penile curve during erection in affected men is usually ventral, and can be so severe (even over 90 degrees) that sexual intercourse may be very difficult or even impossible (fig1).

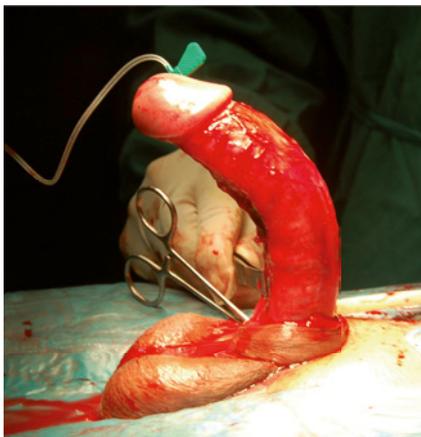


Fig. 1. Congenital penile curvature

Surgical approach is indicated in all these cases, and so far has been carried out using several techniques such as plication-based, Nesbit, 16-dot and others. The overall success rate in terms of straightening is quite good with all techniques. However, penile shortening is the major complaint after congenital curvature surgery with the techniques traditionally employed, and is usually proportional to the degree of curvature. A new technique was published in 2006 by Dr. Shaeer (2), based on the rotation of the corpora cavernosa, and updated by the same author in 2008 (3). This innovative technique reduces the shortening effects of traditional techniques with the same correction of the curvature. Since we started using this technique in 2008,

and after several years of experience, some further modifications needed to be addressed in order to eliminate certain drawbacks and limitations of this procedure. The modifications introduced will be described below.

In short, a longitudinal dorsal incision was made in the dorsal part of each corpus cavernosum. By double suturing the internal and external parts of the incision, a rotation of corpora cavernosa is induced, with excellent penile straightening (figs. 2.1 and 2.2).



Fig. 2.1. (Shaeer O. J. Sex Med. 2008;5:2716-2724



Fig. 2.2. (Shaeer O. J. Sex Med. 2008;5:2716-2724

Step by step:

1. After penile local anesthesia (all cases are done under local anesthesia), the penis is degloved. Contrarily to the original technique, the neurovascular bundle is dorsally dissected

(fig.3), avoiding any potential neurological damage (specially if any additional plication or procedure is needed), and potential vascular damage, either to the dorsal arteries or to the deep dorsal vein (incorporated into the suture in the original technique).



Fig. 3. Neurovascular bundle is dissected dorsally

2. Two superficial longitudinal incisions have to be made on the dorsal part of the corpora cavernosa, involving only the outer longitudinal layer of the tunica albuginea, preserving the inner circular layer (fig.4).

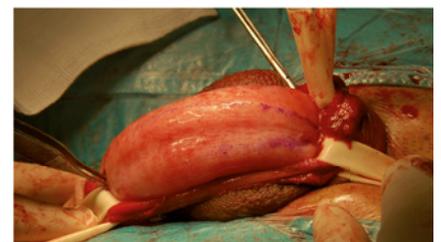


Fig. 4. Two superficial longitudinal incisions on the dorsal part of the corpora cavernosa

These two incisions, described in the original technique, should be slightly curved rather than parallel, with greater separation in the central part of the incision. In fact, in my experience, the more severe the curvature we have, the greater the separation we will need.

3. We first close the interior or medial edges with a continuous suture (fig.5). And then a second continuous suture will approximate the lateral edges (fig.6).

At this point, we prefer 3-0 (or 4-0) absorbable monofilament suture instead of vicryl-0 (described in the original technique). Monofila-

Key from Kols: Treatment of congenital penile curvature by corpora cavernosa rotation. Modifications of Shaeer's technique. A new surgical approach with minimal penile shortening

ment has low tissue reactivity and maintains high tensile strength.



Fig. 5. Continuous suture for the interior or medial edges



Fig. 6. Continuous suture for the exterior or external edges

In vivo tensile strength is 60% at 2 weeks, and less than 30% after 30 days for Vicryl. It is completely hydrolyzed by 90 days. Poliglecaprone 25 (Monocryl) has 70% of in vivo tensile strength at 2 weeks and 40% after 30 days. It is completely hydrolyzed by 119 days (4). Polydioxanone (PDS) suture has greater pliability than polypropylene suture and greater strength than that of other monofilament sutures. In the body, polydioxanone suture retains its strength for longer periods than other synthetic absorbable sutures: 58% at four weeks, and 14 – 25% versus zero at eight weeks. It elicits a low order of tissue response and is absorbed by simple hydrolysis in 180 days (5). More recently, PDS-II has been particularly useful where the combination of an absorbable suture and extended wound support (up to 6 weeks) is desirable (PDS-II strength retention profile in table I) (6).

Weeks	In Vivo Strength Retention		Absorption Profile
	4/0 and Smaller	3/0 and Larger	
2 Weeks	60%	80%	182 – 238 days
4 Weeks	40%	70%	
6 Weeks	35%	60%	

Table I. PDS-II strength retention profile

The breaking strength retention profile of the suture is particularly interesting in these procedures due to the youth of these patients and the hardness of their post-operative spontaneous erections. We prefer PDS-II for these procedures. These new monofilaments allow us to use finer sutures, with fewer infections and slight or minimal tissue reaction.

4. Pre and post artificial erection and penile measurement was made to assess potential residual curvature and penile shortening (fig.7 and 8).

5. Closure of Buck fascia and skin with quick absorption sutures, urethral catheter and compressive dressing.

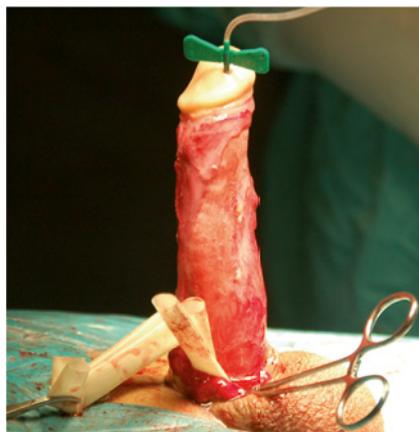


Fig. 7. Artificial erection with excellent penile straightening



Fig. 8. Penile measurement. Minimal shortening of the penis

Ten patients with congenital penile curvature and 60 – 90 degrees ventral curvature have been operated between jun-2009 and jun-2011 in my department by rotating the corpora cavernosa and using this modified technique. More than 90% penile straightening was observed in all cases, with minimal shortening of the penis (0.5 – 1cm.), with high patient satisfaction, and without postoperative complications.

In conclusion, the rotation of the corpora cavernosa, published by Dr. Shaeer, is a novel and useful alternative treatment, which should be considered as the technique of choice for these patients, given the ease of performance and its excellent results. These new proposed modifications have improved its cosmetic and functional results. They are particularly useful in cases of severe congenital penile curvature (60 – 90 degrees). It reduces penile shortening and avoids some complications such as palpable nodules, scars in the corpora cavernosa and penile pain.

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Key from Kols: Endothelial dysfunction in erectile dysfunction etiology – current knowledge

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The endothelium, formerly considered as a simple anatomical passive barrier, is currently recognized as a highly metabolically active organ. By playing important autocrine, paracrine, and endocrine roles, the endothelial monolayer has revealed crucial in regulating systemic and penile vascular homeostasis. Consequently, any impairment on its biological activities is thought to alter endothelium ability to responde to changes, a condition referred to as endothelial dysfunction (EDys). The key feature of EDys is the decreased responsiveness to vasodilator mediators or the increased sensitivity to vasoconstrictor molecules, affecting the normal regulatory role of the vascular endothelium. Since the penis is a highly vascularized organ, a close link between EDys and erectile dysfunction (ED) has been suggested in recent years. The penile endothelial bed is a specialized extension of the peripheral vascular system, responding similarly to the action of endothelium-derived molecules, which regulate cavernosal vascular and smooth muscle contractile tone, essential for erectile functionality. When the endothelium becomes dysfunctional its vasodilator potential is reduced, and vascular structures are unable to fully dilate in response to

the appropriate stimuli. Generally, this decrease in endothelial vasodilation is caused mostly by a diminished synthesis and/or lost of endothelial Nitric Oxide (eNO) bioavailability/bioactivity in the vasculature, accompanied by late structural vascular alterations and altered hemodynamics. The pathologic impairment of eNO-dependent vasorelaxation mechanisms and EDys result from the damaging actions of several vascular risk factors (VRFs). Diabetes mellitus, hypertension, hypercholesterolemia, the more recently recognized metabolic syndrome (MetS), and also aging, have been identified as conditions involved in the development of EDys, ED and cardiovascular disease. Actually, it has been suggested that the deleterious effects of these VRFs in the vasculature, may manifest at an earlier stage as loss of erectile function. In such cases, ED may not be considered only as a clinical manifestation of a pathology affecting the penile circulation, but also as a potential sign of a more generalized vascular systemic disorder. This awareness may reveal important for the prevention of cardiovascular events in patients with asymptomatic coronary artery disease. A vascular etiology of ED is in fact closely associated with the existence of VRFs, which affect endothelial physiology, NO-dependent vasorelaxation, and therefore interfering with the response to phosphodiesterase inhibitors type 5 (PDE5i) therapies. It is the case of diabetic patients, in which ED besides involving alterations in the nervous system, presents primarily as a vascular dysfunction. Diabetic-ED is a hard-to-treat complication, where hyperglycemia and increased oxidative stress, besides

impairing eNO functional activities may also affect endothelial viability by promoting apoptosis. In collaboration with Dr Ronald Virag, we have reported in 2009 in the JSM (6:826-835) that cavernosal tissue of diabetic patients with ED have increased endothelial cell death as compared with non-diabetic non-ED individuals. The elevated apoptosis levels correlated with EDys assessed in the preoperative stage by the Penile NO Release Test (PNORT) and duplex scan ecography. This study indicated that severe lesions on the endothelium are directly related with lack of endothelial functionality and consequently decreased responsiveness to PDE5i. Interestingly, even when EDys is not the major etiology of ED, the endothelial monolayer reveals to be an important player. In ED after radical prostatectomy (RP), a post-surgical role for cavernosal endothelium has been suggested. Prolonged penile flaccid state after RP is thought to lead to irreversible damage to the cavernosal tissue due to hypoxia and fibrosis. Although still somehow debatable, it has been proposed that the use of PDE5i after RP may improve EDys related to ischemia reperfusion and/or denervation, and ameliorate post-operative ED associated-cavernosal fibrosis. Given the crucial role of the endothelium as direct or indirect etiology of ED, future research will focus in providing novel strategies to improve cavernosal endothelial function and ED. Although molecular strategies involving gene therapy and stem cells are still in their infancy, they should be regarded as promising potential treatments aimed at rehabilitating cavernosal endothelial-erectile function.

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Interview with Ronald Virag Dr. Juan I. Martinez-Salamanca (JIMS)



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Dr. RONALD VIRAG, an internationally known figure and Pioneer in the field of Sexual Medicine. He is a Vascular Surgeon and was the discoverer of therapy by intracavernosal injections (ICT) with Alprostadil. For me and for all ESSM Members is a real pleasure and honor having you here.

JIMS: Dr. Virag, could you remember for us what was the situation for the treatment of ED before you described the use of ICT?

The only available treatment of ED – called impotence at that time- was the implant. At the initiative of the late Adrian Zorngniotti (later with him Wagner, Furlow Michal and myself, we founded ISIR), a group, already multidisciplinary met in 1978 in New York around Vaclav Michal's proposal to revascularize the penis, as a reconstructive procedure, as an alternative to the implant. It was really a group of pioneers, eager to understand the pathophysiology of ED. You must understand that at that time ED was considered by the medical world as psychogenic in 90 % of the cases and they were almost no tools to evaluate the patients. Michal, a vascular surgeon, as me had brought that, similar to what was occurring for the heart, the penis'arteries or the penis tissue should be revascularized: he proposed 1st the Michal I direct anastomosis to the CB, and the Michal II to the dorsal artery. I proposed soon the DDVA (deep dorsal vein arterialization) having demonstrated, using artificial erection and cavernosography that the venous side of erection could be as preminent as the arterial one. Two years later in 1980 the group met again in Monte Carlo. I establish then a

strong collaboration with the Danish group lead by Gorm Wagner. Understanding in depth erection and ED was our main goal and remains the same nowadays. The key point to understand the story of ICI is what occurred when we developed artificial erection with saline mixed with cavernosography as a diagnostic procedure (1977 – 1982): some patients (later we found that all had arterial diseases) claimed that they were improved after having experienced artificial erection. I thought that something was going on inside the CB and started to use chronic artificial erection with saline as a treatment for such patients.

JIMS: How was the process to blow-out your idea?

The "papaverine story" is well-known of course. In early 1980 during a Michal I procedure, I had injected 80mg of papaverine in the CB through the epigastric artery directly implanted in one CB. A full erection occurred and lasted for two hours. Moreover it lasted even after the clamping of the epigastric artery. Having suspected the role of the drug, I repeated positively the test on myself. Then I did 2 things:

1. I introduce papaverine to better study the penile arteries during ultrasound tests arteriography and cavernosography.
2. To treat the patients, we used papaverine mixed with saline in the office to enhance natural erections and we allow patients to have sex, in a hotel close to our institute to be able to control the erection duration!

The first scientist aware of the discovery was Gorm Wagner. In 1982, I was preparing an in-depth manuscript for Vascular Surgery, when Gorm urged me to publish sooner my first results in a larger audience Journal. The now famous letter to the Lancet was prepared with him in Copenhagen, accepted and published two weeks later. One year later, Brindley reported his own experience in the British J. of Psychiatry. From The Lancet letter and Brindley's spectacular presentation during the 1983 AUA meeting everything changed in the way ED was evaluated and treated. Papaverine alone or with phentolamine was widely used. I met then Ganesh Adaikan and we shared our findings, he in animal studies, and me in human trials. Many substances were tested including PGE1. Cératine and Trimix came across to enhance the intracavernous injections' performance. Long term results were reported in the J of Urology. And we are still there for many patients who do not respond to PDE5inhibitors.(see below)

JIMS: What do you think about the role of vascular penile surgery nowadays in the treatment of ED?

I think that the role of vascular surgery should be reevaluated in multicenter studies with clearly define parameters to select the patients and evaluate the results. I strongly think that there is a room between ICT and implants, for vascular procedures. We must differentiate the arterial insufficiency and the caverno-venous leaks. Modern imaging eases and improves the evaluation of lesions, especially with what we have called "Caverno CT imaging" proposing a new classification of caverno-venous leaks. (see Virag and Paul J Sex Med. 2011 May;8(5):1439-44.). There is growing evidence that young patients suffering of difficulties to maintain full erection since early sexual life, may have abnormal venous drainage and may benefit from surgical reduction of the venous outflow. In other hands, on the arterial side, the lesions are mainly located

Interview with Ronald Virag

on the pudendal arteries, generally occluded or heavily infiltrated. Desobstruction or bypass is seldom possible. As usual, it is the patient who asks for improvement. In that aspect, we see more and more individuals who ask for a “total repair” even if they respond well to pharmacological treatment.

JIMS: In your practice, what is the role of ICT in the era of PDE5 Inhibitors ?

The role of ICT in my practice is still essential for two reasons: first of all because of its efficacy and also because in a specialized centre like mine, we see a lot of patient's none or poor responders (including those who complain of side effects) to PDE5 inhibitors. In any case, the indications are mainly dependant on the evaluation and demand of the patient. Oral therapy in “fresh” ED patients should remain a first line therapy. Nevertheless when from the history or the hemodynamic studies I have a strong feeling that PDE5 inhibitors will not work I recommend ICT immediately. Two examples: 1-after radical prostatectomy: I always start with ICT; 2-In patients who constructs or rebuild a new couple and have a very high performance anxiety asking to be sure to succeed. Generally speaking, when I think that ICT is more suitable for the patient I propose it bypassing a possible unsuccessful trial with PDE5 inhibitors which would increase performance anxiety.

JIMS : From a formal point of view, what is your choice: Andrology ?, Sexual Medicine ? Global Male Health ?

Dealing since so many years with sexual medicine and having understood soon that erection is an essential link of male general

health, I think that restoring sexual function in a man contribute widely to his well being. Long term follow up of such patients has been the occasion to extend sexual medicine to preventive medicine especially in vascular diseases (CHD), urology (i.e. prostate); and anti aging (hormonal and metabolic adjustments). I do not forget the psychological aspects, being, since the beginning of my experience a strong supporter of pluridisciplinary approach of ED and now of global medicine for men's health.

JIMS: Dr. Virag, do you strongly believes that the Endothelial Dysfunction is the real link between risk factors and development of the disease ?

We have learned that the endothelium is the larger organ in the body. Provided that the penis is full of endothelial tissue it is quite logical to think that the deterioration of this tissue should initiate ED in patients with vascular risk factors. Aware of that I have introduced PNORT in 2002 a specific test to evaluate the penile endothelial function (J Mal Vasc. 2002 Oct;27(4):214-7 and Int J Impot Res. 2004 Feb;16(1):39-42) Later, with Carla Costa, we have shown the grade of endothelial apoptotic cells in the diabetic erectile tissue of patients operated with penile implants. We have now enough material to go further and see if endothelial dysfunction is an early defect in ED and how it combines with general endothelial dysfunction measured by hemodynamic or biological tests. Is there a specific penile endothelial function as we have different locations for atheroma? This demand large clinical research not only focused on epidemiology.

JIMS: On the other hand, which do you consider the most important challenges for the journal over the next 10 years ?

I am convinced that in the next ten or twenty years we shall see the success of local therapy either medical and/or surgical. Such easily accessible organ shall see “rejuvenating” medicine reshaping it: We should be able to deliver locally medications without needles through tiny intracorporal electronic devices. Stem cells, tissue engineering, auto-reconstructed penis through biodegradable scaffolds are candidates to make our sexual life almost endless. But don't forget education which is a prominent challenge: education of all doctors. Too many everywhere neglect sexual medicine and leave many patients still desperate when we have already all the tools to treat them. Education of the public through the media. Education of the youth.

A large program for our society. Remember that in 1980 in New York the attendance of our first meeting was as much as 32 guys.

It was a real pleasure to do this interview; I'm sure your p points of view, fruit a whole life dedicated to your work, will be highly appreciated by our readers, thanks once again.



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The Patient's Corner by Milly Lemos



ESHA activities

Over the years The European Sexual Health Alliance (ESHA) has used St Valentine's Day, a special day devoted to love and romance to draw attention to the problems of sexual dysfunction and the suffering they produce. Through our patient support centres we are acutely aware of the difficulties people have in coming to terms with these problems, breaking their silence to talk to their partners and their doctor and embarking on the path to finding a solution. In this article we mention the recent activities of two of the ESHA centres.

In Spain the message this year has been "talk to your partner about sex", highlighting the importance of communication within the couple as one of the most important factors in finding solutions to problems of sexual dysfunction. It seemed the perfect opportunity to remind people that it is not just important to talk about romance but also to open up about any problems affecting the sexual health of the couple and this way open the door to a solution. A press release was sent to the media with interviews by Dr Martinez Salamanca the general secretary of the AESS (Spanish Association for Sexual Health) and Cristina Martinez a psychologist who collaborates with the AESS.

2012 is also the year that marks the 10th anniversary of the foundation of the Turkish Association ASAD : Family Health Research Association. In the last 10 years, they have undertaken many activities and they have observed that one of the greatest challenges they face is that of misin-

formation in the general public fuelled by the countless media and internet resources. The most common urban legends encountered so far through their help line and internet questionnaires concern erectile dysfunction (ED)'s relationship to age, comorbidities, concurrent medications and PDE5 inhibitors. It is also clear to that there is still a very low percentage of ED patients that are clinically evaluated and treated correctly. The majority seek information online or through friends and take medicines accordingly without talking to their doctors or getting the correct medical evaluation. There is even a new term for the resource used by these patients, so called "internet doctors".

It is for this reason this year the ASAD decided to use internet short movies for their awareness campaign. These provide information about such an important subject as counterfeit drugs but also other common misconceptions about ED. The campaign was a huge success and lasted a whole week in a wide range of websites, primarily news and health sites. It was backed-up by press releases from Prof. Dr. Halim Hattat as President of the ASAD.

The campaign's primary aims were to protect and inform ED patients and their partners not only by stressing the importance of accessing safe and legitimate medicines, but also by raising their awareness about the facts and fiction surrounding ED and its treatment options. This project has been very successful. Their data shows that the number of visitors to these websites has been in the tens of thousands.

We believe this may be a very effective tool for ESHA to use in the future in terms of organising a combined European activity using a carefully selected range of web sites.

Milly Lemos
European Sexual Health Alliance

In **Portugal** a big truck was placed in the heart of the three major cities. It was parked two days in each city. Lisbon, Coimbra, Oporto. Inside there was a comfortable waiting room and two other rooms: one for a check up on the risk for cardiovascular diseases (a nurse did this) and another room where a sexologist gave out information, advice and referral to those interested in sexual dysfunction. It was available from 9 to 19:00. All five more important television stations gave full coverage of this event, with a lot of live/local interviews on air. There were a total of 254 male visitors, 26 female and 17 couples just for the sexology advice. On the 14th morning there was a Press Conference given by Prof Nuno.

Also on the 14th there was a special edition on the topic of sexual disorders released together with the two major daily newspapers one in Lisbon and another in Oporto. It included 16 pages covering the topics of physiology, prevalence, therapeutic, psychological perspective and history of ESAE events to date. 140 000 samples were distributed. The back cover of this special edition featured the ESDA poster.

On the 14th there was an opening night for a theatre play on the topic of erectile disorders "O Efeito Laranja". Some of Portugal's most popular theatre actors and actresses took part in it. The programme of the play included the helpline number in it.

On Saturday, the most popular TV station showed a 35-minute news piece on female sexual disorders during prime time.

The Patient's Corner



The **Greek** centre's TV spot was shown on 10 TV channels throughout the whole of February, promoting the message that common conditions such as diabetes or obesity can be associated with ED and sexual health problems. The above, combined with the publicity generated by the launch of their new website and the press release on the 14th of February, which received very good coverage in all newspapers, has resulted in a dramatic increase in the number of calls received at their centre.

Meanwhile the campaign poster was distributed to all urologists in **Germany** (about 4000), and a press release was sent out on the 14th announcing the hotline and offering the possibility of radio interviews with experts.

In **Turkey** a very comprehensive press conference was held at the Ritz Carlton followed by lunch. 4 of the main TV stations and many newspapers covered the event and interviews with

the professors (namely Prof. Hattat, Prof. Akkus and Prof. Oner - President of Turkish Urology Association). The results of a questionnaire with approx. 2000 pharmacists and their sales people were announced. These included hints about their knowledge on ED drugs, treatment options and the type of medical education they prefer. As their preference turned out to be Andrologists organising meetings with them including Q and A Sections, ESDA Turkey now plans to go to between 10 and 20 Anatolian cities in 2006. After this announcement at the press conference, the first meeting was organized for the on 16th of Feb in Izmir. It was a huge success; nearly 400 people (both pharmacists and the sales people) attended the meeting followed by a dinner. The meeting attracted both local and main media coverage.



In **France** leaflets were distributed to GPs giving information about ED and this was reinforced by a timetable of television spots which are on-going.

The SDA in the **UK** issued a press release to the British media which focused on "Sex and the Heart". Several stories were published in the glossy magazine sector. As a result the helpline fielded three times the amount of calls in the

week after the release. The SDA also announced that it is changing its name to "Sexual Health UK" as from June 2006. This appears to have gained a good reaction from most sectors of the media and with the members of the organization.

In **Spain** a press release was sent out on the 8th February. The press conference was held on the 14th February. Participants were Dr Ignacio Moncada (President of the Spanish centre, AESS), Dr Martin Morales (General Secretary AESS) and Dr. Cristina Fernández-Micheltorena a GP physician working in primary care and a member of the AESS Board of Trustees.



Press release headline was "Four years of silent suffering for men and nearly five for women before they decide to seek help for their sexual dysfunction". Main messages: "Love and an active sex life improve people's the quality of life" and "Highlight the importance of communication within the couple as one of the most important factors in finding solutions to problems of sexual dysfunction". Press material included a 3-page press release and a PowerPoint presentation with results of the calls received at the helpline in 2005. The press attracted very good media coverage, including TV news channels, general and specialised press.

Campaign posters were distributed to health centres throughout Spain.

Have you read? Best of the Best: Clinical

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



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Erectile Dysfunction

Corona G et al: Phosphodiesterase type 5 (PDE5) inhibitors in erectile dysfunction: The proper drug for the proper patient. J Sex Med. 2011 Dec;8(12):3418-32.

Erectile dysfunction (ED) is a very common multidimensional disorder affecting men worldwide. Physical illness, reaction to life stresses, or an unhappy couple relationship influence clinical outcome. Phosphodiesterase type 5 (PDE5) inhibitors are recognized as efficacious and well tolerated, and are the first-line treatment for ED. Sildenafil, tadalafil, and vardenafil are the most widely used and studied PDE5 inhibitors. Data acquired during a routine diagnostic workup for ED should be taken into account when choosing the best PDE5 inhibitor for the individual patient, creating an individualized treatment plan, and going beyond “experience-based” subjective opinion and unfounded ideas and prejudice regarding currently available drugs. As the process of matching a given patient’s profile to any selected PDE5 inhibitor often relies more on physician’s personal convictions than on solid evidence, the aim of this review is to identify the main clinical, demographic, and relational factors influencing the choice of the PDE5 inhibitor to be used for the treatment of ED. A systematic literature search and current treatment guidelines were evaluated in a systematic manner. The main clinical, cultural, and demographical factors to be considered for the treatment of ED have been identified. Main factors influencing the choice of the treatment for ED have been described. A short list of items that may help in choosing the right PDE5 inhibitor for the treatment of different patients in daily clinical practice has been prepared. The simple algorithms prepared should

be a useful tool to be used in daily practice, which may help in choosing the right treatment for each subject affected by ED.

HPV

Hartwing S et al: Estimation of the epidemiological burden of human papillomavirus-related cancers and non-malignant diseases in men in Europe: A review. BMC Cancer. 2012 Jan 20;12(1):30.

The role of human papillomavirus (HPV) in malignant and non-malignant genital diseases in women is well known and the corresponding epidemiological burden has been widely described. However, less is known about the role of HPV in anal, penile and head and neck cancer, and the burden of malignant and non-malignant HPV-related diseases in men. The objective of this review is to estimate the epidemiological burden of HPV-related cancers and non-malignant diseases in men in Europe. The annual number of new HPV-related cancers in men in Europe was estimated using Eurostat population data and applying cancer incidence rates published by the International Agency for Research on Cancer. The number of cancer cases attributable to HPV, and specifically to HPV16/18, was calculated based on the most relevant prevalence estimates. The annual number of new cases of genital warts was calculated from the most robust European studies; and latest HPV6/11 prevalence estimates were then applied. A literature review was also performed to retrieve exhaustive data on HPV infection at all anatomical sites under study, as well as incidence and prevalence of external genital warts, recurrent respiratory papillomatosis and HPV-related cancer trends in men in Europe. A total of 72,694 new cancer cases at HPV-related anatomical sites were estimated to occur each year in men in Europe. 17,403 of these cancer cases could be attributable to HPV, with 15,497 of them specifically attributable to HPV16/18. In addition, between 286,682 and 325,722 new cases of genital warts attributable to HPV6/11 were estimated to occur annually in men in Europe. The overall estimated

epidemiological burden of HPV-related cancers and non-malignant diseases is high in men in Europe. Approximately 30% of all new cancer cases attributable to HPV16/18 that occur yearly in Europe were estimated to occur in men. As in women, the vast majority of HPV-positive cancer in men is related to HPV16/18, while almost all HPV-related non-malignant diseases are due to HPV6/11. A substantial number of these malignant and non-malignant diseases may potentially be prevented by quadrivalent HPV vaccination.

Disorders Of Ejaculation

Cindolo L et al: The influence of ejaculation and abstinence on urinary flow rates. NeuroUrol Urodyn. 2011 Nov;30(8):1571-5.

To investigate the relationship between urinary flow rate and ejaculation in healthy young men. Young men were voluntarily enrolled in the study. All subjects were healthy, and sexually active, without neurological diseases, genital, or urethral surgery and they were not under any medications. Subjects were evaluated with ultrasound, uroflowmetry, and post-void residual urine (PVR) measurement. All subjects were followed for 22 days (T) with daily uroflowmetry, and were instructed to ejaculate only on specific days (0, 6 and 22) during the study period. On days 0, 6 and 22 uroflow measurements were performed between 2 and 6 hr following ejaculation. Uroflowmetry parameters before and after ejaculation and during abstinence were compared. Data presented a non-normal distribution and the non-parametric Wilcoxon-match-paired test and Kruskal-Wallis test were used for statistical analysis. 18 subjects (mean age 27.4 years) completed the study. A total of 414 uroflow charts were collected. A statistical significant increase in Qmax was observed after ejaculation (T-1 Qmax: 22.7 ± 5.4 vs. T0 Qmax: 25.7 ± 8, P = 0.002; T5 Qmax 23.2 ± 5.4 vs. T6 Qmax 25.4 ± 8, P = 0.031; T21 Qmax 21 ± 4.8 vs. T22 Qmax 24.5 ± 7.9, P = 0.031). Sexual abstinence resulted in a progressive, statistically significant decline in Qmax rates (T0 Qmax 25.7 ± 8 vs. T5 23.2 ± 5.4 P = 0.035; T6 Qmax 25.4 ± 8

Have you read? Best of the Best: Clinical

vs. T21 Qmax 21 ± 4.8 , $P=0.01$). PVR did not change during the study period. Our results suggest that in young healthy men micturition might be influenced by ejaculation. Our findings, if confirmed in larger series of patients with LUTS, should support that sexual status and activity could represent an important confounding factor in the interpretation of uroflowmetry traces.

FSD

Leeman LM, Rogers RG.: Sex after childbirth: Postpartum sexual function. *Obstet Gynecol.* 2012 Mar;119(3):647-55.

Pregnancy and childbirth bring many changes to the health and well-being of new mothers. Postpartum sexual health is a common concern that is often not discussed during prenatal or postpartum care and has received little attention from either clinicians or researchers. In this article, we review current theories of female sexual response, the epidemiology of postpartum sexual dysfunction, and the use of screening tools to identify women with sexual health concerns. Specifically, we present a review of published data regarding the effect of mode of delivery, perineal lacerations, postpartum depression, and breastfeeding on postpartum sexual activity and function. Finally, suggestions for how to screen for and approach the treatment of postpartum sexual problems are presented.

FERTILITY

Hoover P and alt: Do men with prostate abnormalities (prostatitis/benign prostatic hyperplasia/prostate cancer) develop immunity to spermatozoa or seminal plasma? *Int J Androl.* 2012 Feb 9.

Prostate is an immunocompetent and not an immunoprivileged organ. It has an active immu-

nologic armamentarium. There are three major prostate abnormalities namely, prostatitis, benign prostatic hyperplasia (BPH) and prostate cancer. In all these abnormalities, infection/inflammation has been implicated. As infection/inflammation of the male genital tract can also be involved in induction of antisperm antibodies (ASA), this study was conducted to examine if these prostate abnormalities lead to the formation of ASA, men with chronic = ASA. Sera were obtained from normal healthy men ($n = 25$), men with prostate cancer ($n = 20$), men with BPH ($n =$ prostatitis ($n = 10$). The presence of antisperm antibodies against = and immunoinfertile men (n lithium diiodosalicylate (LIS)-solubilized human sperm extract (HSE), seminal plasma and synthetic peptides based upon sperm-specific antigens namely fertilization antigen (FA-1) and YLP(12), were analysed using the sperm immobilization technique (SIT), tray agglutination technique (TAT), enzyme-linked immunosorbent assay (ELISA) and indirect immunobead binding technique (IBT). All the sera from normal men and men with prostate abnormalities (chronic prostatitis/BPH/prostate cancer) were found to be negative in SIT and TAT. In ELISA, a few sera from men having prostate abnormalities (4 – 24 %) showed a weak positive immunoreactivity (2 – 3 SD units) with some of the spermatozoa/seminal plasma antigens. Majority of the samples did not show any immunoreactivity (<2 SD units) in ELISA. Even the samples that showed a weak positive immunoreactivity in ELISA did not bind to live human sperm in IBT, indicating lack of sperm binding antibodies in these sera. In all these assays, the sera from immunoinfertile men were positive. Our findings indicate that chronic prostatitis, BPH and prostate cancer do not induce antibodies to spermatozoa, sperm-specific antigens and seminal plasma components. Although prostate is an immunologically competent organ, and its abnormalities cause a rise in circulating prostate-specific

antigen (PSA), it appears that there is no concomitant induction of immunity to spermatozoa/seminal components including sperm-specific fertility-related antigens, thus not causing ASA-induced immunoinfertility. This is the first study to our knowledge reporting the absence of ASA in men with BPH and prostate cancer.

Penile Surgery

Garaffa G et al: The management of residual curvature after penile prosthesis implantation in men with Peyronie's disease. *BJU Int.* 2011 Oct;108(7):1152-6.

To report our experience in the management of residual curvature after implantation of a penile prosthesis in men with Peyronie's disease (PD). From January 1985 to June 2009, 62 (29%) of the 209 patients with PD that have undergone the insertion of a penile prosthesis have required an additional straightening procedure to correct the residual curvature after the insertion of the cylinders of the implant.

- ▶ The types of additional manoeuvres, their success in correcting the residual curvature and eventual complications have been reported. Among the additional straightening procedures, modelling was more successful in achieving straightening when performed on an inflatable device (84 %) than on a malleable implant (54 %).
- ▶ If the curvature persisted after modelling or if the curvature was ventral, straightening was achieved with tunical plications or incision with or without grafting. Although it is common for the simple implantation of cylinders alone to straighten the penis, some patients will present a residual curvature that must be successfully corrected with additional straightening procedures.

Have you read? Best of the Best: Research

by Dr. Javier Angulo



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Erectile function – Modulation of nitreergic responses

Activation of muscarinic receptors inhibits neurogenic nitric oxide in the corpus cavernosum

Senbel AM, Hashad A, Sharabi FM, Daabees TT. *Pharmacol Res* 2012; 65: 303-311.

Rapid release of nitric oxide (NO) from parasympathetic nerve terminals in corpus cavernosum and penile arteries is likely the first local event triggering an erection. Modulation of this nitreergic neurotransmission would therefore importantly influence erectile function. Senbel and collaborators have investigated the effects of cholinergic modulation on erectile responses in rats and on nitreergic relaxations as well as the influence of sildenafil-induced effects on these responses.

Enhancement of cholinergic transmission with intravenous neostigmine complexly influences erectile responses in rats, causing inhibition at low dose and potentiation at higher doses. This potentiating effect is observed at low frequencies of stimulation but is lost at the highest frequencies. This puzzling picture could be explained by a stimulation of muscarinic M3 receptors in endothelium promoting NO release and favoring erectile responses. The potentiating effect would decline due to feedback regulation by excessive NO/cGMP production. This hypothesis is supported by the inhibitory effect driven by atropine (muscarinic antagonist) on erectile responses. However, acetylcholine seems to exert different actions on NO/cGMP pathway function in

corpus cavernosum. Neostigmine at low doses (0.1 μ M) causes inhibition of nitreergic relaxations suggesting a negative modulation of nitreergic responses by acetylcholine. In contrast, a higher dose (10 μ M) promotes potentiation of nitreergic relaxations. The fact that atropine blunts the inhibitory effect of neostigmine together with the observed potentiation of nitreergic relaxations by nicotine led to the conclusion that cholinergic transmission modulates nitreergic responses through inhibitory muscarinic receptors while a larger cholinergic stimulation would increase NO synthesis through nicotinic receptors. This would also explain the reduction caused by neostigmine in the potentiating effects induced by sildenafil on nitreergic responses in vivo and in vitro.

The existence and functional relevance of cholinergic neurotransmission in human corpus cavernosum has been known for a long time (Sáenz de Tejada et al. *Am J Physiol* 1998;254:H459-67) while a negative modulation of NO release through activation of prejunctional muscarinic receptors in nitreergic nerve terminals has been demonstrated in monkey corpus cavernosum (Ayajiki et al. *Hypertens Res* 2009;32:685-9). The work by Senbel and collaborators points to a complex effect exerted by cholinergic stimulation on NO/cGMP pathway in erectile tissue driving both stimulatory and inhibitory effects at different levels. Modulation of cholinergic control on nitreergic responses could obviously have therapeutic implications in erectile dysfunction, mainly when both cholinergic and nitreergic innervations coexist (if not being the same structural entities) in corpus cavernosum. However, a previous step would involve the characterization of specific muscarinic receptor subtype involved in inhibition of nitreergic responses to use antagonists targeting the subtype inhibiting NO release from nerves but lacking activity on M3 receptors (assuming both subtypes are different) that promote NO release from the endothelium.

Erectile physiology – A role for urotensin II

Endogenous urotensin II selectively modulates erectile function through eNOS

d'Emmanuele di Villa Bianca R, Mitidieri E, Fusco F, D'Aluto E, Grieco P, Novellino E, Imbimbo C, Mirone V, Cirino G, Sorrentino R. *PLoS One* 2012;7:e31019.

Urotensin II (Ull) is an 11 amino acid cyclic peptide originally isolated from the goby fish. The amino acid sequence of Ull is exceptionally conserved across most vertebrates. Ull binds to a G protein-coupled receptor, the urotensin receptor (UT). Ull and its receptor, UT, are widely expressed throughout the cardiovascular, pulmonary, central nervous, renal, and metabolic systems. Although it is considered the most potent endogenous vasoconstrictor, Ull is also able to cause vasodilation in some vascular beds. In fact the authors of the present article have previously reported that UT is expressed in the endothelium of human corpus cavernosum (HCC) and that Ull causes HCC relaxation and increases intracavernosal pressure in vivo in rats (*J Sex Med* 2010;7:1778-86).

In the present work, d'Emmanuele di Villa Bianca and collaborators detect gene expression of Ull in HCC, demonstrating local synthesis of Ull. They also confirm the involvement of NO pathway on relaxant effects driven by Ull. Stimulation with Ull triggers interaction of UT with eNOS as shown by co-immunoprecipitation. Consistent with eNOS activation, Ull increases nitrite+nitrate (NO derivatives) in HCC. The Ull-induced stimulation of NO production by eNOS is produced by promoting phosphorylation of eNOS at Ser1177 residue (a more active conformation) through phosphatidylinositol-3 kinase (PI3K)/Akt pathway as demonstrated by increased ratio of phosphorylated eNOS content and by the reversion of both phosphorylation and relaxation by an inhibitor of PI3K (wortmannin). The activation

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process is also dependent on the participation of Hsp90 which is a known factor involved in eNOS activation.

This paper proposes a role of endogenous Ull in erectile physiology and suggests the existence of a novel target having potential pharmacological implications in the therapy of erectile dysfunction.

However, although Ull/UT pathway is convincingly demonstrated to activate eNOS and promote relaxation of HCC, this interesting investigation opens the door to novel questions. First, **considering the potent vasoconstrictor effects of Ull in some vessels, the effects of Ull in penile arteries which are fundamental for hemodynamics of erection should be determined.** On the other hand, it is necessary to consider the fact that **levels of Ull have been demonstrated to be elevated in pathological conditions such as hypertension, atherosclerosis and diabetes which are also associated to erectile dysfunction.**

Diabetic ED – Altered expression of angiogenic factors

Differentially expressed angiogenic genes in diabetic erectile tissue – Results from a microarray screening.

Castela A, Soares R, Rocha F, Medeiros R, Ribeiro R, Monteiro C, Gomes P, Vendeira P, Virag R, Costa C. *Mol Genet Metab* 2012;105:255-262.

Erectile dysfunction associated to diabetes is one of the main focuses in preclinical research in erectile dysfunction. Defective production/activity of angiogenic factors has been proposed to contribute to cavernosal alterations leading to erectile dysfunction in diabetes. In fact, administering or enhancing expression of angiogenic factors (vascular endothelial growth factor - VEGF, fibroblast growth factor - FGF, insulin-like growth factor-1 – IGF-1) results in improved cavernosal and/or erectile function in diabetic animals.

Castela and co-workers have evaluated the angiogenic molecular changes occurring with the course of diabetes in corpus cavernosum from streptozotocin-induced (type 1) diabetic rats and they have confirmed the results in corpus cavernosum from diabetic patients. Determinations in rats were performed at 2 and 8 weeks to analyze the influence of diabetes duration on molecular alterations in corpus cavernosum. Cavernosal samples were analyzed using a microarray system to determine mRNA expression of a broad spectrum of genes mainly related to angiogenesis and vascular function. No significant molecular alterations were observed after 2 weeks of diabetes but 8 weeks after induction of diabetes 10 angiogenesis-related genes were down-regulated in corpus cavernosum from diabetic rats. These include genes involved in angiogenesis (Nrp1, Serpinf1, Igf1, Pdgfa), cGMP generation (Npr1), chemokine activity (Ccl2, Ccl11, Tnfsf12), proteolysis (Plau) and inflammation (Ptgs1). Interestingly, VEGF and VEGF receptors genes were not altered. Reduced expressions of genes codifying for IGF-1 (Igf1) and natriuretic peptide receptor-1 (NPR-1; Npr1) were also demonstrated by quantitative RT-PCR. Down-regulation of IGF-1 was also confirmed by immunohistochemistry and dual immunofluorescence for IGF-1/ α -smooth muscle actin (α -SMA) in human corpus cavernosum from diabetic patients with ED. IGF-1 was localized in smooth muscle cells (SMC) and some endothelial cells. These methodologies also confirmed the reduced expression of NPR-1 in cavernosal specimens from diabetic ED patients. NPR-1 was localized in trabecular fibroblasts and SMC.

This work supports the idea that angiogenic factors are important in preserving cavernosal function and structure and down-regulation of these factors in advanced stages of diabetes (8 weeks-diabetes in this model is associated with erectile dysfunction) would contribute to a dysfunctional cavernosal tissue.

In fact, gene therapy targeted to increase IGF-1

has been shown to improve erectile responses in diabetic rats. On the other hand, NPR-1, a cGMP-generating receptor was shown to promote vascular regeneration and cavernosal relaxation.

Then, strategies directed to prevent loss of angiogenic factors in diabetic corpus cavernosum would favorably impact erectile function in diabetes even though that angiogenic factors could contribute to preserve cavernosal cell architecture rather than to promote neovascularization.

Diabetic ED – Increased number of endothelial progenitor cells by melatonin

Mobilisation of endothelial progenitor cells: one of the possible mechanisms involved in the chronic administration of melatonin preventing erectile dysfunction in diabetic rats.

Qiu XF, Li XX, Chen Y, Lin HC, Yu W, Wang R, Dai YT. *Asian J Androl* 2012 [Epub ahead of print].

While the previous paper points to a deficit in angiogenic factors as a possible pathophysiological manifestation of diabetic ED, the present paper deals with another player in angiogenesis, the endothelial progenitor cells (EPCs). Qiu and collaborators evaluate the effects of melatonin administration on circulating EPC number in the same above mentioned rat diabetic model.

Intraperitoneal administration of melatonin for 8 weeks (10 mg/kg/day) partially prevented the reduction on circulating EPC number in diabetic animals and also partially preserved erectile responses in these animals. The loss of endothelial cell content in cavernosal tissue of diabetic rats is significantly attenuated by melatonin administration while smooth muscle content in this tissue, which is also reduced by diabetes, is not modified by melatonin treatment. These positive effects on erectile function and endothelial cells by melatonin is not related to an improvement of systemic blood glucose homeostasis but it is associated with preservation of the activity

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of the superoxide scavenger, superoxide dismutase, in bone marrow. This is parallel to attenuated elevation of the oxidative stress marker, malondialdehyde, in bone marrow from diabetic rats. Since EPCs are thought to be derived from bone marrow stem cells **the study proposes that oxidative stress induced by diabetes would compromise generation of EPCs by bone marrow while the antioxidant effects of melatonin in bone marrow would maintain production of EPCs. This effect would therefore be responsible for the beneficial effects of melatonin on cavernosal endothelium and erectile function in diabetic rats.**

There is no doubt about the association of reduced circulating EPC with aging as well as with cardiovascular risk factors as diabetes.

In fact, reduction of circulating EPC correlates with impaired endothelial vasodilation in such conditions. Erectile dysfunction has also been associated with reduced number of circulating EPCs. However, we have to consider that all those evidences provide associative but not causal relationships. The role of EPCs in vascular and cavernosal function still present some gaps. For instance, although the role of EPCs in angiogenesis is well established, the involvement of EPCs in preservation and/or repair of endothelial cells is not completely elucidated. In addition, EPCs seem to be composed by a relatively heterogeneous cell population. The cell population evaluated in the present study (CD34+/KDR (VEGFR2)+) is probably the most widely used cell population for determining circulating EPCs but a consensus on the

markers that EPCs have to present has not been achieved.

Although the molecular mechanism is not fully established, melatonin is considered to act as an antioxidant. Melatonin has been previously reported to have an impact on sexual function. It is known its role at nervous central system level in sexual behavior but melatonin has shown to improve cavernosal function in pro-oxidant situations such as ischemia-reperfusion and diabetes in animal models. **Thus, in addition to the demonstrated increasing effect on number of circulating EPCs in diabetic rats, a potential positive impact of melatonin at cavernosal level could also account for the beneficial effects of melatonin on erectile responses in these animals.**

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Case reports from ISSM list

by Javier Romero Otero, Eduardo Garcia Cruz



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Ability to document true erectile dysfunction

Dear lecturers, this number I would like to reproduce a conversation held in the ISSM list about one interesting and practical issue: how to document true erectile dysfunction. The expert comments are coming from Dr. Natalio Cruz, one of our most important and active andrologists. Hope all of you will find as interesting as we did this issue.

Have a question regarding the ability to document the presence of true erectile dysfunction vs alleged erectile dysfunction for secondary gain... such as a workers compensation case or a malpractice case. I have seen several patients over the years with complaints of erectile dysfunction after such things as a motor vehicle accident, a fall while at work, etc. ...and also with occasional allegations of negligence or malpractice. Along that line, I am not sure how best to document the presence of true ED in this setting, as patient may have secondary gain (financial or otherwise) in alleging the presence of this problem as part of damages. I wonder whether a rigi-scan, snap gauge, etc. is good enough, and reliable enough to confirm the presence of his erectile dysfunction. I had a rigi-scanner in the past, but got rid of it years ago.

Barry Rossman, MD
Assistant Clinical Professor of Urology
University of Medicine & Dentistry of New Jersey
University Medical Center at Princeton

I am using the Rigiscan less day by day. In my experience, the Rigiscan's results are trust less and highly variable depending on the clinical setting (patient, place where the patient sleeps, ...). So I only consider its results when they support my clinical judgement. Thus, which is the point in

asking if the result will not make the difference? Nowadays, I only ask for it to support my diagnosis in males with suspected psychological ED. If we consider Rigiscan for legal documentation, I would be even more critic considering the fact that non sleeping would be equalled to severe ED.

Eduard García-Cruz
Unidad de Andrología / Andrology Unit
Hospital Clínic de Barcelona, Spain

In situations of suspected secondary gain or in cases of professional liability litigation, it is imperative that an attempt be made to objectively document erectile function or dysfunction. Nocturnal Penile Tumescence Monitoring (NPTM) is one of the ways that one can go about getting this information. The Rigiscan measures (NPTM) and is a tool which may be helpful in providing objective (NPTM) information. Though not perfect, it can give valuable information if properly employed in the proper setting. It can be programmed, to allow the investigator an opportunity to know if the instrument has been tampered with during the study, thus rendering the information useless. Ideally, it could be done in a sleep lab where an independent observer is verifying the information simultaneously with the Rigiscan. At least two nights of study should be done and where the information is contradictory, even a third night should be considered. Obviously, a sleep lab is more expensive, but where hundreds of thousands or millions of dollars may be at stake, the cost is minimal by comparison.

Don Mode, M.D.
Associate Clinical Professor of Urology
Medical College of Georgia

The Rigiscan fell out of favour several years ago, but I have continued to use it, and find it quite useful. Like any test-eg, PSA, prostate biopsy, pharmacodynamic penile US- it has its strengths and limitations. It is especially helpful in assessing a man with possible psychogenic ED, since the presence of one or more rigid, well-sustained erections during nocturnal testing is compelling evidence of adequate neurovascular erectile function. However there may be multiple reasons why a study may show poor or absent erectile activity, which is why its use is limited in legal cases where a man wishes to show he has ED. In those cases, it may be preferable to refer the man to a formal sleep lab, many of which are still able to monitor for erection with a strain gauge while documenting sleep patterns.

Abraham Morgentaler, MD, FACS
Director, Men's Health Boston
Associate Clinical Professor of Urology
Harvard Medical School

The cost of the "new" regiscan (I am presuming used just a little) only serves to emphasize how little utility it really has in the setting of ruling in or out ED for secondary gain, or even in our practice for patients who don't have those sorts of issues. In a court case (workers comp as well) one has to demonstrate a medical "probability" (defined as greater than 50% chance) in order to prevail on an issue. Almost anything is a medical possibility (defined as anything greater than a 1% chance). So in cases of slips and falls, MVAs, etc there is no device that is going to establish without question a causal relationship between ED and the "incident". One person has suggested sleep labs in combo with a rigiscan and if an insurance company would be willing to pay for all of that then it might be helpful but a good defense attorney is going to blow a million holes in the false positive/negative rates associated with those studies. As the founder of the Medicare Carrier Advisory panel for the AUA some 15 years ago it became quite clear that "testing" to prove ED wasn't really very cost

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effective (there are a few exceptions – which especially those who own and do a lot of penile duplex ultrasonography will probably {remember > 50 % likelihood} be quick to defend). There are medical/surgical instances where we know without a lot of testing that what the patient tells us during our history taking is medically “probable” {10 year hx of IDDM, pelvic surgery-colon, rrp, etc, pelvic crush injuries, AAA repairs, etc} there are other instances where we just don’t know with that same degree of “probability” (slips and falls, MVAs, etc). So Medicare has ruled most of those studies are NOT medically reasonable or necessary in those cases (IDDM, AAA, RRP, cystectomy, etc) – and that means they don’t/won’t pay. So I have come to the conclusion that it is a good thing that we are Docs and not private investigators or trial attorneys who want/need black and white answers (not to mention our testimony) and we are left taking our patients’ word. At the end of the day, since we do have to sleep night, I believe we have to tell those who ask us that we don’t know with certainty if the patient is being honest with us or not and no test exists that is absolute.

Marty Dineen

I had an interesting case in this area a few years ago. I was asked by a defense attorney to examine a patient who was accused of rape and claimed innocence on grounds that he was impotent. I performed penile Doppler after injecting him with a standard dose of pge1. The results were quite clear and showed little or no erectile reaction and very poor hemodynamics even after a repeat injection. In court, the District Attorney who was prosecuting

(and the presiding judge) would not allow me to conclude that the patient could not have committed the crime because he was impotent – although that is what I would have said. I did describe the test and results to a jury but I’m not sure they understood. In follow up, the man was convicted and imprisoned. Shortly thereafter the D.A. who had prosecuted was shot and killed. I still wonder about a connection. I think a properly performed Doppler can prove true ED beyond reasonable doubt when the impotence is severe. Obviously, it would be less useful in marginal cases.

Fred Grossman MD
Male Care Center – Denver, CO USA

In my opinion, whatever method you use must be done in a controlled setting (not at home) with an available observer and be performed on several occasions. I think that snap gauges are not sensitive enough and I should think that Rigiscans are probably the most sensitive and reliable items out there. The units do have to be checked for reliability every so often. TIMM medical does calibrate these for a year.

S.A.Liroff, M.D.
Senior Staff
Vattikuti Urology Institute

A normal rigiscan shows a normal capacity but as with all else in ED there is so much supra tentorial input that a negative response can easily be a false negative. Throw in avarice with conniving patients and you can get a false negative if they put it on

a rubber phallus and leave it on all night. I have used Doppler’s to document the presence (or absence) of a normal flow and even a normal erectile response to injectables. That does not mean they do not have a physical problem as they may have anxiety in a sexual setting leading to elevated circulating catecholamines etc. however, if they are claiming damage to the vascular tree from an accident and they have a normal vascular response it often gives the judge something to think about. As well if they claim curvature due to a traumatic induced peyronies plaque and the shaft is straight when rigid you can also disprove their claim. My most interesting claim was someone accused of rape and he was sent to me as his defense was a severely curved penis, which the “rapee” when asked said it was a normal looking penis. I was able to document an almost 180 degree curve.

Nachum M. Katlowitz, MD
Director of the Division of Urology
in the Department of Surgery
Staten Island University Hospital, Staten Island,
New York

It was Dr. Ismet Karacan who developed and validated NPT as a meaningful diagnostic tool for men complaining of ED. This development followed his decades of using NPT to evaluate sleep disorders which was his primary research interest. When we developed the inflatable penile implant at American Medical Systems we needed a reliable means to differentiate between physical versus emotional causes of ED; the NPT monitor we developed at AMS was the first commercial product available to meet this need. I

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merely added the capability of measuring hardness or rigidity of the erectile episodes when the man was suspected of having a progressively deteriorating erectile capability due to chronic hypertension or diabetes or some similar condition. In the 4000+ males Dr. Karacan studied in his fully equipped sleep lab he found that none of them could go for three nights without sleeping; hence the recommendation that NPT and Rigidity monitoring be done for three nights. Later research has shown that there may be confounders in the differential diagnosis, however, such as certain mental or sleep disorders in which little or no tumescence activity is observed. Hence when involved in a litigation issue you need to be able to rule out these possibilities. I know that my former company, Timm Medical Technologies which purchased this former Dacomed product, still services them and may also know how you could obtain access to one for your purposes. Here is contact information for TMT:

Marcus J Raphael,
Gerald W. Timm, PhD
President and Founder GT Urological, LLC, and
Professor of Urological Surgery
University of Minnesota

I have read with interest, the remarks of others regarding the pros and cons of Rigiscan utilization. As with any method of study we currently use in the management and treatment of ED; they all have their pluses and minuses. None are pure and accurate 100% of the time, i.e., penile doppler studies, cavernosometry, cavernography, Rigiscan, hormone studies. We use them as “tools” accepting their shortcomings and interpreting them in conjunction with the

patient’s history and physical findings (as aids in diagnosis and management). It doesn’t mean we should give them up, nor employ each and every test in each and every patient; yet trying to improve on them and use them when appropriate. Thanks for the enlightening discussion by all and to Dr. Rossman for “revisiting” this subject.

Don Mode, M.D.
Associate Clinical Professor of Urology
Medical College of Georgia

This topic is particularly interesting for several reasons:

- ▶ The first is because throughout our practice all professionals who are dedicated to Sexual Medicine have been, or will be, in a similar situation at some time where we have to determine a man’s erectile function or dysfunction as experts on the subject. Sometimes it may be to clarify whether the cause is iatrogenic, while on other occasions the aim is to provide evidence for legal procedures. Finally it could just be from a medical standpoint as part of the diagnosis process. It will always be extremely difficult to determine the exact erectile function of an individual.
- ▶ The second is derived from the very nature of Sexuality, which is always conditioned by subjective factors related to the individual’s circumstances, the spontaneity of sex, the couple, the background, etc. These factors affect their sexual response.
- ▶ The third is related to the evaluation of the erectile function. No test is completely reliable, unquestionable and infallible in this regard.

Taking into account all these aspects, we appreciate these very valuable and interesting contributions from different colleagues, the ISSM-list contributors. The Rigiscan should be evaluated with caution: It should be used with the highest level of objectivity, under the necessary conditions to ensure reliability of the results (sleep laboratory for three consecutive nights, etc.). These are not always available at some centers. Personally I think that color duplex ultrasound doppler, which provides a very rough picture of penile vascular status, tends to be more objective and feasible in all centers. We must not forget blood tests, and, of course, individual sexual and clinical records especially focused on whether there is any spontaneous erection in any circumstances at any time (even not related to sexual arousal).

The completion of an expert medical report on erectile function has to be taken as an approximation, as close as possible to reality, with the maximum amount of objective data we have available at that moment: Rigiscan, Doppler, Lab, etc. Furthermore, we can’t confirm anything about the previous sexual function. In conclusion we and everybody else must accept that this report will never reflect the reality, taking into account that personal sexual response with a partner in real life will always be different from any test in a hospital environment or lab.

Natalio Cruz / Head of the Andrology Unit
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Meetings and Events Calendar 2012



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MAY 2012

10th Annual meeting of Mediterranean Society for Reproductive Medicine Symposium. Mediterranean Society for Reproductive Medicine – MSRM in association with Montenegro Society for Human Reproduction
May 10 – 12, 2012
Location: Budva, Montenegro
Website: <http://www.msrm2012.org>

7th Annual General Meeting Association of Biomedical Andrologists (ABA)
May 18, 2012
Location: Marriott Hotel, Leeds, UK
Website: <http://www.aba.uk.net>

AACE 21st Annual Meeting and Clinical Congress
May 23 – 27, 2012
Location: Marriott Philadelphia Downtown and the Pennsylvania Convention Center, USA
Website: <http://www.aace.com>

JUNE 2012

2012 Joint International Congress of the ASRI and the ESRI
May 31 – June 2, 2012
Location: Hamburg, Germany
Website: www.asri-esri-2012.de

Taking Liberties: Sex, Pleasure Coercion (1748 – 1928)

June 15 – 17, 2012
Location: Newcastle upon Tyne, United Kingdom
Website: <http://conferences.ncl.ac.uk/taking-liberties/>

JULY 2012

ESHRE 2012
July 1 – 4, 2012
Location: Istanbul, Turkey
Website: www.eshre.eu

Society of Reproduction and Fertility 2012 Conference
July 09 – 11, 2012
Location: The John McIntyre Conference Centre, Pollock Hall, Edinburgh, UK
Contact: srf@portland-services.com
Website: www.srf-reproduction.org/meetings.aspx

International Congress on Cell Biology (ICCB2012) / joint with the Meeting from the Brazilian Society of Cell Biology and International Federation of Cell Biology
July 25 – 28, 2012
Location: Rio de Janeiro, Brazil
Website: www.sbbc.org.br/iccb2012

Biennial Meeting Association for Applied Animal Andrology (AAAA) "Andrology QA / Biosecurity"
July 28 – 29, 2012
Location: Vancouver Community College, Vancouver, BC, Canada
Website: <http://www.animalandrology.org/futuremeetings.htm>

AUGUST 2012

VI Congresso Internacional de Estudos sobre a Diversidade Sexual e de Gênero.
August 1 – 3, 2012
Location: Salvador (BA), Brazil
Website: <http://www.abeh.org.br/>

SSR's 45th Annual Meeting Applied Reproductive Biology: Making it Relevant
August 12 – 15, 2012
Location: The Pennsylvania State University State College, Pennsylvania, USA
Website: <http://www.ssr.org/Meetings.shtml>

SMSNA/ISSM Joint Annual Meeting.
Sponsor: Sexual Medicine Society of North America
August 26 – 30, 2012
Location: Sheraton Chicago Hotel and Towers, Chicago, IL, USA
Website: www.smana.org

The First Qualification Examination and Preparation Courses 2012



Fellow of the European Board of Sexual Medicine (FEBSM)

Sexual Medicine is a discipline concerned with the impact of physiology and pathophysiology, psychology and psycho-pathology, relationships, socio-cultural influences, developmental effects, sexual identity, sexual behaviours, gender identity and inter-gender differences on the sexuality of men and women of all ages, both as individuals and within the context of their relationships. Its aim is the restoration of sexual health, a state of complete physical, mental, and social well-being with respect to sexuality, as well as the management of sexual problems.

The Multidisciplinary Joint Committee on Sexual Medicine (MJCSM) was established by the UEMS specialist sections of Urology, Obstetrics and Gynaecology and Psychiatry and functions within the framework of their respective statutes and bylaws. The main objective is to guarantee the highest standards of health care in the field of Sexual Medicine in the countries of the European Union and associated European countries, by ensuring that the training in Sexual Medicine is raised to the optimal level. The MJCSM shall recommend the content of training programmes, the access for training, and professional knowledge and skills for Sexual Medicine.

The MJCSM issue a certificate of recognition of quality of the training programme. Prior to entry into training in Sexual Medicine, candidates should be accredited in a medical specialty relevant to the practice of Sexual Medicine. Such specialties include Urology, Obstetrics and Gynaecology, Psychiatry, Internal Medicine and General Practice, although this is not a comprehensive list.

The MJCSM determine the standards for training and assessment in Sexual Medicine. Successful candidates will be awarded on behalf of the MJCSM the title of "Fellow of the European Board of Sexual Medicine" (FEBSM).

This year the first qualification examination of the MJCSM will take place on **5th December 2012 in Amsterdam**.

Eligibility

The exam is set under the auspices of the UEMS but all nationalities, including countries outside the EU, are able to apply for the exam. The application will be reviewed by the examination committee of the MJCSM.

Who can apply?

▶ FEBSM is a particular qualification in Sexual Medicine awarded under auspices of the UEMS, the EU organisation with responsibility for specialist medical practice. Consequently, only registered medical practitioners, who are accredited as medical specialists in their country of practice, or who are General Practitioners with more than 5 years' clinical experience of unsupervised independent practice, are eligible to apply.

The applicant should deliver:

- ▶ CV with description of his/her educational and clinical experience in the field of Sexual Medicine.
- ▶ A list of publications in the field of Sexual Medicine (not obligatory).
- ▶ All applicants should deliver authenticated proofs of their qualifications.
- ▶ Letter of recommendation by an ISSM/ESSM member is appreciated.

For updates and further information please visit the website

www.essm.org

The First Qualification Examination and Preparation Courses 2012

Examination form

The exam duration will be 3 hours and include 150 MCQ in 5 domains of Sexual Medicine:

- 1. Basic science (including psychology) of the sexual response including sexual development**
- 2. General sexual issues**
 - a. Impact of gender
 - b. Impact of aging
 - c. Sexual orientation
 - d. Ethical and legal aspects
 - e. Historical aspects
- 3. Diagnosis and management of male sexual dysfunctions**
- 4. Diagnosis and management of female sexual dysfunctions**
- 5. Other sexual disorders**
 - a. Gender identity disorders
 - b. Problematic and variant sexual behaviours
 - c. Impact of other conditions including STD, cancer and cancer treatments

The contents will be according to the curriculum of Sexual Medicine defined by the MJCSM. The contents will be described in the syllabus of Sexual Medicine, which will be published in July 2012 by the ESSM educational committee.

Examination fee: EUR 400

ESSM Exam Preparation Courses

This year, ESSM will offer a number of examination preparation courses for medical practitioners intending to take the first FEBSM examination in December 2012.

The courses are intended for physicians with experience of specialist practice in Sexual Medicine who wish to increase their chance of passing the exam.

Preparation courses of 4 days are being planned; these will provide an overview of all subjects in the MJCSM curriculum of Sexual Medicine that may be included in the examination, as well as advice about exam-taking skills and practice in completing a Sexual Medicine MCQ. Specific preparation courses may be offered for physicians who usually work exclusively with one gender or patient group, so that they might have access to extra content to refresh their knowledge of Sexual Medicine with respect to other groups, and couples.

The course teaching faculties will include experts in the field of Sexual Medicine.

The location and specific dates will be published shortly on the essm.org website.

Application will be made for CME recognition for these courses, so that participants may gain CME credits.

Registration fee: EUR 300

Exam date:	5 December 2012
Location:	Amsterdam, The Netherlands
Registration deadline:	5 September 2012

The ESSM School of Sexual Medicine



An invitation to ESSM members...

The 6th ESSM Oxford Sexual Medicine Course, 2012

St Catherine's College Oxford, United Kingdom

Monday, 23th July – Friday 3rd August 2012

and

Sexual Medicine course during the Amsterdam ESSM 2012 Congress

Amsterdam, The Netherlands (with the 2012 ESSM Scientific Congress)

Thursday, 6th to Sunday, 8th December 2012

Dear ESSM Member,

On behalf of our President, Professor Hartmut Porst, and the Executive Committee of ESSM, and the Educational Committee of the ESSM I invite you to apply for the 6th European School of Sexual Medicine programme. A number of ESSM bursaries are available to support the attendance of ESSM members from low-income countries, or those who are experiencing financial hardship; for more information, please see below.

This exclusive benefit is available only to ESSM members.

Background

The European School of Sexual Medicine was a joint venture established by the European Society for Sexual Medicine and the European Federation of Sexology. The first "Oxford Course" was run in 2007; this year, we will deliver a learning curriculum based upon the UEMS Joint Committee for Sexual Medicine syllabus. Our programme is intended for clinicians seeking to acquire the knowledge and skills essential for specialist practice in Sexual Medicine. Medically-qualified participants should find the programme helpful when preparing for the **Fellowship of the**

European Board of Sexual Medicine examination, which will be set for the first time in 2012.

So far, over one hundred and twenty physicians from Europe, Asia, Africa, Australia and the Americas have taken part in the Oxford Programme; they include specialists in andrology, endocrinology, family medicine, gynaecology, internal medicine, psychiatry and urology. Participants will have the opportunity to learn the essentials of sexuality in both men and women that are necessary for effective clinical practice, even for those whose usual practice is exclusively with one gender.

Programme

The Oxford Programme is primarily intended for medically-qualified persons with post-graduate experience in any relevant clinical specialism. Interest in and enthusiasm for Sexual Medicine are the essential qualifications; whilst previous experience in the clinical practice of Sexual Medicine is an advantage, the programme is also suitable for those starting out in this fascinating and rapidly developing area of medicine. Spe-

cial skills in surgery or psychotherapy are not a requirement for participation. Psychologists and therapists are welcome to join the programme but are not eligible to sit the UEMS Fellowship of the European Board of Sexual Medicine exam.

Requirements

Participants must enter the 2012 Oxford Programme at the two-week, residential "Oxford Course" in July/August 2012. This covers a wide range of Sexual Medicine topics and provides the essential background learning from which clinical experience can be developed. A second programme will be held in Amsterdam in December 2012, in conjunction with the ESSM Annual Scientific Congress, so that participants can attend both events. All sessions during the programme will be conducted in the English language; participative learning techniques for skill development will be used, as well as didactic teaching. Working with simulated patients, there will be practical training in Sexual Medicine consultation techniques and history-taking, and in the basic use of sex therapy techniques in Sexual Medicine.

The ESSM School of Sexual Medicine

The academic programme will include

- ▶ sexual development
- ▶ psychology and physiology of sexual desire, arousal and response
- ▶ impact of gender on sexuality
- ▶ ageing and sexuality
- ▶ sexual dysfunctions in men and women
- ▶ problematic sexual behaviour
- ▶ gender identity disorders
- ▶ impact of medical treatments and other health problems on sexuality
- ▶ clinical skills in Sexual Medicine
- ▶ clinical management of sexual disorders
- ▶ sexually transmitted diseases – STD
- ▶ genital dermatology
- ▶ ethical and legal aspects of Sexual Medicine
- ▶ research methods related to Sexual Medicine
- ▶ history of Sexual Medicine
- ▶ standards of care in Sexual Medicine

The course not only aims to add to your knowledge of Sexual Medicine but also to enable you to change your clinical practice with the acquisition of new skills to apply to providing services for patients and to have more confidence in assessing and helping men and women with common sexual concerns.

The two-week course is held at St Catherine's College, a modern College offering high-quality accommodation for participants; it is within 10 minutes walk of Oxford city centre. There

will be an optional and very informal social programme run throughout the course. This is a friendly course and we hope that participants will make new friends, as well as learn about Sexual Medicine. Because the number of participants is strictly limited (see below), there is plenty of opportunity to meet and talk informally with teaching faculty members; group members have the option of joining us for evenings together in Oxford after dinner at the College. Although two weeks may seem a long time to be away from home at a course, feedback from previous groups suggests that loneliness and boredom are not a problem. We are fortunate to be studying such an interesting subject!

The actual running cost of the complete Oxford Programme is more than EUR 3,300.00 per person but it is part-subsidised by generous support from the European and International Societies for Sexual Medicine.

- ▶ The registration fee for the complete programme is EUR 1,500.00, inclusive of tuition fees for both the Oxford and Amsterdam courses, meals and accommodation for the two-week Oxford course, and lunch and refreshment breaks at the Amsterdam course; accommodation costs in Amsterdam, and all travel costs, are not included. In addition, participants will be offered free registration for the 2012 ESSM Congress in Amsterdam.

- ▶ ESSM members from low-income countries, or those who are experiencing financial hardship, may apply for special bursaries, which can cover up to two-thirds of the registration fee.
- ▶ The number of participants in each year of the Oxford Sexual Medicine Programme is limited to 40, so early application is advisable. Bursary applications should be received no later than 31st March 2012; successful applicants will be notified of award of bursaries by 23rd April 2012.

ISSM is likely to offer a similar bursary scheme for ISSM members who are NOT also ESSM members, to assist those from low-income countries, and those who are experiencing financial hardship. A separate letter of invitation and application form will be sent by ISSM to its non-ESSM members.

All ESSM member applicants, whether seeking a bursary or not, should apply using the form below, which must be returned by e-mail to jan@sexualmedicine.org or by fax to **+44 1364 72935**

For further information, please email the Programme Director Dr John Dean c/o jan@sexualmedicine.org

For updates and further information
please visit the website www.essm.org

OXFORD Sexual Medicine Programme 2012

Two-Week Residential Course On Sexual Medicine

St Catherine's College Oxford, United Kingdom

Monday, 23rd July – Friday 3rd August 2012

APPLICATION FORM FOR ESSM MEMBERS

(Non-ESSM members of ISSM should request an ISSM Application Form)

Forename:	Surname:	Title:
Preferred name for delegate badge:		
Place of work:		
Address for correspondence:		
Current Speciality (e.g. urology, family medicine):		
Professional qualifications:		
Mobile:	Email:	
Are you an ESSM member?	Are you applying for an ESSM bursary?	<input type="radio"/> yes <input type="radio"/> no
Do you belong to a national Sexual Medicine society? If yes, please specify:		
Nationality:	Country where you work:	
Any special dietary or other requirements?		
Name and email-address of an ESSM/ISSM member that we may contact, who would be willing to provide a short reference for you:		

You will be notified of the grant amount as soon as possible after 23rd April 2012. If you are not an ESSM member, you MUST join as a full or associate member before a grant can be awarded. You need not delay your application for a grant but the membership fee must be received by the relevant Society before any grant is confirmed.

To join ESSM, visit www.essm.org or contact your national affiliated society.

Current Professional Status (e.g. consultant gynaecologist, specialist trainee in urology, family physician, etc.):



Post-graduate studies (qualifications, dates):

Relevant experience in sexual Medicine:

Research interests and achievements (thesis, grants, publications):

Applicant's Personal Statement

Provide a personal statement describing how participation in the Oxford Summer School will be of benefit to you and to your academic career in particular (maximum 200 words).

If paying the cost of the full course fees would cause you financial hardship, please describe why the grant is of importance to you (maximum 100 words).

Please return your application to: jan@sexualmedicine.org

PAYMENT OF THE ESSM MEMBERSHIP FEE 2012

To be sent back to:

ESSM secretariat – c/o AIM Congress
Via Ripamonti 129 – 20141 Milano, Italy
www.essm.org

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

Membership goes from January to December

New Member
 Member since: _____

Title: _____

Name: _____ Surname: _____

Date of Birth: _____ Nationality: _____

Position held: _____

Institution: _____

Postal address: home work

City: _____ Zip code: _____ Country: _____

Telephone: _____ Fax: _____

Email: _____

First Specialty: _____ Second Specialty: _____

Membership category:

Full Member
 Associate Member

Membership type:

Simple ESSM EUR 50,00
 Combined ESSM + ISSM EUR 120,00

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 2012 by:

Herewith confirms the payment of EUR 120,00 for the ESSM and ISSM membership cost for the year 2012 by:

Bank transfer to AIM Congress srl/ESSM

Bank: Banca Popolare di Milano – Ag. 24 – Milano, Italy
Account N.: 000000024845
Bank codes: CIN K
ABI 05584
CAB 01624
IBAN IT81K055840162400000024845
SWIFT/BIC BPMIITM1024

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

Credit Card: Visa American Express Master Card Eurocard

Credit Card number: _____

Expiration date: _____ CVC Number _____

Holder _____

Holder's Signature _____

Privacy and treatment of personal data

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

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

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

Date _____ Signature _____

For more information please visit www.essm.org



Announcement for the next Congress

15th CONGRESS OF THE EUROPEAN SOCIETY FOR SEXUAL MEDICINE

6 – 8 December 2012, RAI Amsterdam Convention Centre, The Netherlands



Preliminary Topics

Male Sexual Disorders (MSD)

1. Preclinical Research
2. Psychosexual Issues and Management
3. ED Epidemiology and Risk Factors
4. ED and Lifestyle Management
5. ED Conservative/Medical Treatment
6. ED Surgical Treatment
7. Prostate Cancer Treatment and Sexual Rehabilitation
8. Peyronie's Disease
9. Penile Congenital Anomalies
10. Rare Penile Disorders (Priapism, Penile Cancer, Skin Lesions)
11. Genital Reconstructive Surgery
12. Ejaculatory and Orgasmic Disorders
13. Prostate and Male Sexual Health
14. Hormones and Male Sexual Health
15. Homosexuality and Gender Identity Disorders
16. Sexually Transmitted Diseases (STD)
17. Miscellaneous

Female Sexual Disorders (FSD)

1. Preclinical Research
2. Epidemiology and Risk Factors
3. Urogenital Surgery and Women's Sexual Health
4. Cultural and Religious Issues
5. Libido, Arousal and Orgasmic Disorders
6. Pelvic/Genital Pain Syndrome and FSD
7. Recurrent Urogenital Infections and Sex
8. Hormones and Women's Sexual Health
9. Cancer (Breast,Uterus) and Sex
10. MSD and Women's Sexual Health
11. Genital Plastic Surgery and Women's Sexual Health
12. Incontinence and Sex Life
13. Sexual Life in the Elderly Woman
14. Drugs for FSD
15. Psychosexual Interventions in FSD
16. Contraception, Pregnancy and Sex
17. STD Manifestations in Women
18. Commerce and Female Sexuality

Deadline for Abstract Submission: 3 September 2012

Online Submission at: www.essm-congress.org

www.essm.org