

NEWSLETTER



EDITORIAL

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- Letters to the Editor

Press, television programmes and countless scientific meetings hover over and around the field of erectile dysfunction, public tributes to its recent growth. Every few months we hear of a new development in the field: oral agents (at least three at an advanced clinical development stage), transurethral delivery (soon to become available world-wide), creams, improvements in existing injectable drugs as well as the development of other injectables with new drugs or drug combinations, etc. There are an impressive number of ongoing clinical trials and the quality of basic and clinical research in erectile dysfunction has improved enormously over the course of the last ten years. But how and why did this happen? Sometimes it is good to stop, look back and examine the early days of what is now a "booming" field. This month Gorm Wagner gives a historical perspective from the privileged point of view of twenty-five-years as a major research figure and as a witness to a substantial period in the short life of the field of male erectile dysfunction.

Let me first express my gratitude for having been given a platform in the ESIR Newsletter without any specific topic or obligations. After 25 years of activity within academic approach to sexual medicine (basic and clinical research, university teaching etc.) and having served as president to Int. Academy of Sex. Res. (1984),

Int. Soc. Impotence 1988-94, and European Society for Impotence Research 1995-97 I now have some general points of view, which I would like to share with our readers.

Perspectives of impotence in the 20th century.

Psychiatry versus Urology.

Since the introduction of psychoanalysis and different surgical interventions early in this century there were fights back and forth about who should treat these patients. It ended up with an all out war in the US between psychiatrists and urologists in the 1930's (1). The psychiatrists came out as winners for a period of around 50 years.

Twenty-five years ago.

The treatment of the patient with erectile dysfunction, (the p.c.-expression for impotence) had come to a standstill twenty five years ago.

If the patient went to his own physician he would most likely get some ordinary non-professional words about his age, "that we are all going to slow down" and the like. Or he would be given testosterone and after that he was given up on.

If the general practitioner believed in referrals there were two options: an implant or sex-therapy.

Implants were done by a handful of specialised urologists but mostly in

post-traumatic or post-priapism patients. A gradual improvement in surgical procedures and implant material and devices finally led to the current almost perfect technical, mechanical solution.

The so-called modern sex therapy which stormed forward in the 1970's ended up leading nowhere, when it came being able to obtain and maintain an erection sufficient for intercourse.

The urologist looked at the penis only and had no diagnostic tools except for palpation and radiographic visualisation of the corpora.

The sexologist (an unidentifiable figure with no globally authorised training), the psychologist, psychiatrist or psychoanalyst did not even look to see if the patient had a penis, but treated him happily in endless sessions.

But then, within a period of only eight years, the whole field was turned upside down. Not by psychiatry and not by urology.

From 1974 to 1982 revascularisation, pudendal arteriography, dynamic cavernosography, blood flow measurements, Doppler methods, visual sexual stimulation, vibration, in vitro studies and finally pharmacological intervention were described and presented by vascular surgeons, plastic surgeons, radiologists, biochemists, clinical and neuro-physiologists and pharmacologists, but mainly for their own peer-groups.

However, one observant urologist sitting on the other side of the Atlantic turned out to be the mediator and was able to bring these people together in meetings from as early as 1978 followed by 1980 and 1982. The development therefore came to the prompt attention of American urologists who then massively engaged themselves in research and development, which in turn drew the interest of scores of young European residents who went to the US research centres. The build up of interest in the field in Europe has been slower but it is now substantial and the scientific interaction between groups has increased. So finally the urologists were the winners.

What next?

Today when a patient goes to his G.P. with impotence he will most likely be referred to a urologist or a centre for impotence treatment, although not all general physicians have knowledge of the broad spectrum of treatment modalities now available.

But if and when the G.P. gets a tool which is effective and safe, what will happen then? If he/she is well-informed about the patient and better trained in broad knowledge of sexual dysfunction, will

there still be need for a referral? On this we can only speculate, but one thing I will hold for certain: That after 100 years of turmoil for this type of patient it is the patients themselves who will be the winners in the next century.

1. Ballenger EG et al. J. Urol 1936,36,250-254.



Gorm Wagner



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España

PHYSIOLOGY OF “PSYCHOGENIC” ERECTION

Benjamin D. Sachs



Penile erection caused by genital touch is usually termed “reflexive” or “reflexogenic,” and laboratory animals have long been studied to analyse the physiology of reflexive erection. Erotic sights, sounds, or smells (whether current, recalled, or imagined) promote so-called “psychogenic erection” (P.E). Until

recently, we knew almost nothing about the physiology of P.E., because only recently did we discover a convenient laboratory animal model of P.E. If it were true (with apologies to Gertrude Stein) that an erection is an erection is an erection, then the lack of an animal model of P.E. would not have been a problem. But there is increasing evidence that the neuroendocrine regulation of erection varies with the “type” of erection, i.e., the context within which erection occurs. This context-sensitive regulation was captured in traditional texts, which asserted that the sacral spinal cord controls reflexive erection via the pelvic nerves, whereas the lumbar cord controls P.E. via the hypogastric nerves. As we shall see, this example is probably incorrect, but the principle of differential regulation appears to be sound.

With the clear exception of the great apes and many ungulates (e.g., horses, elephants, various antelopes), most mammals do not have erections before mounting and thrusting. None of the common laboratory animals, including rats, cats, and dogs, were known to exhibit P.E. At least for rats, that is no longer true. Male rats placed in a chamber with a receptive female that can be seen, heard, and smelled, but not touched, exhibit intermittent erections. This context satisfies definitions of P.E., and intracavernosal pressures during these erections are similar to those occurring during copulation or reflexive erections. Our exploration of the neural regulation of rat P.E.’s and, by implication, of sexual arousal, has relied mainly on lesions of peripheral nerves or in the brain, and I have space here only for a sampling of results. It has long been known that lesions in the male medial preoptic area (MPOA) permanently eliminate copulation in every species studied. But why? One persistent hypothesis is that the males are no longer sexually aroused. However, we found that MPOA lesions have no effect on P.E. — and pre-

sumedly arousal — in rats. Lesions in the medial amygdala (MeA), a key structure with efferents to the MPOA, disrupt copulation (e.g., more insertions required for ejaculation) but leave the male’s attempts to copulate unaltered. However, MeA lesions eliminate P.E. It remains to be seen whether these lesions interfere only with the olfactory processing that is essential for P.E. in rats, or whether they have a more general effect on sexual arousal. Endocrine studies reveal another dissociation: estradiol maintains erection in copula in castrated rats, but does not maintain P.E. or reflexive erections. As for the peripheral nerves, transection of the hypogastric nerves, long reputed to be essential for P.E, has no detectable effect in rats, whereas pelvic nerve transection dramatically reduces the incidence of P.E., reflexive erection, and erection in copula.



Collectively, our experiments (several conducted in collaboration with colleagues in France, Mexico, and Japan) confirm that the neuroendocrine regulation of erection varies with the context in which erection occurs, but we have found no support for the traditional view of context-dependent participation by the peripheral nerves in erection. The small proportion of lower-motor-neuron paraplegics who retain P.E. may do so via parasympathetic fibers coursing with the hypogastric sympathetic nerves, or via pro-erectile fibers in the paravertebral sympathetic chain.

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KARL-ERIK ANDERSSON AND FRANÇOIS GIULIANO

BASIC RESEARCH HIGHLIGHTS

Meetings Calendar and reports.



Edoardo Pescatori

Dear Colleagues,

The second ESIR Newsletter is being published just in time for the XIIIth EAU Congress in Barcelona. This gives me the opportunity to point out some events of andrologic interest, besides the specific podium and poster sessions, that will take place during the Convention:

Saturday, March 21 09.10 - 09.50

- State of the Art Lecture (**5th International Meeting of the ESRU in conjunction with the XIIIth EAU Congress**): Treatment of Erectile Dysfunction. A. Allona, Madrid (Spain)

Sunday, March 22 12.15 - 13.15

- **Special Round Table Session 1: Peyronie's Disease.** Chairman: E. Austoni, Milano (Italy)

Monday, March 23 17.00 - 19.00

- **Satellite Symposium #7: Sexual function and other complications of managing BPH patients.** Chairman: J. Fitzpatrick, Dublin (IRL)

I am also proud to announce that the Matula Prize has been awarded to Dr. Francesco Montorsi, presently Secretary General of ESIR.

I would like to remind all the Colleagues involved in the field of Erectile Dysfunction about the call for abstracts for the forthcoming 8th World Meeting on Impotence Research and the 11th Symposium on Corpus Cavernosum Revascularization, August 25-28, 1998 Amsterdam, The Netherlands. Please note that April 1, 1998 is the deadline to have your abstracts considered for evaluation.

Finally, the next ESIR Meeting is shaping up! The Organizing Committee has been formed, and our Turkish Colleagues are getting ready to welcome all of us to Istanbul in October 1999. See below for details.

*Again, any contribution concerning specific events not included in the following list, as well as suggestions or comments, are very welcomed.
(E-mail urolpoli@unimo.it).*

1998

**March 21-25, 1998 Barcelona, Spain
European Association of Urology - XIIIth Congress**

Contact: EAU Congress Office
Tel. +31 24 6452510
Fax +31 24 6450769
Email eau@bpc.nl

**March, 28-31, 1998 Long Beach, California - USA
American Society of Andrology Annual Meeting**
Contact: ASA Executive Offices
Tel. +1 415 7644823

Fax +1 415 6744915

Email 105037.1120@compuserve.com

March, 30-31, 1998 Florence, Italy

Ist International Conference on Penile Diseases

Contact: Scientific & Organizing Committee

Tel. +39 55 417645 or +39 5527582986

Fax +39 55 4377755 or +39 55 2758395

Organizing Secretariat

Tel. +39 55 476377

Fax +39 55 476393

Email os@mediahouse.it

April, 6-8, 1998 Sitges, Barcelona - Spain

1st International Interdisciplinary Symposium on Genitourinary Reconstructive Surgery in Congenital Malformations, Transsexuals and Impotence

Contact: Dr. Joaquim Sunol

Fax +34 3 4145313

Email jsunol@secre.org

Congress Organization

Tel. +34 3 4908715

Fax +34 3 4906766

Email simposia@ipras.org

April 30 - May 2, 1998 Palma de Mallorca, Spain

VII International Symposium of Andrology

Contact: Dr. Rosselló Barbará

Tel. +34 9 71714733

Fax +34 9 71726519

Email cuasba@atlas-iap.es

May 29 - June 4, 1998 San Diego, California - USA

American Urological Association 93rd Annual Meeting

Contact: AUA Convention Dept.

Tel. +1 401 2234308

Fax +1 401 2234372

Email convention@AUAnet.org

During the convention:

**May 31, 1998 Marriott Hotel, San Diego Ballroom, 1-6 pm
Society for the Study of Impotence-Annual Scientific Meeting**

Contact: Ira D. Sharlip, Secretary-Treasurer

Tel. +1 415 2020250

Fax +1 415 2020255

Email isharlip@aol.com

July 25-29, 1998 Caracas, Venezuela

XVII International Congress on Urology

Venezuelan Society of Urology

Contact: Congrex Venezuela

Tel. +58 2 2639733

Fax +58 2 263 8443

Email congreca@ven.net

August 25-28, 1998 Amsterdam, The Netherlands

THE 8TH WORLD MEETING ON IMPOTENCE RESEARCH AND THE 11TH SYMPOSIUM ON CORPUS CAVERNOSUM REVASCULARIZATION

Contact: Congress Secretariat, Ms. Marianne Mulder

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Nijmegen P.O. Box 9101, 6500 HB Nijmegen, The
Netherlands
Tel. +31 24 3613920
Fax +31 24 3541031
Email m.mulder@uro.azn.nl

**September 17-20, 1998 Singapore, Republic of
Singapore**
4th Asian Congress on Urology
Contact: Congress Secretariat
Tel. +65 297 7633
Fax +65 297 7560
Email wocp@pacific.net.sg

1999

October 3-6, 1999 Istanbul, Turkey
**3rd MEETING OF THE EUROPEAN
SOCIETY FOR IMPOTENCE RESEARCH**
Contact: Congress Secretariat
Tel. +90 212 2305535
Fax +90 212 2304923
Email scrpilh@antmarin.com.tr

Topic: Postoperative Erectile Dysfunction. 2- transurethral prostatectomy and internal Urethrotomy

Chen, G.L., Berger, R.E.: Treatment of impotence
resulting from internal urethrotomy.

J. Urol 158:542, 1997

Gerstenberg, T., Schou, J.: Is erectile dysfunc-
tion after transurethral resection of the prostate
(TURP) caused by heat to the penile nerve? Int.
J. Impotence Res. 6, Suppl.1:D192, 1994

Hanbury, D.L., Sethja, K.K.: Erectile function follo-
wing transurethral prostatectomy.

Br. J. Urol. 75, 12-13, 1995

Jiaan D.B., Lee, Y.H., Huang, J.K.: Incidence and
risk factors of impotence after transurethral
resection of prostate. Int. J. Impotence Res.
8, No. 3, 142:D79, 1997

Tscholl, R., Largo, M., Poppinghaus, E., Recker, F.,
Subotic, B.: Incidence of erectile impotence
secondary to transurethral resection of benign
prostatic hyperplasia, assessed by preoperative
and postoperative snap gauge tests. J. Urol
153, 1491-1493, 1995.

The incidence of erectile dysfunction after tran-
surethral resection of the prostate ranged be-
tween 8,2 % out of 98 patients (Tscholl et al),
22,2 % out of 180 patients (Hanbury et al) and
32,1 % out of 766 patients (Jiaan et al), who
reported intact erectile capacity prior to opera-
tion. Surgery-related risk factors were small
adenomas < 10-30 gm respectable tissue
(School et al, Jail et al) as well as breach of the
prosthetic capsule with 28,1 % impotence vs. 10
% in patients without capsular perforation
(Banbury et al). All three papers emphasise the
fact, that transurethral resection of prostate
bears a non-negligible risk of postoperative
erectile failure about which the patients must be

informed. Especially in younger
males in whom sexual activities
are of important interest, the indi-
cation for transurethral resection
of prostate adenomas should be
very carefully discussed. The
underlying etiology of postoperati-
ve erectile dysfunction after
TURP remains to be clarified as
Gerstenberg and Schou were
able to prove by means of transperineally
applied thermosensors placed near the nerves
at the level of the verumontanum that in no
patient the temperature exceeded 37.5° during
the transurethral resection. Therefore direct
heat damage to the cavernous nerves seems
not to be responsible and other alternative cau-
ses such as fluid extravasation with postoperati-
ve extensive scar tissue formation around the
cavernous nerves must be presumed.



HARMUT PORST

A quite different cause of postoperative impo-
tence after transurethral procedures (here inter-
nal urethrotomy) is the manifestation of fistula
between corpus spongiosum and corpus caver-
nosum, which was successfully repaired with a
perineal approach and closure of the defect
(Chen). Impotence can be a complication of
internal urethrotomy reported in up to 11 % of
patients in literature. In my own experience I
have encountered 4 cases with spongiosal-
cavernosal leakage after "forced internal ureth-
rotomy". Urologists should be aware of this risk,
especially in severe strictures and redoings.

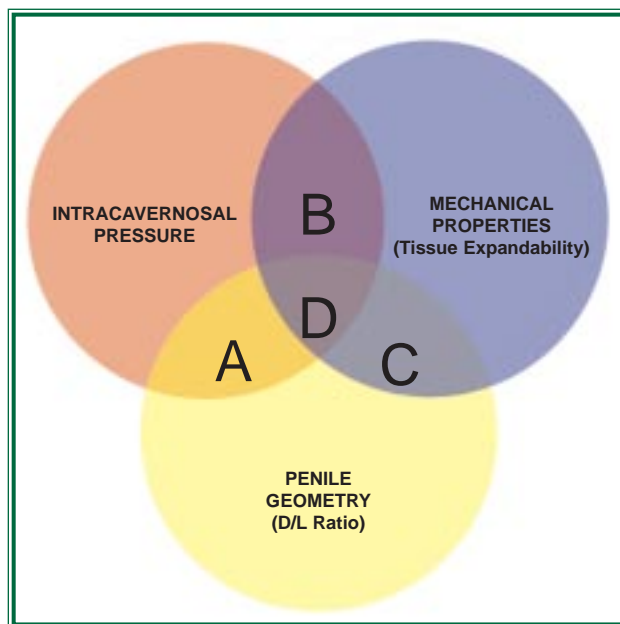
DETERMINANTS OF PENILE RIGIDITY:

Some considerations on the pathophysiology of impotence.

*Dimitrios
Hatzichristou*

The past fifteen years have witnessed considerable advances in the development of sophisticated diagnostic procedures for the evaluation of impotent men with significant enhancement of our understanding of the pathophysiology of erectile dysfunction. Specifically, as vasculogenic impotence is the most common cause of organic impotence, hemodynamic testing such as duplex ultrasonography and pharmacocavernosometry, have gained wide popularity among researchers and clinicians in the evaluation of both the arterial inflow and the venous outflow in the corpora cavernosa. Potency however, defined as the ability to attain an erection of adequate rigidity for coitus, is best characterised by the presence of axial rigidity, rather than hemodynamic parameters. Several studies for example noticed that the magnitude of intracavernosal pressure associated with rigidity varies widely (1). In addition, recent data have shown that a rigid/functional erection is not always associated with normal hemodynamics. On occasions the contrary also being true i.e. Normal hemodynamics have been noticed in patients with inadequate penile rigidity. In that sense, diagnostic procedures for vasculogenic impotence, offer valuable information on the hemodynamic integrity, but are incomplete in characterising the "potency status".

A recent engineering investigation by Udelson and collaborators at Boston University (2) on the relationship between hemodynamics and penile structural components identified 3 factors affecting penile rigidity: intracavernosal pressure, mechanical properties of erectile tissue and penile geometry. Two new important parameters were introduced. Firstly, expandability (X) of the erectile tissue, implying the ability of the corpora to achieve its erect volume at low intracavernosal pressures. Easily reaching the erect volume of the corpora, is probably critical to the full activation of the veno-occlusive mechanism. This is why poorly expandable erectile tissue (fibrotic tissue) results in veno-occlusive dysfunction. Secondly penile aspect ratio, defined as the ratio between penile diameter and length (D/L ratio). A significant negative correlation was observed between D/L ratio and the intracavernosal pressure necessary to achieve penile rigidity, such that penises with a large diameter and short length (high D/L ratio) required lower intracavernosal pressures than penises with a low D/L ratio. The range of intracavernosal pressure necessary to achieve rigidity could be enormous, from 50 to over 100 mmHg. Such findings



were independently confirmed by Moncada and Sáenz de Tejada (3).

Based on these findings, a conceptual model on the pathophysiology of impotence was proposed (see figure), in which impotence may be due to reduced intracavernosal pressure, altered tissue mechanical properties, unfavourable penile geometry (D/L) ratio or any combination of these:

- A.** Normal tissue expandability, low intracavernosal pressure and low D/L ratio.
- B.** Normal penile geometry, low intracavernosal pressure and altered tissue expandability properties.
- C.** Normal intracavernosal pressure altered tissue expandability and low D/L ratio.
- D.** Low intracavernosal pressure value, altered tissue expandability and low D/L ratio.

It is anticipated that the recognition of the factors affecting rigidity may lead to the development of new diagnostic and treatment strategies for impotent men with impaired penile rigidity.

References:

1. DG Hatzichristou, I Sáenz de Tejada, S Kupferman, S Namburi, ES Pescatori, D Udelson and I Goldstein.
In vivo assessment of trabecular smooth muscle tone, its application in pharmaco-cavernoso

metry and analysis of intracavernous pressure determinants.

J. Urol, Vol. 153, 1126-1135, April 1995.

2. D. Udelson, A Nehra, DG Hatzichristou, K Azadzoï, RB Moreland, J Krane. I Sáenz de Tejada, and I Goldstein. Engineering analysis of penile hemodynamic and structural-dynamic relationships:

Part I- Clinical implications of penile tissue mechanical properties. Int. J. Impot Res. 1997, 8 1-11.

Part II- Clinical implications of penile buckling. Int. J. Impot Res. 1997, 8, 1-11.

Part III- Clinical considerations of penile hemodynamic and rigidity erectile responses.

Int. J. Impot. Res. 1997, 8, 1-11.

3. I Moncada, C Hernández, E Lledó, J Jara, G. Escribano and I Sáenz de Tejada.

Clinical value of measuring flaccid penile diameter/length ratio as a predictor of the intracavernosal pressure required for rigidity. J. Urol. Supplement Volume 157, # 691 April 1997.

Dimitrios Hatzichristou

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Thessaloniki, Greece.

Clinical Cases

Michael Sohn

A 54-year-old patient consulted for erectile dysfunction lasting three to four years.

A thorough anamnesis revealed that he has a stable relationship with his wife. Sexual desire was reported to be the same as years before without any deterioration on either side. The main problem was initiating erection and achieving the degree of peak rigidity sufficient for sexual intercourse. Furthermore the patient reported a loss of morning erections and similar problems during masturbation.

In general he noted a loss of erectile activity and spontaneity spanning the last 3 to 4 years.

Physical examination could not reveal any suspicious lesions or pathologies of the penis and scrotum.

Blood chemistry showed regular values for lipids, glucose and liver enzymes. Testosterone was measured four times during the day and only reached subnormal values between 2.2 to 2.7 µg /ml. FSH, LH and prolactine were evaluated within the normal range.

Duplexsonography of penile vessels was performed after i.c. injection of 5 µg PGE1; both deep cavernosal arteries were shown to have normal flow-rates with no signs of venous leakage. The erection observed after i.c. injection was complete and lasted 45 minutes.

NPTR-measurements using a Rigiscan® device for three consecutive nights revealed only two regular erectile events with 90% rigidity and suf-

ficient tumescence at penile base and tip during a 24 hour registration.

Diagnosis: We suspected an apnoea syndrome from anamnesis and from NPTR- results. NPTR-measurements were repeated under continuous EEG-monitoring: a severe apnoea syndrome was confirmed with serious loss of oxygen saturation.

Re-evaluations after this period revealed a return of spontaneous morning erections and normal erections under sexual stimulation.

The level of general erectile activity and spontaneity improved and the patient was reported to be in good physical and psychological shape again.

Testosterone levels returned to normal values between 3.0 and 4.5 µg/ml during serial measurement.

Conclusion: Sleep apnoea should be suspected as the origin of erectile dysfunction when certain anamnestic details coincide with reduced NPTR events, mild hormonal depression and normal reaction to i.c. drug injection. Only EEG and parallel NPTR registration can confirm this diagnosis.

Treatment with continuous oxygen supply delivered with positive pressure during sleep can reverse all associated symptoms.



A contribution from Spain

Ignacio Moncada

Things were so much simpler fifteen years ago. Urologists could not really do very much for a person seeking advice on erectile dysfunction. All they could do was to give hormones a try, or send the patient to the psychiatrist. Only a few experienced urologists were able to implant penile prosthesis. A former professor in my department used to say “al que Dios se la dé, San Pedro se la bendiga”, or “if still potent, lucky you...”. Now things are different, even in Spain. Since the introduction of effective medical treatments, impotence has turned out to be one of the most frequent reasons for medical consultation. Medical practitioners now agree on treating patients with erectile dysfunction. If we give eyeglasses to people as they age to maintain visual acuity, why not give them remedies to retain sexual potency?

Medical care to impotent patients is provided essentially by urologists and andrologists. The Spanish Association of Urology and Spanish Association of Andrology include erectile dysfunction in their areas of interest and most medical practitioners dealing with impotence are members of both associations. These two associations share scientific interests and clinical objectives, but an emerging problem has been the appearance of injection clinics with very aggressive marketing. They personify, in our country, the most blatant commercialisation of a medical condition.

Specialists agree that most patients do not need a lengthy and costly workup, but do need a workup. Medical history, physical exam, sexual questionnaire and hormonal screening make up the standard assessment on the patient's first visit. The second visit normally includes the intracavernosal injection of prostaglandin E to test the hemodynamics of erection and to measure penile rigidity. In a few cases some kind of vascular assessment is considered necessary, and a doppler ultrasound or, more infrequently, a cavernosometry is performed.

The only medical treatment approved for organic impotence in Spain is Caverject (alprostadil from Pharmacia-Upjohn) in presentations of 10 and 20 mcg. Social security partially reimburses (60%) this drug to those affected and completely (100%) to pensioners, but to apply for this reimbursement the patient needs to have a document stating the diagnosis of erectile dysfunction issued by a specialist, usually working in a hospital environment.

Many expectations have been created through lay press articles about the urethral suppository

or the pill for impotence. Everyone is now concerned about when these less invasive therapies will obtain the health authority's approval and become widely available. In the meantime it seems that the idea of injections does not discourage many men from therapy as around 20.000 units are used monthly. To this we would have to probably add, an equal number of uses of other vasoactive combinations most of which are sold in the above mentioned injection clinics.

Penile prosthesis are an option that has not changed too much since the introduction of Caverject. With the introduction of new hydraulic models, mechanically more reliable, and the refinement of surgical techniques, the implanting option remains important for patients in whom medical therapy is ineffective. The price of the devices is a problem, it is too high for both public hospitals with a restrained budget and for the private patient. Nevertheless, around 400 penile prosthesis are implanted annually in Spain, mostly in public hospitals.

Vacuum devices are not popular in Spain, doctors are not convinced that this is a good option and in many cases this treatment option is not even mentioned to the patient. Vascular surgery is only performed at very few hospitals and is therefore not widespread.

To sum up, Spain is a country in which impotence is now considered a commonly occurring disease, predominantly dealt with by urologists, but also by other specialists and where the options available are primarily intracavernosal injections and penile prosthesis. Public opinion is aware of new emerging treatments, particularly the pill taken one hour before sex, and everybody, it seems, would like to give it a try.



NEW PRODUCTS



Injectable products on the European market.

CAVERJECT (*Pharmacia & Upjohn*)

* Registered in: Austria, Belgium, Bulgaria, Cyprus, Czech Republic, Denmark, Finland, France, Germany, Greece, Hungary, Iceland, Ireland, Israel, Italy, Luxembourg, Malta, Netherlands, Norway, Portugal, Russia, Slovak Republic, Slovenia, Spain, Sweden, Switzerland, Ukraine and United Kingdom

* Awaiting registration in: Croatia, Estonia, Kazakstan, Latvia, Lithuania, Poland, Turkey and Uzbekistan

* Formulation: Alprostadil 5,10,20 mcg

* Special devices attached to medication: A disposable syringe prefilled with diluent, a 5,10,20 mcg vial of Caverject® sterile powder, two needles Becton Dickinson MICROLANCE 3 (27G x 1/2 and 22G x 1 1/2), two alcohol swabs. Peninject® 2.25, an autoinjector device, is also distributed by Pharmacia & Upjohn for exclusive use with Caverject®.

ERECNOS (*Fournier*)

* Registered in: France and Great Britain

* Awaiting registration in: Austria, Belgium, Denmark, Finland, Germany, Greece, Ireland, Italy, Luxembourg, Portugal, Spain, Sweden and Holland

* Formulation: 10 mg/1 ml and 20 mg/1 ml Chlorhydrate of Moxisylyte

* Special devices attached to medication: dual chamber preloaded syringes.

VIRIDAL (*DUO /EDEX - Schwarz Pharma*)

* Registered in: France, United Kingdom, Ireland, Russia, Germany, Finland and Denmark

* Awaiting registration in: Italy, Spain, Sweden and Norway

* Formulation: (Alprostadil-alfadex [prostaglandin E1 - (cyclo-dextrine)])

* Special devices attached to medication: Ampoules, reusable applicator, 30 G needles, alcohol swabs, two chamber carpules (10, 20 mcg), vials (5,10,20 mcg)

ANDROSKAT (*Byk Netherland bv*)

* Registered in: Belgium Luxembourg, Germany, Spain, Denmark, Finland, Italy and Portugal

* Available on the market: The Netherlands and Austria

* Formulation: Per 1ml 15mg Papaverine Hydrochloride 0.5mg Phentolamine Mesylate

* Special devices attached to medication: Available in the form of ampoules and cartridges. Kits include syringes with long needles and short needles, alcohol swabs and in the case of Andropen® an autoinjection device which is easy to use for the patient. Andropen® can only be used together with cartridges

Interview with Dr. Ronald Virag

Hans Hedlund

Professor Virag, based on your great experience within the field of impotence, we would like you to please give us your opinion on the following questions:

Almost twenty years have elapsed since papaverine was first introduced as a diagnostic and therapeutic tool in male erectile dysfunction (ED). Today, there is world-wide experience with self-injection programmes. On the other hand, intra-urethral application is already in the market, and very soon oral therapy will be available to patients and doctors. How much has pharmacological development changed our attitude and consideration for impotent patients, and how much will the global aspect of ED change, when oral therapy comes on the market?

It is true to say that the possibility of achieving erections by injection of vasoactive agents into the cavernous bodies has dramatically changed the way impotent patients are approached for both diagnosis and treatment. For doctors an easy tool was made available to them for the day-to-day evaluation; for the patients, a relief from the fear of failure, the main symptom of erectile dysfunction was now under control. Clinical research was also boosted. Many patients who had been reluctant to undertake more invasive tests and surgery sought treatment when they heard about the new technique. The medical community, at the beginning, was less enthusiastic about intracavernous injections (ICI) because they seemed to bypass the psychological aspects of ED and carry the risk of severe complications. Almost twenty years later, despite the fact that the innocuity and efficacy of the procedure have been largely demonstrated, both attitudes are still common in non-specialised doctors. Thus it is an accepted fact that no more than 20% of the patients suffering from ED seek treatment. Oral therapy, when available on the market should bring large amounts of patients, who would otherwise not consult, to the doctor. But we should be aware that the medical world is clearly not ready for that second revolution in the treatment of ED. Prescribers if untrained, would cause much deception for the non-responders in exactly the same way as we have observed with ICI. Specialists should consider that, now more than ever before, a careful evaluation of the aetiology of ED is mandatory even with the availability of such easy treatment as a pill.

We have accepted a high drop-out rate in men following self-injection programmes, specifically during the first treatment period. Based on your experience do you have any practical advice to help reduce the number of drop-outs?

It has been reported for example, that the use of more "friendly" application systems such as autoin-

jectors have considerably reduced the early drop-out rate. What is your view?

Personally, I have never accepted a high drop-out rate in men following self intracavernous injection programmes (SICI). I have identified several reasons for early drop-out: lack of education concerning the ICI technique, improper use of the vasoactive agents, fear of priapism, concern about what has to be said to the partner, economic worries, lack of follow-up and perspectives for the long-term programme.

Taking into account the above list and addressing each of the elements properly would dramatically reduce the drop-out rate of SICI programmes. Among others I would suggest four main tips:

** Use an automatic injector for the first test: it "defuses" the fear of the injection*

** Use the appropriate drug with the smallest volume*

** Provide the patient with an auto-treatment for a potential priapism: it "defuses" the fear of prolonged erections*

** Manage information provided to the partner carefully as in more than 50% of the cases resistance to the treatment comes from her. Even in well-established couples, partner information might be unnecessary.*

The use of an automatic injector increases by 25 to 30% the acceptance of SICI programmes. Nevertheless, we frequently observe that after a while patients abandon the device for the more discrete manual injection.

Intracavernosal injection therapy is now accepted as the gold standard treatment for ED. Do you believe, we run the risk of forgetting the deeper and main aspects of sexual disturbances and become more concerned with creating erectile athletes?

No. In my personal experience it has always been a major concern to integrate SICI programmes in each patient's individual history, not only sexual but affective. When we look carefully at the very long-term results (i.e. over 5 years use of ICI) we can observe three major facts:

** Patients keep up the same pace of sexual activity*

** Patients do not modify their previous habits significantly in terms of partnership and affections*

** In more than 6000 patients involved in SICI programmes, we did not observe one case of sexual violation*

Within a wider perspective, the results of vascular surgery for ED are not encouraging, although some young patients with insufficient arterial inflow may restore their erectile function with revascularization. Should we try to treat such patients medi-

La petite morte

cally - with intracavernosal or intra-urethral alprostadil today and with oral medication such as sildenafil tomorrow - without any work-up, or shall we refer them directly to national centres with a certain surgical expertise?

I do not recommend vascular surgery as a first line treatment in ED except on very rare occasions: patients aged below 55 years, without neurological involvement, no diabetes, non-smokers and expressing a clear caverno-venous leak responding poorly to ICI. Otherwise, and specially for young patients with arterial insufficiency, I always start with a conservative therapy for at least 6 months. The same applies to caverno-venous leaks. In those cases, the patients should be referred to national centres with considerable expertise (i.e. a sufficient annual rate of such surgical procedures) in practising direct arterial surgery and deep dorsal vein arterialisation.

With regard to diagnostic and therapeutic strategy, there is still variation between centres handling ED. Do you think that we are far from reaching a consensus?

Yes. On the one hand, consensus in the medical community is more philosophical and economic than creative. I do think that we should not tend towards too much consensus, specially in this field, where ED is only one part of the whole process of sexuality. On the other hand I do think that in the day-to-day practice, we should observe equilibrium between zero evaluation and exhaustive work-up when unnecessary. Evaluation of ED should be carried out at two different levels:

1- Erection, where pharmacological testing (including duplex scan) should be the gold standard examination, providing it mimics the real sexual situation as closely as possible, by using low dose of vaso-active agents, and sexual stimulation. More complicated tests such as artificial erection, cavernosometry and DICC should be applied only in the case of poor responders to the former ones.

2- Etiological and general factors which are mandatory because of their therapeutic consequences (hormones, arterial risk factors) or prognostic (neurologic and psychological). The answer to ED should, in no case, be simple prescription treatment such as giving a patient with a headache a painkiller.....

“You will go blind”, “It will be the death of you”.

These and other popular sayings have all at one time or another been associated with overindulgence in sexual activity. They all share a moralising element linked to the pernicious and possibly fatal effects of allowing yourself to fall to seedy depths. From literature to popular satanic rituals, sex and death seem to be inextricably linked. The French language, perhaps because the French are famously well versed in bed manners, has been fast to pick up on this and has found an appropriate expression for orgasm, “la petite morte”. Perhaps this is due to the feeling of weakness following sexual climax or simply a way of making death seem a bit more attractive, who wouldn't welcome a sweet death in the arms of a lover following amorous combat. Whatever the explanation, the fact is that some scientific interest is now being shown in finding possible connections between sexual activity and mortality. The field is open to major controversy, involving social religious and personal issues which are far from objective. If sex is medically proved to be good for one's health then we might find ourselves caught up in an avalanche of sexual activity that could have far-reaching consequences on our social and economic structures. Productivity, aerobics, eating out and going to the cinema could all become things of the past. Time-consuming social rituals would be sacrificed in the name of orgasmic, rejuvenating sex and the civilised network which it has taken centuries to build, could disintegrate overnight in favour of more primitive healthy pursuits. This is alarmist I know, someone would eventually set up a sex regulation “body” that would recommend standard quantity and quality, ban it from the workplace and ultimately apply VAT to it. On a more serious note, there is some scientific evidence to suggest that frequent sexual activity appears to have a protective effect on men's health. In the case of women the main negative impact on health seems to be the quality of their sex lives. This confirms the old idea that men are interested in quantity whereas women are more concerned with quality, perhaps each instinctively knows what's sexually good for them.

