PROCEEDINGS OF THE 5th EURASIAN ANDROLOGY SUMMIT

5-6 March 2010, Kiev - UKRAINE

UKRAINIAN
ASSOCIATON OF ANDROLOGY
AND SEXUAL MEDICINE

PROFESSIONAL ASSOCIATION OF
ANDROLOGISTS OF RUSSIA
(Founded in 1995)

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Editor: **Selahittin Çayan, MD**

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SCIENTIFIC PROGRAM

5 March 2010, Friday

08:30-08:50 **Opening Ceremony**

V.V. Lazoryshynec (Ukraine) / *The First Deputy Minister of Health of Ukraine*

V.F. Moskalenko (Ukraine) / *Rector of the National Medical University, corresponding member of AMS of Ukraine*

D.D. Dyachuk (Ukraine) / *Head doctor of the Scientific-Practical Center of Prophylactic and Clinical Medicine of the State Administration of Affairs*

P. Scheplev (Russia) / *President of the Eurasian Andrology Summit, President of the Professional Association of Andrologists of Russia*

M. Boiko (Ukraine) / *President of the Ukrainian Association of Andrology and Sexual Medicine*

Ö. Yaman (Turkey) / *President of the Turkish Society of Andrology*

A. Kadıoğlu (Turkey) / *Secretary General of the Eurasian Andrology Summit*

08:50-09:00 Past and today of the Eurasian Andrology Summit / **A. Semerciöz (Turkey)**

09:00-10:00 **Panel: Evaluation and treatment of male sexual dysfunction**

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Standard and further evaluation to diagnose erectile dysfunction / **M. Boiko (Ukraine)**

Update on the treatment of ED with PDE-5 inhibitors **/ S. Deveci (Turkey)**

New classification and novel treatment of premature ejaculation **/ E. Can (Turkey)**

Hypogonadism, erectile dysfunction and lower urinary tract system

C. Adayener (Turkey)

10:00-10:30 **COFFEE BREAK**

10:30-12:00 **Panel: Andrological video surgery**

Moderators: **M. Boiko (Ukraine), A. Bölükbaşı (Turkey)**

Surgical treatment of urethral strictures and hypospadias / **A. Lyubchak (Ukraine)**

Correction of penile curvature during hypospadias surgery

C. Germiyanoğlu (Turkey)

Penile curvature surgery for congenital penile curvature**/ M. Çulha (Turkey)**

Penile prosthesis implantation in Peyronie's disease / **P. Scheplev (Russia)**

Penile prosthesis and sphincter implantation surgery / **M. Çakan (Turkey)**

Management of penile fracture **/ B. Gümüş (Turkey)**

12:00-13:00 **LUNCH**

5 March 2010, Friday

13:00-13:45 **Panel: Oncologic Andrology**

Moderators: **A. Zhuravchak (Ukraine), İ. Nane (Turkey)**

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Nerve sparing radical retropubic prostatectomy **/ Ö. Dillioğlugil (Turkey)**

Nerve sparing laparoscopic radical prostatectomy **/ İ. Yavaşçaoğlu (Turkey)**

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Life-style behavior and sexual and reproductive health **/ E. Özbek (Turkey)**

Future of the treatment for male erectile dysfunction **/ M. Kendirci (Turkey)**

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14:45-15:30 **Panel: Effect of different conditions on male sexual and reproductive functions**

Moderators: **G. Okyar (Turkey), A. Gör (Turkey)**

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Effect of medical and surgical treatment for BPH on sexual functions in men with lower urinary tract symptoms **/ A. Atan (Turkey)**

Effect of radiotherapy and chemotherapy on male infertility / **İ. Özbey (Turkey)**

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Sex transforming in children / **A.B. Okulov (Russia)**

Hypospadias: controversies in the strategy and methods of treatment **A. Matar (Russia)**

Circumcision in Russia: social, medical and ethical aspects / **A. Matar (Russia)**

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6 March 2010, Saturday

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10:30-11:30 **Panel: Adolescent Andrology**
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Contemporary management of undescended testis / **M. Dayanç (Turkey)**
Contemporary management of adolescent varicocele **/ A. Fazlıoğlu (Turkey)**
Principals and rules of urethral surgery / **P. Scheplev (Russia)**

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Moderator: **A. Kadıoğlu (Turkey)**
Panelists: **M. Boiko (Ukraine), I. Ahmedov (Azerbaijan), B. Rispaev (Kyrgyztan),**
E. Uçaner (Northern Cyprus), S. Shavakhabov (Uzbekistan), M. Usta (Turkey)

CLOSING REMARKS

TEXT OF THE PRESENTATIONS

STANDARD AND FURTHER EVALUATION TO DIAGNOSE ERECTILE DYSFUNCTION

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Scientific-Practical Center of Prophylactic and Clinical Medicine of the State Administration of Affairs, Kiev, Ukraine

The fundamentals of assessment for any patient are the history, the physical examination and special investigations.

The essential step in the management of ED is the taking of a comprehensive sexual medical and psychological history of the patients and his partner when possible [1, 2].

Enquiries should also be made about sexual development and any possible relationship difficulties, together with an assessment of the patient's and his partner's attitude to the problem.

The initial enquiry about medical history allows a more relaxing atmosphere to be established and permits questions about erectile function and other aspects of sexual history to be asked more easily, even when men do not volunteer to describe their problem.

The first step should be to estimate sexual history. Patients are often confused by the terminology used to describe MED. It is important to clarify exactly what the patient's symptoms are. The sexual history may include information about previous and current sexual relationships, current emotional status, onset and duration of the erectile problem and possible previous consultations and treatments. Detailed descriptions of the quality of both erotic and morning erections, in terms of rigidity and duration, as well as arousal, ejaculation and orgasmic problems should be discussed. The use of validated questionnaires, such as the international index for erectile function, may be helpful. [3]. Once these points are clarified, diagnostic features indicating either a psychogenic or an organic cause of the problem can be sought.

A detailed medical history is critical as many common disorders are associated with ED, including hypertension, diabetes mellitus, myocardial disease, lipidaemia, hypercholesterolemia, renal insufficiency, hypogonadism, neurological and psychiatric disorders, and indeed any chronic illness. Genitourinary and rectal surgery, as well as many drugs, particularly anti-hypertensive and psychotropic drugs may cause ED. The chronic use of alcohol, marijuana, codeine, meperidine, methadone and heroin is associated with a high percentage of ED [4]. Evaluation has revealed vasculogenic alteration to be the most consistent organic erectile abnormality in radiotherapy [5].

A focused physical examination must be performed on every patient, with particular emphasis on the genitourinary, endocrine, vascular and neurological systems [1]. The examination of a man with erectile dysfunction will be directed to a certain extent by knowledge gained from his history. However, it is important to assess the external genitalia, the endocrine and vascular systems, and the prostate gland in all patients.

The presence, location and size of the testes, together with an assessment of secondary sexual characteristics will usually be enough to identify obvious hypogonadism.
Vascular assessment should include measurement of blood pressure, cardiac status and lower extremity pulses. The penis should be carefully palpated to exclude the presence of fibrous Peyronie's plaques.

Laboratory testing (blood glucose and testosterone) should be carried out in the majority of the patients and selectively in other patients when lipid profile, prolactin and prostate-specific antigen (PSA) assessment should be considered [6-8].

On that occasion the physician examines the results of the blood tests. If any abnormality is observed, further investigation by referral to another specialist may be necessary.

Clinical investigations of men with ED can be classed as essential, general and specialized The only essential investigation is to exclude undiagnosed diabetes mellitus, using a serum glucose estimation. General investigations include serum concentrations of testosterone, sex hormone binding globulin (SHBG), prolactin, thyroid hormones, creatinine and fasting lipid levels. Special investigations are not always required, but may be necessary if patients fail to respond to minimally invasive treatments, before other options can be explored. Unless the problem is obviously psychogenic, most patients will have a trial injection of an intracavernosal vasoactive agent and their response assessed.
Specialized investigations need only be performed when a detailed knowledge of the cause of erectile dysfunction is required, and the patient and his partner have expressed an interest in pursuing corrective therapy. Also young patients with a history of pelvic or perineal trauma who could benefit from potentially curative vascular surgery. Specific tests may be indicated at the request of the patient or his partner for medico-legal reasons.

The presence of nocturnal erections, which is used to differentiate psychogenic from organic impotence, can be detected using devices placed around the penis during sleep. This is known as nocturnal penile tumescence (NPT) testing. The intracavernosal injection test offers limited information regarding vascular status. Positive response may be considered to be associated with normal arterial and veno-occlusive haemodynamics [9]. In all other cases, the test is inconclusive, and a duplex ultrasound of the penile arteries should be requested.

Colour Doppler imaging provides information about penile haemodynamics after maximal smooth muscle relaxation has been induced with a vasoactive agent. Its aim is to distinguish arterial insufficiency from other causes of erectile failure. The velocity of blood in the cavernosal artery in the dynamic state can be measured during systole and diastole, and organic impotence can be differentiated from psychogenic impotence. It can also suggest the presence of a venous leak, although further studies are necessary to confirm this.If the result of the duplex examination is normal, the vascular investigation stops. When it is abnormal, arteriography and cavernosometry should be performed only for patients who are considered potential candidates for vascular reconstructive surgery.

Failure of the veno-occlusive mechanism to provide adequate venous outflow resistance can be demonstrated by pharmacocavemosography. This measures the blood flow required to maintain a pharmacologically stimulated erection. Contrast medium injected into the corpora will identify the location of any leak, which usually originates in the deep dorsal vein of the penis.
Patients with psychiatric disorders will be sent to a psychiatrist particularly interested in ED. Patients with penile abnormalities, such as hypospadias, congenital curvature or Peyronie's disease with preserved rigidity, may require surgical correction with very good success.

The possible useful diagnose procedures in the future can become:

- detecting of adenosine level [10];
- detecting of reactive oxygen metabolite concentrations and plasma total antioxidant status to indicate antioxidant defense [11];
- detecting of the circulating levels of endothelial progenitor cells phenotypes (CD34+, KDR+) [12];
- detecting of enzyme level (endothelial and neuronal NOS) [13];
- detecting of homocysteine level (as an important regulator of NO synthase) [14].

REFERENCES:

1. Davis-Joseph B, Tiefer L and Melman A. Accuracy of the initial history and physical examination o establish the etiology of erectile dysfunction. Urology 1995; Mar;45(3):498-502.
2. Burnett AL. Erectile dysfunction. A practical approach for primary care. Geriatrics 1998; Feb;53(2):34-5, 39-40, 46-8.
3. Rosen R, Riley A, Wagner G, Osterloh IH, Kirkpatrick J and Mishra A. The international index of erectile function (IIEF): a multidimensional scale for assessment of erectile dysfunction. Urol 1997; Jun;49(6):822-30.
4. Benet AE and Melman A. The epidemiology of erectile dysfunction. Impotence. Urol Clin North Am, W.S. Saunders Company 1995; Nov;22(4):699-709 22, 4: 699.
5. Goldstein I, Feldman MI, Deckers PJ, Babayan RK, Krane RJ. Radiation-associated impotence. Aclinical study of its mechanism. JAMA 1984; Feb 17;251(7):903-10.
6. Zonszein J. Diagnosis and management of endocrine disorders of erectile dysfunction. Impotence. Urol Clin North Am 1995; Nov;22(4):789-802 .
7. Citron JT, Ettinger B, Rubinoff H, et al. Prevalence of hypothalamic-pituitary imaging abnormalities in impotent men with secondary hypogonadism. J Urol 1996; Feb;155(2):529-33.
8. Carter HB, Epstein JL, Partin AW. Influence of age and prostate-specific antigen on the chance of curable prostate cancer among men with nonpalpable disease. Urology 1999 Jan;53(1):126-130.
9. Meuleman EJ, Diemont WL. Investigation of erectile dysfunction: Diagnostic testing for vascular factors in erectile dysfunction. Impotence. Urologic Clinics of North America 1995 Nov;22(4):803-
10. Phatarpekar PV, Wen J, Xia Y. Role of Adenosine Signaling in Penile Erection and Erectile Disorders. J Sex Med. 2009 Nov 3. [Epub ahead of print].
11. Barassi A, Colpi GM, Piediferro G, Dogliotti G, D'Eril GV, Corsi MM Oxidative stress and antioxidant status in patients with erectile dysfunction. J Sex Med. 2009 Oct;6(10):2820-5. Epub 2009 Apr 23.
12. Esposito K, Ciotola M, Maiorino MI, Giugliano F, Autorino R, De Sio M, Jannini E, Lenzi A, Giugliano D. Circulating CD34+ KDR+ endothelial progenitor cells correlate with erectile function and endothelial function in overweight men. J Sex Med. 2009 Jan;6(1):107-14.
13. McCarthy HO, Coulter JA, Robson T, Hirst DG. Gene therapy via inducible nitric oxide synthase: a tool for the treatment of a diverse range of pathological conditions. J Pharm Pharmacol. 2008 Aug;60(8):999-1017.
14. Demir T, Comlekçi A, Demir O, Gülcü A, Calypkan S, Argun L, Seçil M, Yepil S, Esen A. Hyperhomocysteinemia: a novel risk factor for erectile dysfunction. Metabolism. 2006 Dec;55(12):1564-8.

UPDATE ON THE TREATMENT OF ERECTILE DYSFUNCTION WITH PDE-5 INHIBITORS

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Phosphodiesterase (PDE) is the enzyme that breaks down the intracellular second messenger of erection cyclic guanosine monophpsphate (cGMP). Type 5 is the predominant form of PDE in the penis thus inhibiting this enzyme enhances penile erection. PDE-5 belongs to a protein family of cyclic nucleotide which is divided into at least 11 families of structurally and functionally related enzymes. There are three PDE-5 inhibitors licenced in the treatment of ED; sildenafil citrate, vardenafil and tadalafil. Sildenafil is the first oral PDE5i approved by FDA and has the most long experience and data confirming its activity and safety. Sildenafil is administered in doses of 25, 50 and 100 mg whereas tadalafil is administered in doses of 10, 20 mg and vardenafil 5,10 and 20 mg. The recommended starting doses are; 50 mg for sildenafil and 10 mg for tadalafil and vardenafil. These starting doses are adopted according to the response to the therapy and side effects. All three agents are effective in patients with organic, psychogenic and mixed etiology of ED (1, 2). Methodological problems prevent comparative preference trials between three PDE-5 inhibitors to be conclusive (3). The main reasons for not responding are; inappropriate timing of sexual intercourse, single dose trial and lack of titration to the recommended highest dose (4-5).

Pharmacokinetics and pharmacodynamics

The terminal half life (T1/2) of sildenafil is 3-5h. The time to peak plasma concentration (Tmax) after oral absorption on an empty stomach is 30- 120 minutes (median, 60 min). High fat meal increases the Tmax concenctraion by 60 min and reduces the peak plasma concentration by 29%. Vardenafil has been shown selective as 25 times greater than that of sildenafil and 48 times than tadalafil in inhibiting PDE-5 in invitro studies. Single dose of oral administrated vardenafil is absorbed with maximum plasma concentration reached within 15 minutes in some men (median, 36-54 min). A high fate meal reduces the absorption rate with an increase T max of 1 hour and reduces the maximum plasma concentration by approximately 18%. Tadalafil is absorbed with a median Tmax of 2 h (0.5-12) and with mean T1/2 of 17.5 h after oral administration. High fat meal and alcohol do not effect the Tmax, Cmax and T1/2 of tadalafil (4-6).

Drug Interactions

PDE-5 inhibitors are metabolized predominantly at the liver by cytochrome P450s (CYP3A4). CYP3A4 inhibitors (Ketaconazole, Erithromycin, Claritromycin, Ritonavir Indinavir, Grapefruit juice) may lead to an increased plasma concentration of PDE5 inhibitors. On the other hand drugs which induce CYP3A4 (Rifampin, phenytoin) may reduce the effectiveness of PDE-5 inhibitors (2-6).

Cardiovascular safety

Of the three PDE-5 inhibitors none of them demonstrated an increase in myocardial infarction rates in aged matched populations in double blind placebo controlled trials. Organic nitrates used to treat angina are still absolute contraindications with the use of PDE-5 inhibitors. According to the results of the Second Princeton Consensus Panel and to the consensus statement of the American College of Cardiology/American Heart Association that a PDE-5 inhibitor is safe for men with stable coronary artery disease who are not taking nitrates. It is suggested that nitrates should be avoided for at least 48 hours after the last tadalafil dose because of its longer half life. The adverse effect of PDE-5 inhibitors is not worsened by antihypertensive agents even with multiple antihypertensive regimens (2, 7-10).

Side Effects

Similiar side effects are seen with the present three PDE-5 inhibitors such as headache, dyspepsia, flushing, and rhinitis. Sildenafil and vardenafil have similiar side effect profile. Tadalafil do not interact with PDE-6 but reacts with PDE-11 (11). The clinical implications of PDE-11 inhibition is not clearly understood yet but the presence of PDE-11 in pituitary ad testes has led to some concern about its effects. Hellstrom et al reported that the long term daily administration of tadalafil either 10 or 20 mg has no adverse effects on spermatogenesis (12). Musculoskletal side effects such as back pain has been reported with tadalafil (11-12). Loss of hearing has been reported with sildenafil, vardenafil and tadalafil with rare reports (13).

There are several reports the association of PDE-5 inhibitors with Non- arteric anterior ischemic optic neuropathy (NAION). The mechanism by which PDE-5 inhibitors might cause NAION is not known. Patients with sexual dysfunction often have vascular risk factors that are also associated with NAION. Patients who have sustained an episode of NAION should be counselled before PDE-5 inhibitor prescription. PDE-6 is present in the retina and has a role in color vision. Sildenafil cross-reacts with the retinal PDE-6 and accounts for the transient "blue vision" side effect reported in a small percentage of sildenafil-treated men. Tadalafil does not appear to disrupt PDE-6 so blue vision has not been reported with this medication. Daily use of either tadalafil or sildenafil does not appear to be associated with retinal toxicity. Table 1 demonstrates the adverse effects of PDE-5 inhibitors (14-17).

Penile rehabilitation after radical prostatectomy

Pharmacological prophylaxis with any of the three PDE-5 inhibitors has a significant role in preserving erectile function after radical prostatectomy. However, there are several problems existing in analyzing the literature. The surgical technique (Bilateral or unilateral nerve sparing, excess use of coagulation, experience of the surgeon), the age, the preoperative erectile capacity and health status (comorbidities) are the main predictors of success to preserve erectile function with PDE-5 inhibitors after radical prostatectomy. The lack of homogeneity in study population and not using validated instruments prevents to determine the precise effect of PDE- 5 inhibitors on post- radical prostatectomy penile rehabilitation (18).

Daily (Chronic) administration of PDE-5 inhibitors:

Daily dosing of PDE-5 inhibitors for penile rehabilitation is a new paradigm shift in the management of erectile dysfunction. The US Food and Drug Administration (FDA) approved 5 mg of daily tadalafil as an alternative therapy of ED in 2008. The advantage of this medication is to allow spontaneous sexual intercourse especially in patients who engage frequent sexual activity. The daily dosing regimen provides a steady state drug level which takes away the relationship between sexual activity and medication (2,4,5).

PDE- 5 inhibitors beyond erectile dysfunction

Recently, a lot of new urologic and non-urologic indications are described for PDE-5 inhibitors. The only FDA- approved use of PDE-5 inhibitor beyond ED is sildenafil for the management of pulmonary hypertension. There are several studies reporting decrease in lower urinary tract symptoms (LUTS) in men with ED treated with PDE-5 inhibitors. The high safety profiles of PDE-5 inhibitors have made researchers focus on investigating the systemic potential indications of this drug (19-25). Table 2 shows the potential urologic and non- urologic indications of PDE- 5 inhibitors.

Endothelial dysfunction= Erectile dysfunction

Vasular endothelium plays important role in the vascular tone control. Endothelial dysfunction is seen in a variety of pathological conditions in addition to atherosclerosis, including hypercholesterolemia, diabetes, hypertension, heart failure, cigarette smoking, and aging. Endothelial dysfunction and vascular ED share the same risk factors and pathophysiologic mechanisms. The inhibition of PDE-5 enhances the NO mediated vasorelaxation and will serve normalization of endothelial function. Thus, rehabilitation of endothelieal function by daily treatment of PDE-5 inhibitors will serve improving erectile function (2,4,26).

Conclusion

ED therapy with PDE-5 inhibitors should be individualized as each PD-5 inhibitor has different clinical characteristics. A variety of new PDE-5 inhibitors with different pharmacokinetics including avanafil, udenafil, lodenafil and mirodenafil are in development for the treatment of ED. The benefit of daily PDE-5 inhibitor usage seems to be promising. Further researches and clinical trials are needed to investigate the potential benefits of PDE-5 inhibitors besides ED.

	Sildenafil	Vardenafil	Tadalafil
Headache	++	++	+
Flushing	++	++	+
Rhinitis	+	+	+
Dyspepsia	+	+	++
Back pain	_	_	++
Visual distortion	+	_	_

Table 1: Adverse effects of PDE- 5 inhibitors

Urologic	Non-Urologic
• LUTS	• Pulmonary hypertension
• Priapism	• Raynaud's Disease
• Premature ejaculation	• Heart failure
• Peyronie's Disease	• Cognitive dysfunction
• Penile rehabilitation after radical vprostatectmy	• Type II Diabetes
• Overactive bladder	• Stroke
• Female sexual dysfunction	• Endothelial dysfunction

Table 2: New potential indications for PDE- 5 inbitors

REFERENCES:

1. Goldstein I, Lue TF, Padma- Nathan H, et al. Oral sildenafil in the treatment of erectile dysfunction. Sildenafil study group. N Engl J Med. 1998; 338: 1397-1404.
2. Wespes E, Amar E, Hatzichristou D, et al.EAU Guidelines on erectile Dysfunction: An Update. Eur Urol 2006, 49; 806-815.
3. Mulhall JP, Montorsi F. Evaluating preference trials of oral phosphodiesterase inhibitors for erectile dysfunction. Eur Urol. 49(2006) 30-37.
4. Hatzimouratidis K, Hatzichristou D. Phosphodiesterase type 5 inhibitors: The day after. Eur Urol. 51(2007) 75-89.
5. Shindel AW. 2009 Update on phosphodiestesrase type 5 inhibitor therapy. J Sex Med 2009; 6:2352-2364.
6. Corbin JD, Francis SH. Pharmacaology of phosphodiesterase inhibitors. Int J Clin Pract. 2002; 56:453-459.
7. Kloner RA. Novel phosphodiesterase inhibitors: Assessing hemodynamic effects and safety parameters. Clin Cardiol 2004; 27:120-125.
8. Kloner, RA, Hutter, AM, Emmick, JT. Time course of the interaction between tadalafil and nitrates. J Am Coll Cardiol 2003; 42:1855- 1860.
9. Lewis GD, Shah R, Shahzad K, et al. Sildenafil improves exercise capacity and quality of life in patients with systolic heart failure and secondary pulmonary hypertension. Circulation 2007; 116:1555-62
10. Kostis, JB, Jackson, G, Rosen, R, et al. Sexual dysfunction and cardiac risk (The Second Princeton Consensus Conference). Am J Cardiol 2005; 96:313.
11. G. Brock, S. Glina, I. Moncada, et al. Likelihood of Tadalafil-associated Adverse Events in Integrated Multiclinical Trial Database: Classification Tree Analysis in Men With Erectile Dysfunction. Urology, 2005;73(4): 756-761.
12. Hellstrom WJ, Overstreet JW, Yu A et al, Tadalafil has no detrimental effect on spermatogenesis or reproductive hormones. J Urol. 170: 887-891.
13. Maddox PT, Saunders J, Chandrasekhar SS. Sudden hearing loss from PDE-5 inhibitors: A possible cellular stress etiology. Laryngoscope. 2009 Aug;119(8):1586-9.
14. McGwin, G Jr, Vaphiades, MS, Hall, TA, Owsley, C. Non-arteritic anterior ischaemic optic neuropathy and the treatment of erectile dysfunction. Br J Ophthalmol 2006; 90:1
15. Thurtell MJ, Tomsak RL. Non-arteric anterior ischemic optic neuropathy with PDE-5 inhibitors for erectile dysfunction. Int J Impot Res. 2008; 20: 537-543.
16. Sponsel, WE, Paris, G, Sandoval, SS, et al. Sildenafil and ocular perfusion. N Engl J Med 2000; 342:1680.
17. Cordell, WH, Maturi, RK, Costigan, TM, et al. Retinal effects of 6 months of daily use of tadalafil or sildenafil. Arch Ophthalmol 2009; 127:367.
18. Muller A, Parkerm, Wates BW et al. Penile rehabilitation following radical prostatectomy: predicting success. J Sex Med. 2009; 6(10):2806-2812.
19. Sandner P, Hütter J, Tunel H, et al. PDE5 inhibitors beyond erectile dysfunction. Int J Impot Res(2007) 19:533-53.
20. Burnett Al, Bivlacqua TJ, Champion HC.,et al. Long term oral phosphodiesterase 5 inhibitor therapy alleviates recurrent priapism. J Urol, 2006; 67: 1043-1048.

21. McMahon CG, Stuckey BGA, Andersen M, et al. Efficacy of sildenafil citrate in men with premature ejaculation. J Sex Med 2005; 2: 368-375.
22. Stief, CG, Porst, H, Neuser, D, et al. A randomised, placebo-controlled study to assess the efficacy of twice-daily vardenafil in the treatment of lower urinary tract symptoms secondary to benign prostatic hyperplasia. Eur Urol 2008; 53:1236.
23. Sommer F, Wolfgang S. Treating erectile dysfunction by endothelial rehabilitation with phosphodiesterase inhibitors. World J Urol 2005 23:385-392.
24. Mulhall JP, Guhring P, Parker M, et al. Assessment of the impact of sildenafil citrate on lower urinary tract symptoms in men with erectile dysfunction. J Sex Med. 2006 Jul;3(4):662-7.
25. Ferrini MG, Kavanecz I, Nolazco G, et al. Effects of long-term vardenafil treatment on the development of fibrotic plaques in a rat model of Peyronie's disease. Br J Urol, 2006, 97:625–33.
26. Vardi Y, Dayan L, Apple B, et al. Penile and systemic endothelial function in men with and without erectile dysfunction. Eur Urol. 2009;55(4): 979-985.

NEW CLASSIFICATION AND NOVEL TREATMENT OF PREMATURE EJACULATION

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Premature ejaculation (PE) is the most common sexual problem observed in men. PE presence does not automatically imply certain sexual disorder. PE prevalence is 4-39%. Between the ages of 18-59 years it is 21% in US and 31% in UK (1). It is estimated that 75% of the male population experience PE at some point in their sexual lifetime.PE is a neurobiological event that results in interpersonal difficulty due to inadequate control over ejaculation and sexual and performance anxiety. At first, it was stated as "Rapid Ejaculation" by Gross in 1887. PE was defined as a clinical entity or a syndrome by Bernard Schapiro (1943). His Type A and Type B definitions were later denominated as Lifelong and Acquired PE by Godpidinoff (1989)(2).

Current PE Definitions: DSM-IV TR: Persistent and recurrent ejaculation with minimal sexual stimulation before, on, or shortly after vaginal penetration before the person wishes it. This disorder may lead to marked distress or interpersonal difficulty (3). **ICD-10:** An inability to delay ejaculation sufficiently to enjoy sexual interaction. Ejaculation occurs before or shortly after the intercourse in the absence of sufficient erection to make intercourse possible (if time limit is required before the sexual intercourse or within in 15 seconds after the beginning of intercourse) (4). **EAU Guidelines:** Premature ejaculation is the inability to control ejaculation for a "sufficient" length of time before vaginal penetration. **AUA Guidelines:** Ejaculation that occurs sooner than desired, either before or shortly after penetration, causing distress to either one or both partners . I**nternational Consultation On Urological Disease:** Persistent or recurrent ejaculation with minimal stimulation before, on, or shortly after penetration and before the person wishes it, over which the sufferer has little or no voluntary control, which causes the sufferer and/or his partner anxiety or distress. I**nternational Society For Sexual Medicine (ISSM-Lifelong PE):** A male sexual dysfunction characterized by ejaculation which always or nearly always occurs before or within approximately 1 minute of vaginal penetration; The inability to delay ejaculation on all or nearly all vaginal penetrations; Negative personal consequences, such as distress, bother, frustration, and/or the avoidance of sexual intimacy(5). DSM-IV and ICD-10 PE definitions acknowledge three core components: short ejaculatory latency, lack of control over ejaculation, lack of sexual satisfaction. In PE assessments, most of the clinicians use IELT which is defined by Waldinger et. al. (1994).Intravaginal ejaculation latency time(IELT)is defined as the time between the start of vaginal intromission and the start of intravaginal ejaculation.Despite all its disadvantages,it is a useful method.IELT values in the normal population vary between countries(Turkey 4.4;England 10 minutes)(6).The IELT threshold value used in the definition shows variety.In the studies Mc Mahon and Waldinger states this value as 1 minute and Mattos et. al. as 90 seconds and less. (Waldinger; 90% - 1 minute or less).IELT is not enough for the evaluation of PE.A study conducted in 5 EU countries with 1115 cases showed that:25% of the PE patients had IELT value of>4 minutes;12% of the Non-PE patients had IELT values of<2 minutes(7). The most important test in the treatment is the satisfaction assessment of the patient and the partner. In PE assessments questionnaires have started to be used which consist of patient reports including sexual satisfaction, control over ejaculation, personal distress and interpersonal difficulty, bother, etc.

NEWLY RECOMMENDED PE TYPES: Life-long PE: Early ejaculations occur at nearly every intercourse, in most cases (80%) it is between 30-60 seconds or 1-2 minutes (%20), continue with nearly every female partner, and most often from the first sexual encounters, in 70% of these men ejaculation remains very quick throughout life; in another 30% it may get even faster with age, control over ejaculation decrease or lacking. **Acquired PE:** The man has usually experienced normal ejaculation before the start of his complaint, the premature ejaculation comes on either suddenly or gradually, early ejaculation starts at some point in a man's life, it may caused by urological dysfunctions (erectile dysfunction ,prostatitis, thyroid dysfunction and psychological or intercourse problems). **Nature variable PE:** Early ejaculations are happen irregularly and are not consistent, and a man's capacity to control his ejaculation may be less than normal or lacking. Reduced control of ejaculation is linked to a short or normal ejaculation time (less or more than 1.5 minutes). **Premature-like Ejaculatory Dysfunction:** Men with this condition subjectively think they regularly or sometimes come far too quickly during sexual intercourse, they may become obsessed with their supposed early ejaculation or lack of control, even though their IELT is in the normal range or even longer (between 5-25 minutes) decrease or lack of ability to control ejaculation(8). **Why PE requires treatment?** Effects of PE on personal distress, partner difficulties, sexual satisfaction and orgasm are more negative than men without PE. This briefly implies treatment requirement of PE .

CURRENT TREATMENT: Psychosexual /behavioral Treatments, Topical Treatment,SSRI/ Tricyclic Anti depressants, PDE.5 Inh.,Tramadol, Surgical Treatment, Others (Dapoxetine).

Behavioral Treatments: It is a method that easily applicable, has almost no side-effect, time-required and unknown-efficacy. In squeeze technique which was first used by James Semans, glans penis is squeezed for inhibition of the ejaculation. This method was popularized by Masters and Johnson in 1970's. Also in stop-start technique (Kaplan) the aim is inhibition of the ejaculation. Short and long term success rates are 45-65 % and 25%, respectively. **Topical Treatment:** Local anesthetics are first used by Bernhard Schapiro in 1943. Lidocain-prilocain (emla) can be administered for reducing the sensitivity of penis. Adverse effects are hypoesthesia of penis, vaginal numbness, burning and pain due to absorption. **Pharmacological Treatment:** Use

of SSRI's made a revolution in PE treatment. SSRI's with similar mechanism of action are citalopram, fluoxetine, fluvoxamine, paroxetine and sertraline. A recently performed meta-analysis indicated that only 14.4 % of the studies were appropriate for evidence based medicine. **Daily use:** Paroxetine, clomipromine, sertraline, fluoxetine (20-40, 10-50, 50-100, and 20-40mg) are used. Paroxetine was the most efficient (8,8 fold increase in IELT). Effect generally begins on day 5-10. Side effects are fatigue, yawning, slight nausea, and soft feces. Adverse effects begin in first week and disappear in 2-3 weeks. **On-demand use:** Drugs are taken 4-6 hours before sexual activity. It is effective and tolerable. Its effectiveness is less than daily use and can be administered in combination(9). **PDE-5 Inh.:** Several authors reported the use of PDE-5 inh.-only or in combination with SSRI and topical anesthetics. Generally it is not recommended except acquired PE secondary to erectile dysfunction. **Tramadol:** It is a centrally acting analgesic. It has a quick absorption and excretion. It may be appropriate for on-demand use. Controlled studies demonstrated that tramadol increases IELT (0.86/6.31)(10). **Surgical Treatment:** Selective dorsal neurotomy is recommended for treatment-resistant lifelong PE. However the role of surgical treatment in PE is controversial. **A NOVEL DRUG DAPOXETİNE (PRILIGY):** Dapoxetine is the first SSRI which is approved for PE treatment. Dapoxetine's mechanism of action is the inhibition of neuronal reuptake of 5-HT (serotonin) and subsequently potantialization of 5-HT activity on pre- and post-synaptic receptors. Maximum plasma concentrations are reached in 1-2 hours. Its metabolites are excreted by urine. In PE Piriligy treatment increases not only IELT, but also perceived control over ejaculation and decreases personal distress and interpersonal difficulties. Most frequent adverse event is nausea but infrequently orthostatic hypotension and syncope can be occurring. With its positive safety profile, Piriligy is found to be an effective and tolerable drug for on-demand treatment of PE (11).

REFERENCES:

1. Mc Mahon CG,Stuckey BGA,Andersen M,Purvis K,Koppiker N,Haughi S,Boolell M.J.Sex Med 2005;2:368-375
2. Godpodinoff,M.L.:Premature ejaculation:Clinical subgroups and etiology. J Sex Marital Ther,15:130,1989
3. American Psychiatric Association.Diagnostic and Statistical Manuel of Mental Disorders, Fourth Edition,Text Revision.Washington,DC:American Psychiatric Association;2000.
4. World Health Organization.International Statistical Classification of Diseases and Related Health Problems:Tenth Revision.Vol 1.Geneva:World Health Organization;1992:355-356
5. Mc Mahon CG,Althof SE,Waldinger MD,et al.An evidence-based definition of lifelong premature ejaculation:Report of the ISSM Ad Hoc Committee for the Definition of Premature Ejaculation. J Sex Med.2008;5(7):1590-1606.
6. Waldinger,M.D.,J.McIntosh et al.,2009,A Five-nation Survey to Assess the Distribution of the IELT among the General Male Population:J.Sex Med(Epub ahead of print)
7. Giuliano F,Patrick DL et al.Premature ejaculation:Results from a five-country European observational study. Eur Urol 2008;53:1048-57
8. Waldinger,M.Premature Ejaculation:Different Pathophysiologies Determine Its Treatment.Journal of Sex&Marital Therapy,34:1-13,2008
9. Waldinger.M.Towards evidenced based drug treatment research on premature ejaculation:a critical evaluation of methodology.J Impotence Res 2003;15(5):309-13
10. Safarinejad MR,Hosseini SY.Safety and efficacy of tramadol in the treatment of premature ejaculation.J Clinic Psychopharmacol.2006;26:27-31
11. Kaufman JM,Rosen RC et al.Treatment benefit of dapoxetine for premature ejaculation: Results from a placebo-controlled phase III trial.BJU int 2008;103:651-58

HYPOGONADISM, ERECTILE DYSFUNCTION AND LOWER URINARY TRACT SYSTEM

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Androgen deficiency in the aging male has become a topic of interest and debate throughout the world. Demographic data demonstrates the increasing percentage of the older age groups. The data also support that testosterone (T) falls progressively with age and that a significant percentage of men over the age of 60 years have serum testosterone levels that are below the lower limits of young adult men.

Late onset hypogonadism (LOH) is a clinical and biochemical syndrome associated with advancing age and is characterized by typical symptoms and a deficiency in serum T levels. It may result in significant detriment in the quality of life and adversely affect the function of multiple organ systems.

Symptoms of LOH are: Diminished sexual desire (libido) and erectile quality/frequency, changes in mood; diminished cognitive functions, fatigue, depressed mood and irritability, sleep disturbances, decrease in lean body mass with associated diminution in muscle volume and strength, decrease in body hair and skin alterations and also decreased bone mineral density resulting in increased risk of bone fractures

Hypogonadism and sexual functions

Men with erectile dysfunction (ED) have lower serum T level than men without ED. T level was below 3 ng/ml in 12% of 7000 ED patients compiled from nine large series (1-3). T is required for pubertal acquisition of gender charactersitics as well as adult sexual behavior and functional capacity, including libido, ejaculation and spontaneous erections in men with severe organic hypogonadism.

From animal studies it is well known that T plays critical role in the peripheral modulation of erectile function. The expression of neuronal and endothelial nitric oxide synthases (NOS) are regulated by androgens (4-5). If the androgen suppressed by castration, NOS activity decreases significantly with the structural changes in penile tissue (reduction in trabecular smooth muscle and accumulation of adipocytes in the subtunical layer of corpus cavernosum) (6). Androgen deficiency causes a structural imbalance in corpus cavernosum which results in venoocclusive dyfunction and ED, reversed by T administration (6-7).

In men, sexual desire and erection seem to have different thresholds at central nervous system and also at peripheral level. Positron emission tomography studies reported the testosterone action sites in the brain (8) and also it is well established that there are androgen receptors in corpora cavernosa (9). Some recent studies reported that T may act as a modulator on the vascular erection mechanism in men. In a study made with color doppler ultrasonography of the cavernosal arteries showed the significant relation between the resistive index and the serum free T levels (10). In a study men with arteriogenic erectile dysfunction, having low to low normal testosterone levels and not responding to sildenafil 100 mg, a significantly enhanced peak systolic velocity was shown after T supplementation (11). In a more recent study a significant improvement was seen in erectile and orgasmic function of sildenafil-nonresponder men after transdermal treatment of testosterone (12).

As a result, testosterone deficiency leads to structural and functional alterations in the corpora cavernosa resulting in erectile dysfunction. Men with erectile dysfunction should be screened for testosterone deficiency specially if they did not respond to phosphodiesterase type 5 inhibitors (PDE5i) and treatment.

Hypogonadism and lower urinary tract system

The epidemiology of metabolic syndrome, erectile dysfunction and lower urinary tract symptoms (LUTS) has been established (13). Although there were many studies about the relation between androgens and benign prostate hiperplasia, only a few studies have investigated the relevance between hypogonadism and LUTS. One study showed that one of the every 5 men with LUTS have hyponadism (14). Litman and coworkers found a relationship between LUTS and plasma T level but this finding disappeared after statistical adjustment for age (15).

It is not easy to put forward the direct effect of T on low urinary tract system. Large extent of androgen receptors were found in epithelial cells of urethra and bladder nearly 15 years ago(16) and the role of T on maintaining the reflex activity of the autonomic nervous system was reported 10 years ago (17). The mediator role of nitric oxide (NO) in erection mechanism and the genital system was well established and also it was reported that nearly 96% of the neurons in the bladder wall contains nitric oxide syntase. The authors of this study claim that NO may be an inhibitory transmitter in the relaxation of the bladder neck (18). A recent study, investigating PDE5 expression and activity in the bladder, demonstrated that PDE5 regulates the

smooth muscle tone. So a PDE5i may be a possible therapeutic option for irritative low urinary symptoms. The authors of this study also reported that PDE5 gene expression in rat bladder found to be decreased after castration and T supplementation restored it (19). Meanwhile a large number of clinical studies showed that PDE5 inhibitors have a beneficial effect on LUTS (20-23).

If we look at the studies about the effects of T on bladder function, the first paper was written in 1993 by Holmang who found an increase in peak urinary flow in a T treated group of men compared to placebo group (24). A recent study confirmed the positive effects (decreased AMS and increased IIEF scores with increased bladder capacity-compliance and decreased mean detrussor pressure at maximal flow) of T gel administration for 12 months (25). Conflicting results were reported in different studies about the form and the treatment period of T in men with LUTS. One study found higher levels of T and lower IPPS in men treated with parenteral T Undecanoate (TU) than with T gel (50 mg/day dose). The authors claimed that there was a relationship between the T plasma level and their effects on LUTS (26). Whereas the other one found no siginificant difference between 12 weeks of parenteral TU and 26 weeks of T gel administration in men by the scores of Aging Male Symptom, IIEF-5 and IPSS (27).

It is very obvious that well designed, placebo controlled and randomised studies are needed to understand the effect of T on the men with LUTS. Also uodynamic investigations may provide more accurate information about the direct and indirect beneficial effect of T on LUTS.

REFERENCES:

1. Buvat J., Lemaire A. Endocrrine screening in 1022 men with erectile dysfunction: clinical significance and cost-effective strategy. J Urol 1997;158:764-767
2. Bodie J, Lewis J, Schow D, Monga M. Laboratory evaluations of erectile dysfunction: an evidence based approach. J Urol 2003;196(6):2262-2264
3. Earle CM, Stucky BG. Biochemical screening in the assessment of erectile dysfunction: what tests decide future therapy? Urology 2003;62(4):727-731
4. Park KH, Kim SW, Kim KD, Paick JS. Effects of androgens on the expression of nitric oxide synthase mRNAs in rat corpus cavernosum. BJU Int 1999;83:327-333
5. Baba K, Yajima M, Carrier S, Morgan DM. Delayed testosterone replacement restores nitric oxide synthase-containing nerve fibres and the erectile response in rat penis. BJU Int 2000;85:953-958
6. Traish AM, Kim N. The physiological role of androgens in penile erection: regulation of corpus cavernosum and structure. J Sex Med 2005;2:759-770
7. Rogers RS, Graziottin TM, Lin CM, Kan YW, Lue T. Intracavernosal vascular endothelial growth factor injection and adeno-associated virus-mediated VEGF gene therapy prevent and reverse venogenic erectile dysfunction in rats. Int J Impot Res 2003;15:26-37
8. Stoleru S, Redoute J, Costes N, Lavenne F, Le Bars D, Dechaud H, Forest MG, Pugeat M, Cinotti L, Pujol JF. Brain processing of visual sexual stimuli in men with hypoactive sexual desire disorder. Pschiatry Research:Neuroimaging 2003;124:67-86
9. Schultheiss D, Badalyan R, Pilatz A, Gabouev AI, Schlote N, Wefr J, von Wasielewski R, Mertsching H, Sohn M, Stief CG, Jonas U. Androgen and estrogen receptors in the human corpus cavernosum penis:immunohistochemical and cell culture results. World J Urol 2003;21:320-324
10. Aversa A, Isidori AM, Martino MU, Caprio M, Fabbrini E, Rochietti-March M, et al. Androgens and penile erection:evidence for a direct relationship between free testosterone and cavernous vasodilation in men with erectile dysfunction. Clin Endocrinol 2000;53:517-522
11. Aversa A, Isidori AM, Spera G, Lenzi A, Fabbri A. Androgens improve cavernous vasodilation and response to sildenafil in patients with erectile dysfunction. Clin Endocrinol 2003;58:632-638
12. Shabsigh R, Kaufman JM, Steidle C, Padma-Nathan H. Randomized study of testosterone gel as adjunctive therapy to sildenafil in hypogonadal men with erectile dysfunction who do not respond to sildenafil alone. J Urol 2004;172(2):658-663
13. Rohrman S, Nelson WG, Rifai N, Kanarek N, Basaria S, Tsilidis KK, Smit E, Giovannucci E, Platz EA. Serum sex steroid hormones and lower urinary tract symptoms in third national health and nutrition examination survey (NHANES III). Urology 2007;69:708-713
14. Schatzl G, Madersbacher S, Temml C, Krenn-Schinkel K, Nader A, Sregi G, Lapin A, Hermann M, Berger P, Marberger M. Serum androgen levels in men: impact of health status and age. Urology 2003;61:629-633
15. Litman HJ, Bhasin S, O'Leary MP, Link CL, McKinlay JB. An invastigation of the relationship between sex-steroid levels and urological symptoms: results from the Boston area community health survey. BJU Int 2007;100:321-326
16. Rosenzweig BA, Bolina PS, Birch L, Moran C, Marcovici I, Prins GS. Location and concentration of estrogen, progesterone and androgen receptors in the bladder and urethra of the rabbit. Neurourol Urodyn 1995;14:87-96
17. Keast JR. The autonomic nerve supply of male sex organs-an important target of circulating androgens. Behav Brain Res 1995;105:81-92

18. Smet PJ, Jonavicius J, Marhall VR, de Vente J. Distribution of nitric oxide synthase-immunoreactive nerves and identification of the cellular targets of nitric oxide in guinea-pig and human urinary bladder by cGMP immunohistochemistry. Neuroscience 1996;71:337-348
19. Filippi S, Morelli A, Sandner P, Fibbi B, Mancina R, Marini M, Gacci M, Vignozzi L, Vannelli GB, Carini M, Forti G, Maggi M. Characterization and functional role of androgen dependent PDE5 activity in the bladder. Endocrinology 2007;148:1019-1029
20. Truss MC, Stief CG, Uckert S, Becker AJ, Wefer J, Schultheiss D, Jonas U. Phosphodiesterase 1 inhibition in the treatment of lower urinary tract dysfunction: from bench to bedside World J Urol 2001;19:344-350
21. Montorsi F, Corbin J, Phillips S. Review of phophodiesterases in the urogenital system: new directions for therapeutic intervention. J Sex Med 2004;1:322-336
22. Uckert S, Hedlund P, Andersson KE, Truss MC, Jonas U, Stief CG. Update on phosphodiesterase isoenzymes as pharmacologic targets in urology: present and future. Eur Urol 2006;50:1194-1207
23. Mc Vary KT, Monnig W, Camps JL, Young JM, Tseng LJ, van den Ende G. Sildenafil sitrate improves erectile function and urinary symptoms in men wit erectile dysfunction and lower urinary tract symptoms associated with bengn prostatic hiperplasia: a randomized, double-blind trial. J Urol 2007;177:1071-1077
24. Holmang S, Marin P, Lindstedt G, Hedelin H. Effect of long term oral testosterone undecanoate treatment on prostae volume and serum prostate specific antigen concentration in eugonadal middle aged men. Prostate 1993;23:99-106
25. Karazindiyanoğlu S, Cayan S. The effect of testosterone therapy on lower urinary tract symptoms/bladder and sexual functions in men with symptomatic late-onset hypogonadism. The Aging Male 2008;11(3):146-9.
26. Saad F, Gooren LJ, Haider A, Yassin A. A dose response study of testosterone on sexual dysfunction and features of the metabolic syndrome using testosterone gel and parenteral testosterone undecanoate. J Androl 2008;29:102-105
27. Kalinchenko S, Vishnevskiy EL, Koval AN, Mskhalaya GJ, Saad F. Beneficial effects of testosterone administration on symptoms of the lower urinary tract in men with late-onset hypogonadism: A pilot study. The Aging Male 2008;11(2):57-61

SURGICAL TREATMENT OF URETHRA STRICTURES, OBLITERATIONS AND HYPOSPADIAS

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Stricture of urethra is viewed as a lesion of urethra wall with impairment of its lumen. Narrowing and obliteration of posterior, supradiafragmatic part of urethra is subject to endoscopic correction. In case of obliteration of prosthetic part of urethra, anasthomotic uretroplasty with urethro-cysto-anastomosis is needed. Obliteration of membranous part of urethra or sphincter-stenosis is eliminated only by means of anasthomotic urethroplasty. Stricture disease of spongious part of urethra is determined by the onflow of infectious process. At spongiofibrosis with lesion depth more than ½ of urethra wall, anasthomotic operatons are ineffective. In this case augmenting or vicarious urethroplasty is recommended. The severity of fibrose alteration of spongious body determines the type of urethroplasty. Separation of bulbous part of urethra from bulbocavernous muscles leads to injury of diaphragma muscle nerve trunks and cavernous nerves, also impairing blood circulation of urethra wall on its dorsal surface.

Staging of urethroplastics is determined by the quality of donor-spot and the possibility of tubularization of the used flap. In order to minimize the operating time on neo-urethra in case of stricture relapses, use of hairless scrotum flaps at bulbo-urethroplasty is recommended.

Ventral postion of vascularized flap would make the anasthomosis and its lumen nondeformable, while the vascular pedicle of the flap would provide better trophic of the urethra wall.
The author performed 211 operations; of wich 167 were primary (no relapses), 44 reoperations (after relapses). Average age of the patients made 35,4 y.o.

66 vicarious operations were performed at strictures and obliterations of subdiaphragmal urethra with use of vascularized penile and scrotile skin flaps, buccal mucosa.

Out of the total number of vicarious operations 53 were primary, 13 secondary; 47 were performed at stricture of stem part of urethra and hypospadias. The average length of stricture made 3 cm (from 1,5 to 5 cm).

At stem hypospadias 7 operations were performed, of which according to: HODSON–2, DUCKETT–3, LANDERRER-RUSAKOV-3.

Urethroplasties performed with ventral position of penile flap according to: Mc. ANINCH -12, HODSON -2, DUCKET -3, JORDAN -4, ORANDY -7, QUARTEY -9, BARBAGLI with ventral position of buccal flap –5, dorsal position –1.

Urethroplasties with ventral position of scrotile flap according to: LANDERRER-RUSAKOV-6, BLANDY-15.

At stricture of bulbous part of urethra 19 vicarious urethroplasties were performed. In 2 cases patients had already had penile-bulbous neourethra formed out of penile or scrotum skin.

Complications in form of re-stenosis were observed in 12 cases and were followed by reoperations in 9 cases and bouginage in 3 cases. Reoperations performed: optical internal urethrotomy (OIU) –5, repeated urethroplasties –4: Mc. ANINCH re-stenosis –1, reoperation: OIU –1; DUCKET – re-stenosis –2, reoperations: OIU –1, urethroplasty –1; JORDAN – re-stenosis –1, bouginage –1; ORANDY – re-stenosis-1, reoperation: OIU –1; QUARTEY – re-stenosis –2, reoperations: OIU-1, urethroplasty –1; LANDERRER-RUSAKOV – re-stenosis – 3, reoperations: urethroplasty-2; BLANDY – re-stenosis -2, reoperations: IOU –1, bouginage –1. In one patient operated according to BLANDY, urethrotomy was performed twice. Four patients at re-stenosis (after urethroplasties according to LANDERRER-RUSAKOV –2, DUCKET –1, QUARTEY –1) were successfully reoperated according to Mc. ANINCH –2, JORDAN –1, LANDERRER-RUSAKOV –1. There were no cases of purulent inflammation processes, urethroplasty-zone fistula, necrotic complications of donor spot, cosmetic or erectile deformity of penis.

There were performed 145 anasthomotic urethroplasties. Primary operations were performed in 114 patients, reoperations were performed in 31 patient. Out of 145 anasthomotic urethroplasties 93 were performed in cases of strictures or obliterations of bulbous part, 49 in cases of strictures or obliterations of membranous part. 3 operations were done according to Solovov-Shalimov (invaginational urethro-cysto-anasthomosis) in cases of obliteration of prostatic urethra after prostatectomy. One operation was done at diverticula with stones at bulbous urethra part. Anasthomosis with spatulation was performed not in all the patients. The average length of stricture made 3 cm (from 1,5 to 5 cm). The complication of anasthomotic urethroplasties was relapse of the stricture in 19 cases, requiring: OIU in 9 cases, bouginage in 5 cases and repeated anasthomotic urethroplasty in 5 cases (2 of them were augmenting operations according to Terner-Warwik with ventral position of the flap).

REFERENCES:

1. Abouassaly R, Angermeier KW Augmented anastomotic urethroplasty. J Urol. 2007 Jun;177(6):2211-5;
2. Advanced Urologic Surgery Rudolf Hohenfellner, John Fitzpatrick, Jack McAninch,Jack W. McAninch 2005 p 175-186
3. Aggarwal SK, Goel D, Gupta CR, Ghosh S, Ojha H. The use of pedicled appendix graft for substitution of urethra in recurrent urethral stricture. J Pediatr Surg. 2002 Feb;37(2):246-50.
4. Al-Rifaei MA, Al-Rifaei A Management of postoperative obstruction after bulboprostatic anastomotic urethroplasty for membranous urethral defects secondary to pelvic fracture Scand J Urol Nephrol.2001 Dec;35(6):491-6.
5. Anastomotic fibrous ring as cause of stricture recurrence after bulbar onlay graft urethroplasty. Barbagli G, Guazzoni G, Palminteri E, Lazzeri M. J Urol. 2006 Aug;176(2):614-9;.
6. Andrich DE, Leach CJ, Mundy AR. The Barbagli procedure gives the best results for patch urethroplasty of the bulbar urethra. BJU Int. 2001 Sep;88(4):385-9.
7. Andrich D. E., Anthony R. Mundy What is the Best Technique for Urethroplasty? European urology Volume 54, Issue 5, Pages 1031-1041 (November 2008)
8. Bellinzoni P, Rigatti P. Comparison of surgical techniques: resection and termino-terminal anastomosis Arch Ital Urol Androl. 2002 Sep;74(3):117-8
9. Barbagli G, Lazzeri M Urethral reconstruction.Curr Opin Urol. 2006 Nov;16(6):391-5.
10. Blandy J.P Urethral stricture Postgraduate Medical journal 1980,56, 383-418

CORRECTION OF PENILE CURVATURE DURING HYPOSPADIAS SURGERY

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Correcting penile curvature is an essential step for hypospadias repair; however, it is challenging for pediatric urologists in cases with significant curvature. During the 20th century, few published reports have provided objective guidelines as to the degree of congenital penile curvature with hypospadias that inhibits sexual intercourse in adulthood. However,a survey of members of the American Academy of Pediatrics Section on Urology attempted to establish a consensus on the management of penile curvature, including determining these verity that mandates intervention, as well as the optimal technique for correction (1). Significant penile curvature is usually thought to be secondary to corporeal disproportion with a shorter ventral surface of corpora cavernosa. A popular approach to penile curvature is to shorten the dorsal surface of the corpora cavernosa (1). In the literature, the correction of penile curvature was achieved with shortening the dorsal side reportec by Nesbit (2). However, Baskin and Duckett reported that a functional penis may be achieved without division of the urethral plate in approximately 90% of hypospadias patients by dorsal placation (3).

The etiology of penile ventral curvature was originally described as tethering from a dysplastic sorpus spongiosum/urethral plate, so-called chordee. Wehereas this concept of chordee mandated urethral plate excision for straightening, modern recognition that all ventral tissues, including shaft skin, dartos, corpus spongiosum/urethral plate and corpora cavernosa, may be shortened but not dysplastic potentially increases the options for straightening while maintaining tha plate (4). Greater than 30-degree VC that persists after penile degloving and ventral dartos dissection leads to multiple dorsal plications vs ventral corporotomy with grafting for straightening (5). Freeing the corpus spongiosum urethral plate from the underlying corpora cavernosa, sometimes combined with proximal dissection of the normal urethra to the bulb, relying on elasticity of these structures to allow the penis to straighten are additional options (4).

Hypospadias is considered arrested development and, given observations that VC normally occurs during penile formation, it follows that all ventral tissues may be relatively shortened compared to the dorsal aspect. Persistent VC after degloving and ventral dartos dissection may reflect a shortened corpus spongiosum/urethral plate and/or corporeal disproportion. Histology of the corpus spongiosum/urethral plate does not support traditional concepts of dysplastic chordee tissues requiring resection for straightening, but rather shows well vascularized tissues that may retain sufficient elasticity to allow straightening without resection.

It was reported that 99% of pediatric urologists would intervene and most would perform some form of dorsal placation for the treatment of moderate curvature (30°-40°) and that severe curvature(>50degrees) was approached ventrally by 54% of pediatric urologists (1). Especially, for severe chordee, corporeal body grafting is recommended. For 25 to 40 degrees of curvature the treatment choice depends on penile size and surgeon preference.

Several grafts are popular. Dermal grafting was tried with limited morbidity and excellent results but dermal graft harvesting may result in keloid formation at the donor site, which is common in Mediterranean and black populations. Experimental and clinical studies suggest that dermal grafts are superior to tunica vaginalis grafts (6). Tunica vaginalis is readily available with an easy harvesting technique. Prior results suggest that the tunica vaginalis free graft shows high failure and residual curvature. In contrast, Ritcheyetal noted excellent results using tunica vaginalis grafts. Tunica vaginalis flap shad results superior to those of tunica vaginalis grafts. Tunica vaginalis flap had better vascularity and decreased morbidity to the donor graft site (7). However the other controversial issue is the scientific terminology of chordee with or without hypospadias. Accordingly, past operations emphasized the need to thoroughly resect ventral tissues for straightening, while modern understanding offers option stop reserve the corpus spongiosum and urethral plate. Today transaction of the urethral plate should be an uncommon maneuver in both hypospadias repair and in operations for'chordee without hypospadias'. Furthermore, the term 'chordee' , which in common usage has meant either fibrotic tissues causing curvature or the actual bending, is inaccurate and imprecise and so should no longer be used in scientific reporting (8).

REFERENCES:

1. Hayashi Y, Kojima Y, Mizuno K, et al. Demonstration of postoperative effectiveness in ventral lengthening using a tunica vaginalis flap for severe penile curavature with hypospadias. Urology articie in press. DOI:10.1016/j.urology.2009.08.080
2. Nesbit RM. Congenital curvature of the phallus: report of three cases with description of corrective procedure. J Urol.1965;93:230-232.

3. Baskin LS, Duckett JW. Dorsal tunica albugine application for hypospadias curvature. J Urol.1994;151:1668-1671.
4. Snodgrass W, Prieto J. Straightening ventral curvature while preserving the urethral plate in proximal hypospadias repair. J Urol 2009;182:1720-1725
5. Bologna RA, Noah TA, Nasrallah PF et al: Chordee: varied opinions and treatments as documented in a survey of the American Academy of Pediatrics, Section of Urology. Urology 1999; 53:608
6. Mokhless I, Youssif ME, Orabi SS, Ehnaiash MM. Corporeal body grafting using buccal mucosa for posterior hypospadias with severe curvature. J Urol 2009;182;1726-1729
7. Ritchey ML and Ribbek M: Successful use of tunica vaginalis grafts for treatment of severe penile chordee in children. J Urol 2003; 170:1574.
8. Snodgrass WT. Management of penile curvature in children. Cur Op Urol 2008;18:432-435

PENILE CURVATURE SURGERY FOR CONGENITAL PENILE CURVATURE

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Congenital bend of the penis is caused by decreased elasticity in one or more of the fascial layers of the penis leading to a shortness of one aspect of the erect corporal bodies. The bend may be ventral, and/or lateral or complex(1). Congenital curvature is mostly ventral. The reported prevelance of congenital penile curvature is 0.04-0.6%. The actual prevelance may be far higher than this because many curvatures are mild and of no clinical significance(2). Fetal development of the penis is regulated by the testosterone produced by the fetal testis and is converted to dihydrotestosterone by the enzyme 5-alpha reductase in the target cells of male external genitalia(1). Congenital penile deviations may be the result of a temporary testosterone deficciency or androjen insensivity during fetal development(3). Patients may not seek treatment until the of the puberty, because often the curvature worsens or does not become apparent until the growth of the penis that occurs during adolescence(1). When congenital penile curvature causes significant emotional disturbance, pain in the erect penis, difficulty with vaginal penetration or pain in the female partner during sexual intercourse surgical treatment is required(4,5). The young men with penile curvature tend to have a stretched penile length greater than average, with a gradual curvature throughout the length of the shaft. Each patient should be asked to bring a polaroid photograph of his erect penis documenting the curvature and also should he screened preoperatively by a sex therapist. Since one of the primary concerns of patients preoperatively is penile length loss(1).

Surgical Options

There are two popular surgical procedures that have been performed since 1947 for the treatment of congenital penile curvature. These are Nesbit and plication techniques(6). These techniques are also named tunical incision and non incision procedures. The advantages of these approaches include short surgical time, no significant negative effect on erectile hemodynamics, good cosmetic outcomes, simple, safe and effecting regarding straightening. The major disadventage is the shortening of the penis(3). Tunical incision procedures involve making incisions in the tunica and excising wedge/elipse (Nesbit procedure), or leaving a intervening segment of the tunica intact and covering it over with a suture line connecting the two tunical incisions(modified corporaplasty), or fashioning a longitudinal incision and closing it in a Heineke-Miculicz fashion transversely(Yachia procedure). The advantages of these modified procedures are that the repair heals by primary intention. However the repair does require an incision in the tunica. The Nesbit procedure was originally developed for congenital penile curvature repair.Plication procedures do not involve making a tunical incision but rather fold the tunica, thus the integrity of the curvature correction is dependent upon the strength of the suture used to imbricate the tunica(3). When performing a Nesbit procedure for a ventral curvature we mobilize the lateral aspects of Buck's fascia and elevate the dorsal neurovascular bundle from the tunica. An artificial erection allows us to mark a narrow elipse of tunica opposite the point of maximum concavity. We plicate the edges of this ellipse with several 5-0 prolene sutures and repeat the artificial erection. İf penis is not perfectly straight we mark and plicate a second and if neccessary a third elipse until the penis is straight. We mark the edges of the ellipses before removing the sutures. During excising and removing the ellipse of the tunica we must be careful not to damage the underlying erectile tissue. The defects are closed with interrupted and running 5-0 PDS. The resultant scar is usually impalpable. After closure another artificial erection is performed to confirm straightening(1). Subcoronal incision and penile degloving is frequently used in both plication and Nesbit procedures. Corporeal plication technique consist of placing longitudinal plication sutures of 2-0 braided polyester(or another nonabsorbable suture) on the convex side of the curvature until the curvature is corrected when the erection is artificially induced(7). In recent years plication procedures mostly advocated for the treatment of congenital penile curvature. The frequently quoted advantages over traditional Nesbit procedure include easier operation and fewer complication(8). Corrective surgery for penile curvature is highly successful. The overall reported success rate with tunica albuginea plication and Nesbit procedure is between 75-100%. Reccurence of the curvature is estimated 0-26%. Penile shortening after the surgery is up to 74% in some series(3). While postoperative satisfaction is the rule, a number of patients find some side effects of the procedure unacceptable, apart of residual curvature frequent reasons for dissatisfaction are unpleasent feelings of bumps under the skin, penile sensory changes and penile shortening. Understanding the penile anatomy, selection of surgical method and the meticulous surgical procedures to preserve neurovascular bundles may be important to improve the long term outcome and reduce complications(9,10).

REFERENCES:

1. Devine CJ, Jordan GH, Schlossberg SM : Surgery of the penis and urethra. In Walsh PC-Retik AB- Stamey TA-Vaughan ED (eds): Campbell's Urology. Philadelphia, Pennsylvania, USA, WB Saunders, 1992, pp 2957-3070.
2. Paez A, Mejias J, Vallejo J, Romero I, Castro M, Gimeno F. Long-term patient satisfaction after surgical correction of penile curvature via tunical plication. Int Braz J Urol. 2007; 33: 502-509.

3. Mulhall J : Surgical treatment of Peyronie's disease. In Porst H-Buvat J (eds): Standart practice in Sexual Medicine, Massachusetts, USA, Blackwell Publishing Inc, 2006, pp 165-173.
4. Erpenbach K, Rothe H, Derschum W. The penile plication procedure: an alternative method for straightening penile deviation. J Urol 1991; 146: 1276-1278.
5. Horton CE, Devine CJ, Mc Craw JB. Penile curvatures. Plast Reconstr Surg 1985; 75: 752-759.
6. Paulsen J, Kirkeby HJ. Treatment of penile curvature-a retrospective study of 175 patients operated with plication of the tunica albuginea or with the Nesbit procedure. Br J Urol 1995; 75: 370-374.
7. Gholami SS, Lue TF. Correction of penile curvature using the 16-dot plication technique : a review of 132 patients. J Urol 2002; 167: 2066-2069.
8. Ho KL, Yip AWC, Leung LS, Law IC. Surgical treatment of penile curvature. Hong Kong Med J 2006; 12: 410-414.
9. Gholami SS, Gonzalez-Gadavid NF, Lin CS, Rajfer J, Lue TF. Peyronie's disease: a review. J Urol 2003; 169; 1234-1241.
10. Carrier S, Lue TF. For Peyronie's disease, act conservatively. Contemp. Urol 1994; 6: 53-65.

PENILE PROSTHESIS IMPLANTATION IN PEYRONIE'S DISEASE

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Indications.

In the past, penile prosthesis were implanted in all patients who had a penile deformity with or without ED. Now surgical therapy is reserved for patients, who fail conservative treatment.

Criteria for all options surgical treatment:

- Severe curvature, narrowing or indentation more than 1 years duration (except for the presence of a calcified plaque, in which case surgery may be undertaken earlier).
- Disease activity must be stable and unchanged for at last 3 months.
- Presence of severe curvature, which prevent sexual intercourse.
- Severe penile shortening. (1)

Surgery approaches

3 main categories:

1. Shortening the convex side (Nesbit, plication, corporoplasty).
   Penile shortening is the most problem despite restore sexual function and normal erection.

2. Lengthening the concave side (incision or excision and grafting).
   Grafting surgery is not recommended for patients with ED (25% PTs - PD + ED).

3. Penile prosthesis implantation (with/without combination procedures 1 or 2). (1)

Grafting surgery

Plaque excision and grafting is a formidable surgical exercise. When a complex repair is necessary, implantation of penile prosthesis is better and more effective. Any procedure that interrupts tunical integrity by incision may lead to impairment of erection and neurovascular bundle injury during dissection). (2)

Indication for prosthetic surgery

1. Significant ED or flaccidity distal to the plaque
2. As an alternative - incision/excision +grafting
3.! Candidate pool for prosthetic surgery can be expanded to include men with short penis and partially ED (taking into account the complications and disadvantages of lengthening and shortening procedures).
4.! All patients with PD over 50 should be considered as candidates to prosthetic surgery (taking into account high frequency ED. (2)

Be careful!

Patients with unrealistic expectations will not satisfied with prosthetic surgery.

Tips and tricks:

- Prosthetic girth is more important than length in correction of curvature (additional girth helps overcome the deformity)
- Surgeon should attempt to place rods the same length in Peyronie's PTs (despite shortening of one side because of PD)
- 0,5 cm downsizing of rod implants will allow better bendability in the presence of extensive scar tissue

Sizing of malleable prosthesis is more crucial than size selection of inflatable one!

- If the rods doesn't straighten - modeling procedure may be used
- The residual curvature to overcome by relaxing incisions with electrocautery
- The tunical defects don't require closure – rods don't expand to herniate through small incision
- Subcoronal approach preferable than traditional penoscrotal (facilitate degloving if need additional straightening by incision).

Which preferable

Two Piece Hydraulic Prosthesis:

AMS –Ambicor, Mentor – Excel (Mark 2)

- Less mechanically reliable
- Inadequate axial rigidity
- not as reliable in straightening

Not recommended for Peyronie's Disease Patients!

Three Piece Prosthesis:

AMS –Ultrex

- Cylinders expanded distally exaggerate the curvature
  - give «S» like configuration

Not recommended for Peyronie's Disease Patients !

Three Piece Prosthesis

AMS –CX, CXM, CXR, (Inhibizone)
Mentor – alpha 1,(Titan), alpha NB,
These types cylinders:
- don't expanded distally,
- give good intrinsic rigidity

Recommended for Peyronie's Disease Patients !

Tips and trics

Not recommended inflatable prosthesis in the presence of a calcified plaque, especially septum (high risk damage cylinders).

Inflatable Prosthesis

Correction deformity:
1 step - modeling procedure;
2 step (if residual curvature)- incision +grafting surgery (preferable) or plicaton.

Modeling: tips and tricks.

- A running closure of the corporotomy more reliable during modeling then interrupted sutures.
- Two modeling sessions are enough for curvature correction.
- Residual curvature of 20 dg is acceptable.
- Don't use Mentor alpha NB (may develop cylinder aneurysm and rupture through the gaping corporotomy. (2)

Grafting surgery

Grafting materials:

Synthetic (heterologous): Dacron, GoreTex, silastic, Pelvicol.

Autologous: dermis, saphenous vein, penile dorsal vein, tunica vaginalis, tunica albuginea, muscular aponeurosis, fascia lata.

Allogenous (cadaveric): pericardium, small intesninal submucosa (SIS), dura mater.

Xenogenous: bovine/ pig pericardium.

Naturally harvested grafts such as dermis and vein are less likely to be successful as they have only one surface available for imbibitions. Syntetic materals - higher risk of prosthetic.

Grafting: tips and trics.

After grafting surgery the prostheses should be kept about 75% inflated within 3 months for good length expansion of the penis. After modeling or grafting surgery the penis should be positioned pointing in the cephalic direction. Healing of scar tissue in the postoperative period will occur in the position in which the penis is kept. It is necessary to keep penis in the functional position, like during erection. Loss penile length is main problem patients with PD after implantation.

Two surgical techniques:

1. Incision and grafting.
2. Release of suspensory ligament during implantation. (3)

Very important.

Despite of widespread acceptance of the efficacy of the prosthesis implantation, less than 10% of urologists perform 90% of the world's penile implants.

«Like in aviation, where pilot error exceeds mechanical failure as a cause of crash, the human factors are more often causes of implant reoperations than mechanical problems» (Steven Karl Wilson, 1997).

Conclusion.

Ideal penile prosthesis - what is it? Ideal penile prosthesis – absence of prosthesis in the penis. But it is my masculine (NOT SURGICAL!) opinion.

REFERENCES:

1. WJG Hellstrom, MF Usta. Surgical approsches for advanced Peyronie's disease patient. International Journal of Impotence Research. v.5, suppl. 5, october 2003, pp 121-124.
2. SK. Wilson, KL. Billips Chapter 13 «Peyronie's Disease and Penile Implants» in book «Urologic Prosthesis» 2002 Humana Press.
3. F. Borges, L. Hakim, C. Kline. J. Sex. Med. 2006; 3;550-553.

DUAL IMPLANTATION OF INFLATABLE PENILE AND ARTIFICIAL URINARY SPHINCTER PROSTHETICS IN THE POST-PROSTATECTOMY BY SINGLE INCISION

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Radical prostatectomy is the most widely accepted form of management of localized prostate carcinoma. Nearly 100.000 radical prostatectomy are performed each year in the United States. Despite major improvement in surgical techniques for radical prostatectomy, postoperative erectile dysfunction and urinary incontinence are the major issues dealing with quality of life after this surgery. Postoperative incontinence of any degree following radical prostatectomy is reported in up to 40% of cases (1). The most common cause of incontinence is intrinsic sphincteric deficiency (2). Erectile dysfunction (ED) is the second distressing problem. Both problems may occur in the same patient. In fact, the common etiologic factor related to neurovascular bundle injury may increase the likelihood of the second complication in a patient who already has one. Both problems are usually evident in the first weeks following surgery. Although most of these patients can be adequately treated with conservative treatment modalities such as pelvic exercises for urinary incontinence and oral and topical agents or vacuum erection devices for ED during the first year after surgery, approximately 2% will elect to have a PP inserted and a higher proportion to have an AUS inserted (3).

Insertion of an AUS and PP, either synchronously or sequentially, appears to be a safe, efficacious (greater than 80%) and long-lasting method of treatment (4). With the development of the single transverse scrotal incision to insert an AUS, the synchronous insertion of an AUS and PP became possible (4). This incision allows adequate access to the bulb of the urethra for cuff placement, both the corpora to place the IPP cylinders and also to the retropubic space through the external inguinal rings for placement of the reservoir and the PRB (5). Specific benefits of synchronous insertion are a single incision and anaesthetics, faster operating time, shorter hospital stay and potentially lower infection rates. A sequential procedure implies that extra care is needed to avoid damaging the components of the existing implant and the added danger of operating in an area with surgical scarring. Another issues that need to be considered before performing a dual implant are patient dexterity and surgeon experience. The patient or partner need to have sufficient dexterity to activate either pump as required.

The patient, a 60-year-old man, had undergone a non-nervesparing radical prostatectomy for prostate cancer in October 2008 at another urological clinic. After one year from the surgery, he admitted to our clinic for both urinary incontinence and ED which were not responded to conservative treatment. In October 2009, simultaneous implantation of the AMS 700CX IPP (Inhibizone) and AMS 800 AUS (American Medical Systems, Minnetonka, Minnesota) through a transverse scrotal approach was performed in this patient. Before component placement the patient was administered antibiotics, including vancomycin and levofloksasin for antimicrobial prophylaxis. The patient was placed supine under general anesthesia with the legs slightly abducted. The pubic hair was completely shaven in the operating room, just prior to surgery, to minimize abrasion and trauma to the perineal skin which can also increase the risk of infection. The patient was scrubbed for 15 minutes with povidone-iodine scrub and paint, and draped in sterile fashion. The bladder was completely drained via a Foley catheter. A double circle Scott retractor was placed around the genitals with the penis pointing cephalad in the larger ring. A transverse incision was made at the penoscrotal junction with a 15 scalpel and extended through the subcutaneous tissue. Blunt stay hooks were placed at the 1, 3, 5, 7, 9 and 11 o'clock positions to secure the scrotal incision and expose the corpus spongiosum and the 2 corpora cavernosa. Metzenbaum scissors were passed just lateral to the ventral side of the spongiosum and a retractor is placed to create deeper ventral exposure. When the septum was fully exposed it was incised with a curved scissor. A right angle clamp was used for careful blunt dissection of the bulbocavernosus to expose the entire bulbous urethra for a sufficient vertical distance to accommodate the 2.0 cuff width. The correct AUS cuff size was then determined using the measuring device and the cuff was placed. The respective tubing needs to be positioned such that tubing from one prosthesis does not interfere with that of the other. Finger was passed just medial to spermatic chord up and into inguinal canal scrotal ring. After ring medial aspect was entered Mayo scissors were pushed down through fascia for approximately 1 to 2 inches. After spreading and withdrawing scissors finger was pushed medial and then down to dissert space for reservoir. Reservoir was then wrapped around surgeon finger and inserted into this cavity. The pump for each device was placed in the ipsilateral hemiscrotum.

Then, the corpora were dilated and sized for the cylinders cautiously in the proximal part of the corpora near the cuff. Once the cylinders were in place, the corporotomies were sutured such that they were water-tight. The reservoir was then placed and the tubing, pump and connections were completed (6). The pump was placed in the scrotum on the same side. The AUS was cycled and left in a deactivated state and the PP was left inflated overnight as usual to minimize bleeding. A Foley catheter was left in place for 24 hours. A drain was placed at the lowest point of scrotal dissection, coming out at the level of the pubic tubercle. It was removed on postoperative day 1. Layers were closed by continuous suture, with care not to damage any prosthetic material and dressing was applied. The patient was discharged after 2 days of the surgery on oral antibiotics. In

postoperative period no complication was developed and , at present, both prostheses are functional. Dual prosthetic implantation is appropriate treatment for men bothered by both refractory erectile dysfunction and urinary incontinence after prostatectomy. It is safe and efficient—minimizing risk and maximizing patient satisfaction. However, performing the dual implantation procedure should be reserved for experienced prosthetic urologists.

REFERENCES:

1. Hussain M, Greenwell T J, Venn S N and Mundy A R: The current role of the artificial urinary sphincter for the treatment of urinary incontinence. J Urol 2005;174: 418.
2. Majoros A, Bach D, Keszthelyi A, et al.: Urinary incontinence and voiding dysfunction after radical retropubic prostatectomy (prospective urodynamic study). Neurourol Urodyn 2006; 25:2–7.
3. Stephenson RA, Mori M, Hsieh Y, Beer TM, Stanford JL, Gilliland FD, et al. Treatment of erectile dysfunction following therapy for clinically localized prostate cancer: patient reported use and outcomes from the surveillance, epidemiology and end-results prostate cancer outcomes study. J Urol 2005;174: 646–650.
4. Wilson SK, Delk JR II, Henry GD, et al: New surgical technique for sphincter urinary control system using upper transverse scrotal incision. J Urol 2003; 169: 261–264.
5. Kendirci M, Gupta S, Shaw K, et al.: Synchronous prosthetic implantation through a transscrotal incision: an outcome analysis. J Urol 2006; 175:2218–2222.
6. Moncada I. Dual implant in patients with incontinence and erectile dysfunction. J Sex Med 2006; 3: 367–370.

MANAGEMENT OF PENIL FRACTURE

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Penil fracture is described as rupture of a tunica albuginea due to trauma of penis on erection. Penis is not effected significantly from trauma during detumescence.On the other hand, if enough force is applied to cause axial or distortion, fracture occurs in errect penis .

An Arabic doctor, Abul Kasem first described penil fracture in Cordoba 1000 years ago. Operational treatment option was first defined by Fernstrom in 1957 (1-2).

ETIOLOGY

The causes of penil fracture etiology alters depending on the countries and sociocultural status of society. In a study including 155 patients it was reported that these contained as sexual liaison %50.3 , masturbation %14.8,direct kunt trauma %14.8 and rolling over in bed %1.6. With another study consisting of 300 patients it was reported to have %60 masturbation, ,%19 sexual relations and rolling over in bed as %21 (3) .

PHYSIOPATHOLOGY

In the tumescent state the corpora cavernosa become enforged with blood and the tunica albuginea thins from 2 mm to 0,5 mm . the normal pressure inside the errect penis is the mean arterial pressure at 100 mm-hg .The intracorporeal pressure that is needed to rupture the tunica or overcome its tensile strength, is 1500 mm-hg (2,5,6).

CLINIC

Penil fracture clinic is highly typical.Diagnosis is usually placed after physical examining.The story of patient includes swelling of penis ,ecimotic , aubergine coloured penis and the deviation of ripped penis on the opposite way. Patients hear the ripping sound of tunica charactristically as popping sound.

Sudden detumescence and pain ocur in almost all patients.
Tunical ripping is usually seen as one-sided, sometimes it is bilateral.Uretral injury is about %10 .Penil vascular injuries (superficial, deep dorsal vein and dorsal artery) are rare.

DIAGNOSIS

Story and physical examination are usually enough to have a diagnosis.For doubtful cases, rupture and hematoma can be determined by ultrason as non-invasive.Cavernosography is invasive and there is a risk of enfection.Diagnosis by MRI is expensive and may not be possible ever time . If there is doubt of ureatral injury, retrograd uretrograpy can be taken or during the operation, clinical diagnosis is described by using flexible uretroscopy.

TREATMENT

Until 1980's, conservative treatment used to be popular in the treatment of penil fracture .However, due to %10-30 of penil deviation , suboptimal erection and coitus difficuly urgent operational treatment has been essentially preffered.There are 3 different way of entering the fractured penis (4).

a) Subcoronal incision
b) Midline incision
c) Penoscrotal incision

Deglove with subcoronal incision is mostly preffered.The advantage of this method is that it is checked by direct vision of each of three corpus.

Uretral catheter is placed with purpose of taking back one day after the operation.Hematoma in degloved penis is cleaned and ripped tunica is covered with interrupted absorbapl suture .
Procedure is completed by placing penrose to fixed area. Wide-spectrum antibiotic is given for a week. After fixing, uretra is followed for 2-3 weeks. One month later coitus can be applied.

REFERENCES:

1. Evangelos M.M,Livadas K,Chalikopoulos D,Bisas A,Deliveliotis C,Skolarikos A Penil fractures:İmmediate surgical approach with a midline ventral incision,BJU inter. 104,520-523,2009
2. Kamdar C,Mooppan UMM,Kiu H,Gulmi FA: Penil fracture:preoperative evaluation nd surgical technigue for optimal patient autcome BJU inter,102,1640-1644,2008
3. El housseing İ,El-Tholoth HS,Mohsen T,Hekal I,El Assmy A Penil fracture :Long-term outcome of immediate surgical intervention,urology 75:108-111,2010
4. Atat R,Sfaxi M,Benslama MR, Amine D,Ayed M,Mouelli SB,Chebil M,Zmerli S Fracture of the Penis:Management and long-term results of surgicaltreatment experience in 300 cases. J Trauma 64 ,121-125,2008
5. Asgari MA,Hossieni SY,Saferinejad MR,Samadzedeh B,Bardideh AR Penil fracture: evaluation,Therapeutic approaches and long-term results. J Urology 155,148-149,1996
6. De Rose AF,Giglio M, Carmignani G Traumatic rupture of the corpora cavernosa:new physiopathologic acguisitions,Urology 57,319-322,2001

FASCIAL ANATOMY RELATED TO CANCER CONTROL AND PRESERVATION OF ERECTION AND CONTINENCE FOR RADICAL PROSTATECTOMY

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The optimal outcome after radical prostatectomy for clinically localized prostate cancer is freedom from biochemical recurrence along with the recovery of continence and erectile function, a so-called 'trifecta', a term described first in 2005 (1,2). And in order to achieve the best 'trifecta' outcome, the treatment of prostate cancer with nerve sparing radical prostatectomy (NSRP) has experienced a substantial improvement in recent years due to new insights in anatomy of the prostate and of the adjacent structures. Knowledge of this specific anatomy is mandatory during NSRP in order to avoid injuries to functional tissue. Above all, these tissues are the neurovascular bundle (NVB) and the urethral sphincter. And herein the available literature on prostatic anatomy related to these structures will be reviewed.

During a radical prostatectomy procedure, the NVB can be injured near the seminal vesicles, at the lateral surface of the prostate and in the area of the prostato-urethral junction. The urethral sphincter may be hampered during dissection of the dorsal vein complex and during dissection of the urethra at the prostatic apex. Finally, the anatomy of the fascias surrounding the prostate is complex and can inter-individually vary substantially, which adds to the technical difficulties of NSRP.

Fascias of the prostate:

Despite extensive research in the field of prostate anatomy and surgical techniques, the exact anatomy of the fascias surrounding the prostate continues to be controversial. In addition there is still no worldwide accepted consensus in the terminology. In a recently published review written by outstanding experts, the fascias surrounding the prostatic tissue is described as follows; *prostate capsule, periprostatic fascia,* and *the endopelvic fascia* (visceral and parietal components) (3). The anatomical relation between these fascias and the neurovascular bundle will be summarized in the following part of the text.

Prostate capsule:

The prostate is surrounded by a capsule-like structure, which is not always well defined in an anatomic sense, but rather is a layer of fibromuscular fascies, primarily smooth muscle, that is inseparable from the prostatic stoma (4). Vessels and nerves penetrate the capsule from the lateral aspect of the prostate. The prostate capsule cannot be clearly identified at anterior aspect of the prostate, which connects with the detrusor apron, as well as at the apex, where it continues with the sphincter, and at the base, where it continues with the detrusor muscles.

Periprostatic fascias:

The fascia on the outer surface of the prostate has been termed as *lateral pelvic fascia, periprostatic fascia and prostatic fascia* by different authors (3). The periprostatic fascia is not a discrete single-layered structure. It is rather a multi- layer structure, consisting of both collagenous and adipose tissue elements. The prostatic fascia can be subdivided into three basic elements according to their location as *anterior, lateral and posterior (Denonvillier's fascia)*.
a) Anterior periprostatic fascia:

It covers the anterior surface of the prostate from approximately 10-o'clock to 2-o'clock positions. It covers the detrusor apron, dorsal vascular complex, and is fused in the midline with the anterior fibromuscular stroma of the prostate (3).

b) Lateral periprostatic fascia:

After opening the endopelvic fascia during radical prostatectomy and deflecting the levator ani muscle, covered by the *parietal endopelvic* fascia, laterally, the outermost fascial layer of the prostate is the *levator ani fascia*. Generally, there is another fascial layer between the levator ani fascia and the prostatic capsule, which is called the *prostatic fascia*. For the operating surgeon, both the levator ani fascia and the prostatic fascia constitute the *'periprostatic fascia'*. On the postero-lateral aspect of the prostate, these periprostatic fascias cover the *neurovascular bundle*. The levator ani fascia component covers the bundle laterally, and the prostatic fascia component covers the bundle medially. Therefore, a surgical nerve sparing dissection performed between the components of the periprostatic fascia (i.e. between levator ani fascia and prostatic fascia) is called *'the interfascial dissection'*. And the dissection technique performed between the prostate capsule and the periprostatic fascia is called the *'intrafascial dissection'* (5,6). But the intrafascial dissection has a higher risk of inadvertent iatrogenic capsular penetration (6).

On the other hand, the relationship between the prostate capsule and the lateral periprostatic fascia may differ depending on interindividual variations (4). In 48% of patients, the levator ani fascia was found to be fused with the prostate capsule, and no areolar tissue was seen between the layers on the lateral surface of the prostate (4). An exception to this fusion was only seen at the posterolateral angle of the prostate, where the NVB was identified as a distinct bundle. This study supports that it is not always easy and possible to distinguish and perform the planned interfascial or intrafascial dissection (6).

c) Posterior periprostatic fascia and seminal vesicle fascia (Denonviller's fascia):

The posterior surface of the prostate and the seminal vesicles are covered by a continuous layer, called the *'Denonviller's fascia'* (or *fascia retroprostatica, septum retrovesicale, prostatoseminal vesicular fascia*) (3). This fascia extends caudally from peritoneal cul-de-sac distally to the prostatourethral junction. At the center, this fascia is fused with the prostate capsule and toward the posterolateral aspect of the prostate, the space between the prostatic capsule and the Denonviller's fascia is filled by areolar tissue, and the NVB is present in it.

Endopelvic fascia:

The endopelvic fascia, covering the pelvic organs, has two components: parietal and visceral. The *visceral* component covers the prostate, bladder and rectum, and is fused with the anterior fibromuscular stroma of the prostate at the ventral aspect (5,6). The *parietal* component includes the fascia of the levator ani muscle (*levator ani fascia*). Along the pelvic sidewall at the lateral aspect of the prostate and bladder, the parietal and the visceral components of the endopelvic fascia are fused as a fascial condensation and this fusion is usually recognized as a whitish line, and named as the *fascial tendinious arch of the pelvis*. This arch stretches from the pubıvesical ligaments to the ischial spine (3). During radical prostatectomy, access to the lateral prostate can be gained by incising this whitish avascular line, although some authors suggest avoiding this incision as a part of the intrafascial nerve sparing technique (7).

The neurovascular bundle:

The neurovascular bundle contains sympathetic (from ganglia T11-12) and parasympathetic (from ventral rami of S2-4) bundles from the inferior hypogastric (or pelvic) plexus, which is responsible for the mechanisms of erection, ejaculation and continence. Fibers of the pelvic flexus surround the lateral aspect of the bladder neck, proximal prostate, and the seminal vesicles in a cage-like fashion, whereas relatively few nerve fibers are found on the anterior surface of these organs (3). The neural anatomy of the neurovascular bundle represents a spray-like distribution along the lateral border of the prostate. The development of BPH also adds substantially to the dispersion of the nerves over the lateral surface of the prostate (8). The nerves are usually dispersed up to 2-o'clock and 10-o'clock positions on the lateral prostate (3). In the apical region, the NVB is located very close to the urethral sphincter and the prostate apex.

REFERENCES:

1. Eastham JA, Scardino PT, Kattan MW. Predicting an optimal outcome after radical prostatectomy: the trifecta nomogram. J Urol. 2008 Jun;179(6):2207-10
2. Bianco FJ Jr, Scardino PT, Eastham JA. Radical prostatectomy: long-term cancer control and recovery of sexual and urinary function ("trifecta").Urology. 2005 Nov;66(5 Suppl):83-94.
3. Walz J, Burnett AL, Costello AJ, et al: A critical analysis of the current knowledge of surgical anatomy related to optimization of cancer control and preservation of continence and erection in candidates for radical prostatectomy. Eur Urol 2010; 57: 179-192
4. Kiyoshima K, Yokomizo A, Yoshida T, et al : Anatomical features of periprostatic tissue and its surroundings: a histological analysis of 79 radical retropubic prostatectomy specimens. Jpn J Clin Oncol. 2004; 34: 463-468
5. Martinez-Pineiro, L.: Prostatic fascial anatomy and positive surgical margins in laparoscopic radical prostatectomy. Eur Urol 51: 598-600, 2007
6. Savera AT, Kaul S, Badani K, et al: Robotic radical prostatectomy with the veil of Aphrodite technique: histologic evidence of enhanced nevre sparing. Eur Urol 2006; 49: 1065-1074
7. Stolzenburg JU, Rabenalt R, Do M, et al: Intrafascial nevre sparing endoscopic extraperitoneal radical prostatectomy. Eur Urol 2008; 53: 931-940
8. Lunacek A, Schwentner C, Fritsch H, et al: Anatomical radical retropubic prostatectomy: 'curtain dissection' of the neurovascular bundle. BJU Int 2005; 95: 1226-31

NERVE SPARING RADICAL RETROPUBIC PROSTATECTOMY

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Introduction and Overview of the Technique:

For over a century, radical prostatectomy (RP) has been an effective way to achieve long-term control of clinically localized prostate cancer. The first radical prostatectomy was performed at the Zurich clinic [1]. This approach was later modified and rapidly adopted by urologists [2, 3, 4]. Later on, Walsh and colleagues developed nerve sparing radical retropubic prostatectomy (NSRRP) in 1982 and various others developed their own techniques in the following years [5-11]. Although details of the techniques vary slightly from eachother, all depend upon meticulous dissection of the neurovascular bundles (NVBs) carefully away from the urethra, apex and lateral surface of the prostate after division of the dorsal vein complex and puboprostatic ligaments. For this operation it is critical to know that the prostate is surrounded by the outermost "Dennonvilliers' fascia" between the prostate and the rectum, and the inner "lateral pelvic fascia" which is composed of "prostatic fascia" on the prostate and the "levator fascia" over the prostatic fascia. NVB travels between the two layers of the lateral pelvic fascia (i.e. inner prostatic fascia and outer levator fascia). It is also critical to use appropriate surgical aids and instruments during the operation. These can been listed as: a fiberoptic headlight, a standard Balfour retractor with both narrow and wide malleable blades or a Turner-Warwick ring retractor, coagulating forceps, small fine and regular right-angled clamps, Metzenbaum and Jamison scissors, and 2.5- to 4.5-power loupes. It is also critical to avoid any cauterisation (monopolar, bipolar etc.) over the NVBs and use of appropriate size hemoclips wherever necessary. It may be useful to use bipolar cautery over the prostate (not over NVB) for the control of some bleeding whenever necessary to avoid nerve injury from monopolar cautery.

Indications for Nerve Sparing:

The patients should be counseled on the nerve-sparing aspects of the operation. Nerve-sparing prostatectomy does not necessarily compromise cancer control in appropriately selected patients. However, patients with poor-quality erections preoperatively, current and future lack of a sexual partner, or other medical conditions that may adversely affect erections (e.g., diabetes mellitus, neurologic diseases, or medications that produce erectile dysfunction) should not be candidates for NSRRP. On the other hand, it is inappropriate in men with advanced disease. Nerve-sparing surgery is questionable when there is extensive cancer in the biopsy specimens, palpable extraprostatic tumor extension, firm nodule especially at the apex of the prostate (where nerves are closer to the prostate and prostatic capsule is weak or deficient) serum PSA level above 10 ng/mL, and biopsy Gleason score higher than 7.

There have been attempts to predict the side of extra prostatic extension (EPE) or organ confined disease so that nerve sparing can be declined or performed accordingly. Graefen et. al. tried to determine organ confined disease preoperatively based on prognostic factors in their "classification and regression tree structures model: CART analysis" study [12]. In this study, low risk patients defined to have total PSA less than 10 ng/ml and less than 3 cores of Gleason 4 or 5 cancer in the biopsies from right or left lobe were found to have organ confined cancer in 90% of the cases. Ohori et. al. tried to develop a nomogram for the selection of prostate side where EPE could safely be avoided [13]. For example, they found 50% EPE in the side where there was a palpable nodule.

NSRRP and Surgical Margins:

Removal of the cancer without positive margins and preservation of the nerves are often competing goals. Cancers most often penetrate the prostatic capsule posterolaterally, directly over the neurovascular bundles [14]. In several series, attempts to preserve the neurovascular bundles has increased the rate of positive surgical margins posterolaterally [15]. In a review of the literature, Abbas and Scardino found that mean positive margin rate was 25% (14% to 41%) in series coming from centers of excellence [16]. In another review, Weider and Soloway noted the remarkable variation in positive margin rates, varying from 0% to 71%, with an overall rate of 28% in radical retropubic prostatectomy series in which no adjuvant hormonal therapy was used before the operation [17]. So, it is clear that utmost care should be exercised to avoid positive margins in attempts of nerve preservation for optimal cancer control, because it has been shown in multivariate analysis that positive margins confer a greater risk of recurrence [18]. In order to avoid from positive margins, the deep (posterior) layer of Denonvilliers' fascia must be deliberately incised during surgery by releasing the neurovascular bundle laterally and allowing a deep plane of dissection along the fat of the anterior rectal wall. The risk of a positive surgical margin will be greatly increased if this deep layer of Denonvilliers' fascia is not included in the excised specimen. The apical dissection can be performed without a catheter in the prostate to give the prostate more mobility.

Various Aspects of NSRRP:

Potency is defined as the ability to obtain an erection that is sufficient for vaginal penetration and sexual intercourse. Current surgical techniques and a more precise understanding of the autonomic innervation of the corpora cavernosa allow preservation of sexual function in many men. Quinlan and associates [9] demonstrated that recovery of potency was quantitatively related to the preservation of nerves. They found that three factors were associated with recovery of potency after radical prostatectomy: age, clinical and pathologic stage, and preservation of the NVBs. Approximately 90% of men younger than 50 were potent if either one or both NVBs were preserved. For men older than 50, return of potency was more likely if both neurovascular bundles were preserved, rather than one. Catalona et al. [6] reported potency in 68% of patients when both nerves were preserved and 47% when one nerve was spared. They also demonstrated a strong correlation between preservation of potency and age.

Scardino et. al. developed a nomogram to predict the return of potency based on a series of 314 previously potent patients treated since 1993 with radical prostatectomy for cT1a to T3a prostate cancer after 1993. Factors significantly associated with recovery of spontaneous erections satisfactory for intercourse included the age of the patient, the quality of preoperative erections, and the degree of preservation of the neurovascular bundles in the operation (Table 1). They also showed that time after surgery was also an important factor in the recovery of potency; the median time to recovery of an international index of erectile function (IIEF) ?17 was 24 months, while 42 months was required to reach an IIEF ?26 [5].

Cutaneous Nerve Graft Interpositio: There is also the possibility of performing cutaneous nerve graft interposition if one or both cavernous nerves must be resected [19-21]. However it should be kept in mind that in most patients with a so advanced cancer that one or both nerves must be resected, postoperative radiotherapy or hormone therapy is likely to be required, which could reversely effect the potential benefits of nerve grafting. Kim et. al. used a technique for placing interposition grafts from the sural nerve to one or both neurovascular bundles [20, 21]. Surgeons have performed nerve grafts successfully for decades to replace damaged or transected peripheral sensorimotor nerves. The basis for nerve regeneration, and consequently for nerve grafting, is the ability of axons to produce axon sprouts. These support the hypothesis that cavernous nerve grafts may restore penile autonomic innervation and the ability to achieve spontaneous erections following deliberate neurovascular bundle resection at the time of radical prostatectomy. One third of patients with bilateral nerve resection and placement of bilateral nerve grafts have had spontaneous, medically unassisted erections sufficient for sexual intercourse. The greatest return of function was observed 14 to 18 months after surgery. Between July 1998 and June 2002, 108 preoperatively potent patients underwent placement of a unilateral interposition cavernous nerve graft. With a median follow-up of 24 months (5 to 52 months), 42% with unilateral nerve resection with a graft and 24% with unilateral nerve resection without a graft were reported to be potent. Completion of a prospective randomized trial comparing nerve grafts to no grafts after unilateral NVB resection should be waited for firm conclusions. Until then, patients should be given informed consent to decide whether a nerve graft is placed when a NVB is damaged or resected during radical prostatectomy.

Technique of High Anterior Release: Recently, a technique called "High Anterior Release" (HAR) of the NVBs has been described. The purpose of this approach was reported to speed up the recovery of sexual function and continence by reducing traction on the branches of the nerves to the cavernous bodies and striated sphincter or avoiding inadvertent transection of the small branches that travel anteriorly. However, this technique is criticised that the risk of positive surgical margins may be increased by this approach, because there is less soft tissue at the apex. It is proposed that this approach should be used only in men who are likely to have organ-confined disease and who are candidates for bilateral nerve sparing until this possibility has been fully evaluated. The surgical procedure begins after the dorsal vein has been ligated distally but not divided. The levator fascia over the anterior apex of the prostate is incised, and the incision is extended distally along the lateral edge of the dorsal vein complex on the anterolateral surface of the prostate, preserving the underlying prostatic fascia [22, 23]. To identify the correct plane and to avoid inadvertent incision into the prostate, it is suggested to have excellent visualization and magnification (4.5-power loupes).

Importance of Accessory Pudendal Arteries: The return of postoperative sexual function after radical retropubic prostatectomy is dependent not only on the preservation of the autonomic innervation to the corpora cavernosa (i.e., the neurovascular bundles), but also on the preservation of the vascular branches to the corpora cavernosa [7]. Arterial insufficiency is a factor contributing to erectile dysfunction in patients after nerve-sparing radical retropubic prostatectomy. Accessory arterial branches that supply the corpora have been described [24, 25]. They travel over the anterolateral surface of the prostate. These arteries have been reported to be found in 70% of cadaveric dissections and in 7% of patients by selective internal pudendal angiography. Large visible accessory pudendal arteries have been found in 4% of men [26]. When these branches are preserved, a normal arterial inflow to the penis postoperatively will be maintained. The surgical technique for preservation of the arteries should begin with division of the endopelvic fascia lateral to the vessels and division of the puboprostatic ligament (the vessels are beneath the puboprostatic ligament). Preservation of these accessory arteries may enable a patient to remain potent after surgery or, for a patient who is impotent, adequate arterial inflow will ensure an adequate response to medical treatment.

The Results of Contemporary NSRRP Series:

Kundu et. al. reported that erections sufficient for intercourse occurred in 76% of preoperatively potent men treated with bilateral (n=1,770) and 53% of men treated with unilateral or partial nerve sparing (n=64) surgery. Adequate erectile function was more common following bilateral than unilateral nerve sparing surgery in men younger than 70 years old (78% versus 53%, p = 0.001) compared with those 70 years old or older (52% versus 56%, p = 0.6). They also showed that recovery of erections were dependent of age and patients < 50 years of age had 92%, < 60 had 85, <70 had 70 and ?70 had 51% erection rate. Patients excluded from potency analysis in this study were men who were not reliably potent before surgery, those who did not undergo a nerve sparing procedure and those who received postoperative adjuvant radiotherapy or hormonal therapy within 18 months of surgery [10].

Walsh reported that three factors are important in the recovery of erectile function after radical prostatectomy: the age of the patient (younger than 65 years), the status of potency preoperatively, and the ability to preserve both NVBs. With use of his technique he reported that at 18 months, 86% of the patients were able to have unassisted intercourse with or without sildenafil citrate. A third of his patients were taking sildenafil citrate, but only 4% of men reported that they could not have intercourse without it. The recovery of sexual function occurred gradually: 38% were potent at 3 months, 54% at 6 months, 73% at 12 months, and 86% at 18 months. He thinks that it is likely to speed up this recovery with HAR of the NVB before the dorsal vein is divided. The recovery of sexual function in his series also correlated with the age of the patient at the time of surgery: 100% in men 30 to 39 years, 88% in men 40 to 49 years, 90% of men 50 to 59 years, and 75% in men 60 to 67 years [27]. His data were recently updated [28]. At 3 months, 42% of the patients were potent; at 6 months, 49%; and at 1 year, 73%. In both series, most patients had both neurovascular bundles preserved.

Huland et. al. reported that 70% of their patients at age <55 and 37% at age >65 had erections sufficient for intercourse after bilateral NSRP [11].

However, all of the studies do not show success as high as studies stated above. For example "Prostate Cancer Outcomes Study (PCOS)" revaled poor results in the evaluated 3533 subjects. 5 year results were reported on 1288 subjects. This was a population based, prospective longitudinal study. At 5 years 14% of the patients were incontinent and 71% were impotent. Sufficients erections were achieved increasingly by the time and 95 of the patients were potent at 6 months, 17% at 1st, 22% at 2nd and 28% were potent at 5th postoperative year [29].

Optimal Results of NSRRP: The most favorable outcome that can be achieved following radical prostatectomy is complete tumor resection (freedom from clinical recurrence) with full recovery of continence and potency ("Trifecta"). In the study performed by Scardino and friends, patients were excluded if they had received previous radiation to the pelvis or neoadjuvant hormonal therapy, or if they were incontinent or impotent prior to surgery. A total of 1746 men operated since 1983 met these criteria and were analyzed for biochemical recurrence, and time to recovery of both continence (defined as not having to wear any protective pads/devices) and potency (full erections with/without sildenafil). They reported that 60% of their patients achieved "Trifecta" at 24 months of follow-up [30]. In another study from the same group published in the same year [31], patients (n=647) operated between 1998 and 2003 were reported. Mean patient age was 58 years while mean pretreatment PSA was 6.9 ng/mL. In this study, "Trifecta" was reported to be achieved in 30%, 42%, 47% and 53% of the patients at the 1st, 2nd, 3rd and 4th years, respectively. Although 93% of the patients were cancer free and continent at the 2nd year "Trifecta" was only 42% because of poor potency results.

REFERENCES:

1. Kuchler H. Uber prostatavergrosserungh. Dtsch Klin 1866;18:458.
2. Young, 1905. Young HH: The early diagnosis and radical cure of carcinoma of the prostate. Johns Hopkins Hosp Bull 1905; 16:315-321.
3. Ansell JS. Radical transvesical prostatectomy: preliminary report on an approach to surgical excision of localized prostate malignancy. J Urol 1959;82:373.
4. Campbell EW. Total prostatectomy with preliminary ligation of the vascular pedicles. J Urol 1959;81:464.
5. Rabbani F, Stapleton AM, Kattan MW, et al. Factors predicting recovery of erections after radical prostatectomy. J Urol 2000;164(6): 1929-1934.
6. Catalona WJ, Carvalhal GF, Mager DE, et al. Potency, continence and complication rates in 1,870 consecutive radical retropubic prostatectomies. J Urol 1999;162(2):433-438 .
7. Catalona WJ, Bigg SW. Nerve-sparing radical prostatectomy: evaluation of results after 250 patients. J Urol 1990;143:538.
8. Walsh PC, Donker PJ: Impotence following radical prostatectomy: Insight into etiology and prevention. J Urol 1982; 128:492-497.

9. Quinlan DM, Epstein JI, Carter BS, et al. Sexual function following radical prostatectomy: influence of preservation of neurovascular bundles. J Urol 1991;145:998.
10. Kundu SD, Roehl KA, Eggener SE, et al: Potency, continence and complications in 3,477 consecutive radical retropubic prostatectomies. J Urol 2004; 172:2227-2231.
11. Graefen M, Walz J, Huland H: Open retropubic nerve sparing radical prostatectomy. Eur. Urol. 2006; 49: 38-48.
12. Graefen M, Haese A, Pichlmeier U, et. al.: A validated strategy for side specific prediction of organ confined prostate cancer: a tool to select for nerve sparing radical prostatectomy. J. Urol. 2001; 165: 857-863.
13. Ohori M, Kattan MW, Koh H, et. al.: Predicting the presence and side of extracapsular extension: a nomogram for staging prostate cancer. J. Urol. 2004; 171: 1844-1849.
14. Rosen MA, Goldstone L, Lapin S, et al. Frequency and location of extracapsular extension and positive surgical margins in radical prostatectomy specimens. J Urol. 1992; 148:331.
15. Killeen KP, Libertino JA, Sughayer MA, et al. Pathologic review of consecutive radical prostatectomy specimens. Nerve sparing versus non-nerve sparing. Urology. 1991; 38:212.
16. Abbas F, Scardino PT. Why neoadjuvant androgen deprivation prior to radical prostatectomy is unnecessary. Urol Clin North Am. 1996; 23:587.
17. Wieder JA, Soloway MS. Incidence, etiology, location, prevention and treatment of positive surgical margins after radical prostatectomy for prostate cancer. J Urol. 1998; 160:299.
18. Hull GW, Rabbani F, Abbas F, et al. Cancer control with radical prostatectomy alone in 1,000 consecutive patients. J Urol. 2002; 167: 528-534.
19. Quinlan DM, Nelson RJ, Walsh PC: Cavernous nerve grafts restore erectile function in denervated rats. J Urol 1991; 145:380-383.
20. Kim ED, Scardino PT, Hampel O, et al: Interposition of sural nerve restores function of cavernous nerves resected during radical prostatectomy. J Urol 1999; 161:188-192.
21. Kim ED, Nath R, Kadmon D, et al: Bilateral nerve graft during radical retropubic prostatectomy: 1-year followup. J Urol 2001; 165:1950-1956.
22. Montorsi F, Salonia A, Suardi N, et al: Improving the preservation of the urethral sphincter and neurovascular bundles during open radical retropubic prostatectomy. Eur Urol 2005; 8:938-945.
23. Takenaka A, Hara R, Soga H, et al: A novel technique for approaching the endopelvic fascia in retropubic radical prostatectomy, based on an anatomical study of fixed and fresh cadavers. BJU Int 2005; 95:766-771.
24. Bahnson RR, Catalona WJ. Papaverine testing of impotent patients following nerve-sparing radical prostatectomy. J Urol 1988;139:773.
25. Breza J, Abuseif SR, Orvis BR, et al. Detailed anatomy of penile neurovascular structures: surgical significance. J Urol 1989;141:437.
26. Rogers CG, Trock BP, Walsh PC: Preservation of accessory pudendal arteries during radical retropubic prostatectomy: Surgical technique and results. Urology 2004; 64:148-151.
27. Walsh PC, Marschke P, Ricker D, Burnett AL: Patient-reported urinary continence and sexual function after anatomic radical prostatectomy. Urology 2000; 55:58-61.
28. Parsons JK, Marschke P, Maples P, Walsh PC: Effect of methylprednisolone on return of sexual function after nerve-sparing radical retropubic prostatectomy. Urology 2004; 64:987-990.
29. Penson DF, McLerran D, Feng Z, Li L, Albertsen PC, Gilliland FD, Hamilton A, Hoffman RM, Stephenson RA, Potosky AL, Stanford JL. : 5-year urinary and sexual outcomes after radical prostatectomy: results from the prostate cancer outcomes study. J Urol. 2005;173:1701-5.
30. Bianco FJ, Scardino PT and Eastham JA: Radical prostatectomy: long-term cancer controland recovery of sexual and urinary function ("Trifecta"). Urology. 2005; 66: 83-94.
31. Saranchuk JW, Kattan MW, Eklin E et. al. : Achieving optimal outcomes after radical prostatectomy. J. Clin. Oncol. 2005; 23: 4146-4151.

NERVE SPARING LAPAROSCOPIC RADICAL PROSTATECTOMY

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Excluding nonmelanoma skin cancer, prostate cancer is the most common form of cancer and the second most common cause of death from cancer in men (1). Prostate-specific antigen screening has led to a downstaging of prostate cancer. Thus clinically localized prostate cancer are affecting younger men more than before. Several treatment modalities are available to meet patient preferences and provide long-term oncologic control. With excellent survival expectations for localized prostate cancer, patients are seeking better functional outcomes and posttreatment quality of life. Radical prostatectomy is a standard treatment option for localized prostate cancer. The preservation of sexual function being one of the main issues of quality of life after radical prostatectomy can be preserved by nerve sparing procedures (2,3). The determination of organ confined tumors suitable for nerve sparing procedures using preoperative nomograms (4,5) and the simultaneous increase in experience with the surgical technique has led to an increase in nerve sparing procedures (6).

All available surgical treatments for prostate cancer share the common goal of curing the cancer by removing the prostate gland and seminal vesicles, and sometimes the pelvic lymph nodes, while at the same time preserving continence and sexual function. Studying pelvic anatomy in the 1980s,Walsh and Donker (7) popularized the technique for sparing the lateral prostatic neurovascular bundles (NVBs) as a means to improve functional outcomes after prostatectomy. Additional modifications have been suggested, but the Walsh and Donker's technique remains the backbone of the open radical prostatectomy.

In their excellent review, Gontero and Kirby notified the anatomical location of the neurovascular bundles as follows (8); The neurovascular bundles that course posterolateral to the prostate consist of a complex structure related to the vascularization of the outer prostatic portion and to the innervation of the prostate, urethra and corpora cavernosa. Small arterial branches originating from the inferior vesical artery and venous vessels draining in the homonymous vein constitute the vascular portion of the bundles. They run in the lateral pelvic fascia, medially to the cavernosal nerve branches (vide infra) to terminate as capsular vessels that pierce the prostatic fascia. The caudal portion of the pelvic plexus, located at the tip of the seminal vesicles, emanates autonomic fibres, which form a dense network with the described vessels. Some of them perforate the prostatic capsula to enter the substance of the prostatic gland. These branches are inevitably sacrificed during an NS approach, but it is believed that they do not contribute significantly to erectile function. The majority of nerve fibres, known as the cavernous branches, travel in a direct route from the pelvic plexus towards the posterolateral base of the prostate, gradually coalescing from a group of fibres approximately 12 mm wide to a more organized bundle approximately 6 mm wide at the level of the prostate (9). At this point, they lie just underneath the lateral pelvic fascia, between the levator fascia and the prostatic fascia. At the level of the membranous urethra, they are located at the 3 o'clock and 9 o'clock position, just beneath the striated sphincter that at this point surrounds both the urethra and the prostatic apex.

Two main NS surgical approaches have been described. In the so-called 'anatomical technique', first reported by Walsh (10), the nerves dissection is initiated at the apical level with primary isolation of the urethra. Ruckle and Zincke (11) have proposed an alternative technique where the neurovascular bundles are primarily dissected off the lateral prostate and only subsequently is the urethra transected. Several variants of this lateral approach to the neurovascular bundles have been subsequently described (12,13,14).

Laparoscopic radical prostatectomy (LRP) was first performed by Schuessler et al. in 1992 (15), but it was in 1998 that Guillonneau et al. (16) reported an initial series of 28 cases using Gaston's standardized technique based on the primary access to the seminal vesicles. The principal advantages of LRP are that it is minimally invasive, has better visualization of the operative field, an exact and watertight anastomosis, the possibility of early catheter removal, potential reduced blood loss and a shorter hospital stay. However, the transperitoneal approach to an extraperitoneal organ might cause intraperitoneal complications, e.g. bowel injuries, peritonitis, postoperative ileus, peritoneal adhesions, intraperitoneal bleeding or intraperitoneal urine leakage (17). Raboy et al.(18) described the first case report of extraperitoneal LRP (ELRP), and Bollenset al.(19) described the first series of cases using this technique. In 2002 Stolzenburg reported their technique and initial experience with the totally endoscopic extraperitoneal radical prostatectomy (20).

Regarding the preoperative indications the majority of authors agrees that the ideal candidate for an NS surgery should be fully potent preoperatively and have an organ-confined cancer, that is, a clinical T1/T2a and T2b disease (21). As the neurovascular bundles lie outside the capsule and fascia of the prostate, cancer control is not compromised by an NS procedure when the tumour is organ confined.T1a and T1b are ideal for NS as they rarely invade the NVB (22). T1c tumours have been reported to have a PSM rate varying from 0 to 59%, so eligibility for an NS should be judged according to PSA and Gleason score. T2a and T2b cancers with a controlateral negative biopsy are considered low-volume localized diseases with a high probability to be organ confined (23).

Even when surgeons believe that they have achieved complete bilateral cavernous nerve preservation, there is inevitably some trauma to the nerves, eg traction. Its well known that neuropraxia ensues from even minor neural trauma. Not all patients in whom the neurovascular bundles are preserved recover erectile function after radical prostatectomy. A significant proportion of these men have vascular abnormalities that can impact erectile function recovery after radical prostatectomy. Mulhall et al described the available evidence supporting the need to spare not only the nerves, but also the arteries to improve erectile function recovery after radical prostatectomy (24).

Suboptimal performance of the surgical technique may effect the outcomes of an NS surgery. The surgeon considering an NSLRP must balance the need for complete eradication of local tumour with the preservation of sexual function. A successful NS technique should combine a high probability of potency recovery with a low PSM rate, particularly at the apex and the posterolateral prostate.

In our series, gradually increasing number of patients are potent (% 55 at the end of 1 year) with lower rates of PSMs as our experience approached 200 patients so far.

REFERENCES:

1. Narain, V., Cher, M. L. and Wood, D. P., Jr.: Prostate cancer diagnosis, staging and survival. Cancer Metastasis Rev, 21:17, 2002
2. Walsh, P. C.: Anatomic radical prostatectomy: evolution of the surgical technique. J Urol, 160: 2418, 1998
3. Catalona, W. J. and Bigg, S. W.: Nerve-sparing radical prostatectomy: evaluation of results after 250 patients. J Urol,143: 538, 1990
4. Ross, P. L., Scardino, P. T. and Kattan, M. W.: A catalog of prostate cancer nomograms. J Urol, 165: 1562, 2001
5. Kattan, M. W., Potters, L., Blasko, J. C., Beyer, D. C., Fearn,P., Cavanagh, W. et al: Pretreatment nomogram for predicting freedom from recurrence after permanent prostate brachytherapy in prostate cancer. Urology, 58: 393, 2001
6. Graefen, M., Haese, A., Pichlmeier, U., Hammerer, P. G., Noldus,J., Butz, K. et al: A validated strategy for side specific prediction of organ confined prostate cancer: a tool to select for nerve sparing radical prostatectomy. J Urol, 165: 857,2001
7. Walsh PC, Donker PJ. Impotence following radical prostatectomy: insight into etiology and prevention. J Urol 1982; 128:492–497.
8. P Gontero RS Kirby Nerve-sparing radical retropubic prostatectomy: techniques and clinical considerations Prostate Cancer and Prostatic Diseases (2005) 8, 133–139
9. Lepor H et al. Precise localization of the autonomic nerves from the pelvic plexus to the corpora cavernosa: a detailed anatomical study of the adult male pelvis. J Urol 1985; 133: 207–212.
10. Walsh PC. Anatomic radical retropubic prostatectomy. In: Walsh PC, Retik AB, Vaughan Jr ED, Wein AJ (eds). Campbell's Urology, Vol 4, Chapter 90, 8th edn. WB Saunders Co.: Philadelphia, PA, 2002, pp 3107–3129.
11. Ruckle HC, Zincke H. Potency-sparing radical retropubic prostatectomy: a simplified anatomical approach. J Urol 1995; 153:1875–1877.
12. Klein EA, Kupelian PA, Tuason L, Levin HS. Initial dissection of the lateral fascia reduces the positive margin rate in radical prostatectomy. Urology 1998; 51: 766–773.
13. Jarow JP, Trock BJ. Anatomic radical prostatectomy: does initial dissection of lateral fascia affects outcomes? J Urol 2002; 167 (Suppl): A1363.
14. Fernandez S et al. Experience with water-jet dissection in nerve sparing radical prostatectomy. J Urol 2002; 167 (Suppl): A1338.
15. Schuessler WW, Schulam PG, Dayman RV, Kavoussi LR. Laparoscopic radical prostatectomy: Initial short-term experience. Urology 1997; 50: 854–7
16. Guillonneau B, Cathelineau X, Barret Eet al.Laparoscopic radical prostatectomy. Preliminary evaluation after 28 interventions.Presse Med1998;27:1570–4
17. Guillonneau B, Rozet F, Cathelineau Xet al.Perioperative complications oflaparoscopic radical prostatectomy: theMontsouris 3-year experience.J Urol2002;167: 51–6
18. Raboy A, Ferzli G, Albert P.Initialexperience with extraperitonealendoscopic radical retropubicprostatectomy. Urology1997;50: 849–53
19. Bollens R, Vanden Bossche M,Roumeguere Tet al.Extraperitoneallaparoscopic radical prostatectomy. Results after 50 cases.Eur Urol2001;40:65–9
20. Stolzenburg JU, Do M, Pfeiffer H, KönigF, Aedtner B, Dorschner W. The endoscopic extraperitoneal radical prostatectomy (EERPE): technique andinitial experience. World J Urol 2002;20:48–55
21. Wieder JA, Soloway MS. Incidence, etiology, location, preventionand treatment of positive surgical margins after radical prostatectomy for prostate cancer. J Urol 1998; 160: 299–315.
22. Schnall MD et al. Prostate cancer: local staging with endorectalsurface coil MR imaging. Radiology 1991; 178: 797–802.
23. Geary ES, Stamey TA. Pathological characteristics and prognosisof nonpalpable and palpable prostate cancers with a Hybritech prostate specific antigen of 4 to 10 ng/ml. J Urol 1996; 156:1056–1058.
24. Mulhall,J.P., Secin,F.P. and Guillonneau, B. Artery Sparing Radical Prostatectomy-Myth or Reality? J Urol.2008 Mar;179(3):827-31

THE ROLE OF MEDICAL COMORBIDITIES IN THE DEVELOPMENT OF ERECTILE DYSFUNCTION

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Erectile dysfunction (ED) is a common male disease increasing rapidly worldwide that significantly impacts quality of life. The association between ED and different diseases (the most common are: cardiovascular diseases (CVD), hypertension, type 2 diabetes (T2D), metabolic syndrome (MS), late onset hypogonadism (LOH), obesity) was shown in various epidemiological studies [1].

Age is considered as main etiological factor of ED. Thus, the prevalence of ED is more than 150 mln men among the whole world, and it's expected to duplicate in nearest 10 years [2]. According to epidemiological data, manifesting in 9-15% men in the age of 40-50 years, ED affects more than 50% men after 60 years of age [3]. In the case of T2D presens the prevalence of ED in the group of 40-50 years of old males is uprising to the higher levels (58%) than in "healthy" man after 60`s. In T2D male patients ED appears 3-10 years earlier then in the groups of the same age men. Different components of MS, such as blood-sugar level, isulin-resistancy and hypertension also cause the increase of ED incident and their cumulative acting in the development of MS produce much more severe forms of ED [4]. Similar, according to our own data the association of T2D and hypertension causes the development of ED in more than 95% of patients. The quantity of MS components influences the prevalence of ED among such male patients [5]. Also, different medications used in treatments of T2D, MS, CVD (such as vasodilatators, hypotensive, etc) cause the development of ED. The severity of CVD, especially the progression of coromary arteries stenosis, led to uprising the prevalence of ED among such patients. Total ED is observed in 28% males with T2D, and only in 9,6% men in the whole population. Now, it's well known that ED shares underlying pathogenic mechanisms with vascular diseases. At comparison of 2 male groups: with ED and without ED was found that in 10 years period CVD were diagnosed in 56% and 32% of men accordingly. There is a strong correlative dependence between the development of CVD risk-factors and ED. ED is diagnosed 25 months earlier than manifestation of coronary heart diseases in more than 70% of males. In 41% in men with acute coronary syndrome ED was exposed in 23 – 26 months earlier.

Male aging is also considered as risk-factor of LOH development [6]. The role of low testosterone (T) levels, including subnormal range, in pathogenesis of ED is yet proven [7, 8]. Patients with T2DM have an impaired sexual life, which is worsened by hypogonadism. Low T in T2DM is in fact associated with more severe ED, hypoactive sexual desire and low intercourse frequency. Testosterone replacement therapy (TRT) has been proven to improve sexual function in hypogonadal men. In addition, TRT improves adiposity, insulin resistance and total cholesterol in men with MS. The low level of testosterone is found in patients with CVD and essential hypertension [9]. The authors observed a direct correlation of testosterone concentrations with waist circumference and an inverse correlation with the levels of atherogenic lipoproteins and depression. In some studies it was shown an inverse relationship between the total T levels and the number of the MS components; the low testosterone levels were strongly related to the fasting glucose levels and the elevated waist circumference measurements [10].

Now much attention is directed at the potential association of ED and microangiopathy in hyperglycaemic states It was found the inverse relationship between penile blood flow, erectile function, which also is significantly related to the number of MS components [11]. This authors found that elevated blood pressure and elevated fasting blood glucose are factors strongly related to penile blood flow. Investigators defined that ED in men with T2D is associated with a marked increase in the metabolic syndrome, central adiposity and microangiopathy Our data have shown presence of macro- and micro vascular insufficiency of the testicular blood-flow in males with LOH and T2D which testify the presence of primary defeat of testicular tissue.

So, the determination of ED in men with different comorbidities may be the key point to prevent and treat further complications (acute coronary state, stroke, etc) that influence not only on life quality, but on life term. Now ED is considered as a portal to men's health, because ED is clarified as a warning signal regarding the presence of MS, CVD and other diseases.

REFERENCES:

1. R.Tamler Diabetes, obesity, and erectile dysfunction // Gender Medicine 2009. – Vol. 6, Part 1. – P. 4-16.
2. Aytac IA et al. // BJU International. - 1999. – Vol.84. - P:50-56.
3. Braun et al. //Int J Impotence Res. – 2000.- Vol.12.- P. 305-311.
4. Svartberg J, von Muhlen D, Sundsfjord J, Jorde R. Waist circumference and testosterone levels in community dwelling men. The Tromso Study. Eur J Epidemiol. 2004. – Vol. 19. – P.657-663.
5. Esposito K, Giugliano F, Martedi E, Feola G, Marfella R, D'Armiento M, Giugliano D. High proportions of erectile dysfunction in men with metabolic syndrome. Diabetes Care. 2004. – Vol.28. – P. 1201-1203.
6. Gooren L. Androgen deficiency in the ageing male: benefits and risks of supplementation. J Steroid and Molecular Biology. - 2003. – Vol. 85.P. 724-731.
7. Zitzmann et al. Association of Specific Symptoms and Metabolic Risks with Serum Testosterone in Older Men // J. Clin.

Endocrinol. Metab. 2006 - Vol. 91(11). – P.4335-4343.
8. Jockenhövel, F: Male Hypogonadism. UNI-MED Verlag Bremen, 2004
9. A. Ya. Kravchenko, V. M. Provorotov // Testosterone level in male patients with coronary heart disease and essential hypertension. http://www.medlit.ru/medeng/pre/pre09e0337.htm.
10. Corona G, et al., Psychobiologic Correlates of the metabolic syndrome and associated sexual dysfunction.// Eur Urol. 2006. – Vol. 50. – P. 595-604.
11. Traish AM, Guay AT. Are androgens critical for penile erections in humans? Examining the clinical and preclinical evidence // J Sex Med. 2006. – Vol.3. – P. 382-407.

LIFE- STYLE BEHAVIOR AND SEXUAL AND REPRODUCTIVE HEALTH

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Incidence and epidemiology of erectile dysfunction

The incidence of erectile dysfunction (ED) increases with age. It is reported that 35% of married men aged 60 years and older suffer from ED. From the prevalence rates reported in the MMAS (Massachusetts Male Aging Study), between the ages of 40 and 70 years, the probability of complete ED increased from 5.1% to 15%, moderate ED increased from 17% to 34%, and mild ED remained constant at about 17% (1)

According to the study of the National Health and Social Life Survey (NHSLS) following prevalence rates for ED were reported: 7% for ages 18 to 29 years, 9% for ages 30 to 39, 11% for ages 40 to 49, and 18% for 50 to 59 (1).

LIFE- STYLE BEHAVIOR AND SEXUAL HEALTH

Obesity and sexual function

Obesity has become a worldwide public health problem, it may decrease life expectancy by 7 years at the age of 40 years and now it is the sixth most important risk factor contributing to the overall burden of disease throught the world. Overweight and obesity may increase the risk of ED by 30-90% as compared with normal subjects. Moreover, women with the metabolic syndrome have an increased prevalence of sexual dysfunctions as compared with matched controls (2). Patients with ED show a higher BMI, WC (waist circumference), and (insulin-resistance) IR and lower levels of TT (total testosterone) and BT (bioavailable testosterone). There is a negative correlation between erectile function and IR and abdominal obesity. The TT levels are lower in patients with increased BMI, WC and IR. Negative correlation was shown only between BT and abdominal obesity (3). Androgen deficiency together with endothelial dysfunction may be responsible from ED in obesity (4).

In rats, penile endonhelial nitric oxide synthase (eNOS) and neuronal nitric oxide synthase (nNOS) expression were found decreased in hypercholeromic cavernousal tissue due to decrease activity of AMP-activated protein kinase (AMPK), which increases the expression of neuronal (n) NOS and endothelial (e) NOS (5).

Diet, exercise and sexual function

Lifestyle factors such as obesity, lack of exercise and smoking play a role in the development, progression or remission not only of erectile dysfunction (ED), but also in cardiovascular disease and the metabolic syndrome.

One-third of obese men with ED can regain their sexual activity after 2 y of adopting health behaviors, mainly regular exercise and reducing weight. The adoption of healthy lifestyles can reduce the prevalence of obesity and the metabolic syndrome, and hopefully the ED (6).

In our experiment we showed that mild to moderate exercise increases penile eNOS and nNOS expression as well as serum total testosterone levels in young and aged rats (7).

Mediterranean-style diets and a reduction in caloric intake have been found to improve erectile function in men with the aspects of the metabolic syndrome. In addition, both clinical and experimental studies have confirmed that combining the two interventions provides additional benefit to erectile function, likely via reduced metabolic disturbances, decreased visceral adipose tissue, and improvement in vascular function (8).

Mediterranean-style diet might be effective in ameliorating sexual function in women with the metabolic syndrome. Lifestyle changes, mainly focussing on regular physical activity and a healthy diet, are effective and safe ways to reduce cardiovascular diseases and premature mortality in all population groups; they may also prevent and treat sexual dysfunctions in both sexes (9). Caloric restriction increases eNOS and nNOS expression in rat penile cavernousal tissues in hypercholestrolemic rats (10).

Alcohol and sexual function

Chronic alcoholism leads to multi organ damage including nervous system, the liver, cardiovascular and the endocrine system. The prevalence of ED is increased in males who chronically abuse alcohol. The alcoholics also had lower plasma levels of testosterone and greater plasma levels of gonadotropins as compared to the nonalcoholics (11).

Ethanol impairs the endothelial function of corpus cavernosum in mouse, and it may lead to erectile dysfunction through a reduced NO release via endothelial impairment (12). Long term and excessive intake of ethanol may cause ED in rats (13).

Smoking and sexual function

Smoking is considered a major public health problem, seriously affecting the quality of life of patients and their partners, chronic smoking is a major risk factor in the development of ED.

Cigarette smoking-induced ED in human and animal models is associated with impaired arterial flow to the penis or acute vasospasm of the penile arteries. Long-term smoking produces detrimental effects on the vascular endothelium and peripheral nerves and also causes ultrastructural damage to the penile tissue, all considered to play a role in chronic smoking-induced ED. Clinical and basic science studies provide strong indirect evidence that smoking may affect penile erection by the impairment of endothelium-dependent smooth muscle relaxation or more specifically by affecting NO production via increased ROS (reactive oxygene species) generation. There are considerable evidence supporting the concept that smoking-related ED is associated with reduced bioavailability of NO because of increased ROS (14).

Drug abuse and sexual function

Drugs of abuse, like alcohol, opiates, cocaine and cannabis, are used by many young people for their presumed aphrodisiac properties. It is well known that, apart from the subjective effects, they negatively affect the sexual response. Alcohol has direct toxic effects on the gonads and the liver (it increases the catabolism of testosterone and its transformation in estrogens). It inhibits the hypothalamus-pituitary-gonads axis (HPG). The opioids inhibit the HPG axis and increase the prolactin levels which, in turn, interferes with the male and female sexual response. The acute effects of cocaine are stimulants mainly for its dopaminergic properties but in the long run it causes ED due to hyperprolactinemia. Cannabis, at high doses, could inhibit the HPG axis and reduce fertility (15).

Environmental factors and sexual function

Exposure to environmental or occupational substances may affect erectile function. Some environmental toxicants, including smoke, lead, organic solvents, and pesticides, are potential hazards, whose effects on the nervous and hormonal systems have been proposed as the leading mechanisms by which environmental toxicants adversely impact erectile function. More studies are needed to identify specific environmental agents that may harm erectile function and to define their exact action mechanisms in this regard (16).

Arsenic exposure could damage peripheral vessels and increase the risk of cardiovascular disease. However, the relationship between arsenic exposure and ED has seldom been evaluated (17).

Several environmental toxicants such as lead, organic solvents, and pesticides have been implicated as possibly hazardous agents. Effects on the nervous and hormonal systems have been proposed as the leading mechanisms by which environmental toxicants adversely impact erectile function. (18).

Several environmental contaminants can interfere with the actions of endogenous hormones and have been termed 'endocrine disrupters.' p,p-DDE, a prominent and persistent metabolite of the insecticide DDT, has been shown to be an androgen receptor antagonist. In rats endocrine disrupter p,p-DDE can markedly interfere with erectile function and demonstrates persistence after a single dose (19).

Socioeconomic factors and sexual function

Effects on sexual arousal of unemployment and acute stress were studied in men. Ten unemployed (high-chronic-stress) and 9 employed (low-chronic-stress) men were exposed to two erotic videotapes in the laboratory. Acute stress was induced by telling the men that they would have to give a talk on their own sexual behavior and fantasies. Half the men were told about the talk before seeing either erotic tape, the other half were told in between the two erotic tapes. Cardiovascular measures confirmed the stressful nature of this manipulation. Results showed that the unemployed men achieved less penile tumescence than the employed men when stressed prior to erotic stimulation. Presentation of the stressor between the erotic videotapes (after sexual arousal occurred) produced no differences between the employed and unemployed men. These results suggest that impairment of erection occurs as a result of a combination of chronic and acute stres (20).

LIFE- STYLE BEHAVIOR AND REPRODUCTIVE HEALTH

Lifestyle factors such as obesity, tobacco smoking or chewing, alcohol and some of the illicit drugs like cocaine, cannabis etc and exposure to extreme heat, have adverse effects on male reproduction. In this era other factors such as use of mobile phone and stress have negative effect on male reproductive health are inadequate and need detailed study.

Obesity and reproductive health

Compared with those with BMI < 30, obese subjects had significantly lower total sperm count and Inhibin B but not FSH. Whether this is cause or effect, i.e. adiposity impairing spermatogenesis or reduced testicular function promoting fat deposition, remains to be determined (21).

Obese men exhibit reduced androgen and SHBG (sex hormone binding globuline) levels accompanied by elevated estrogen levels. This complexly altered reproductive hormonal profile suggests that endocrine dysregulation in obese men may explain the increased risk of altered semen parameters and infertility (22,23).

Alcohol and reproductive health

In the testes, alcohol can adversely affect the Leydig cells, which produce and secrete the hormone testosterone. Studies found that heavy alcohol consumption results in reduced testosterone levels. Alcohol also impairs the function of the testicular Sertoli cells that play an important role in sperm maturation. In the pituitary gland, alcohol can decrease the production, release, and/or activity of luteinizing hormone and follicle-stimulating hormone. Alcohol can interfere with hormone production in the hypothalamus (24).

In experimental study marked Sertoli cell vacuolization and germ cell degeneration were observed in the testes of ethanol-treated rats (ETR) by both light and electron microscopy. Enhanced apoptosis of germ cells in ETR was also detected (25).

Smoking and reproductive health

Cigarette smoking has negative effects on male fertility. Recent studies showed an active transfer of several components of cigarettes through the blood-testis barrier. The presence of these components in the seminal plasma may induce a degradation of sperm parameters and nuclear quality of spermatozoa, and compromise the chances of pregnancy. Moreover, smoking may have a negative impact on the smokers'offspring: poor quality embryos, development of childhood cancers. Oxidative stress-induced DNA damage seems to be one of the major causes of sperm quality alteration (26).

Heavy smoking was associated with low sperm count, motility, and morphology and increased seminal cadmium levels. Zinc therapy improved sperm quality and increased seminal IL-4, but reduced TNF-alpha and IFN-gamma. A zinc-deficient diet led to high cadmium testicular accumulation comparable with those supplemented with cadmium (27).

Environmental toxins and reproductive health

The impact of environment and occupation on male fertility is still under debate. Epidemiological studies have shown that exposure to glues, solvents or silicones, metals and physical agents in the past, as well as current exposure to glues, solvents or silicones and physical agents are associated oligoasthenoteratozoospermia and infertility (28).

Farmers and painters/varnishers showed a significantly higher proportion of reduced sperm counts and severely reduced sperm concentrations compared with the entire group of infertile men; in addition, significantly more farmers presented with a history of maldescended testes than other occupational groups. Metal workers/welders formed significantly higher proportions of patients with reduced sperm motility. The relatively poor semen parameters of the painters/varnishers could be caused by exposure to toxins (29).

Cell phone and reproductive health

Use of cell phones decrease the semen quality in men by decreasing the sperm count, motility, viability, and normal morphology. The decrease in sperm parameters was dependent on the duration of daily exposure to cell phones and independent of the initial semen quality. Increase in ROS level, and decrease antioxidant capasity and sperm DNA damage may be responsible from infertility (30,31).

Psychologic stress and reproductive health

Emotional stress plays a detrimental role on fertility. Stress causes necrosis, apoptosis and reduces the number of "healthy" sperm. Treatment significantly improves sperm parameters and infertility indicating that stress is an additional risk factor for idiopathic infertility (32). It is reported that psychological stress significantly reduces sperm guality in men undergoing IVF (33). In a different study determining the relationship between psychological stress and semen quality among men undergoing in-vitro fertilization (IVF) it is reported effect of stress only on fecundability, and this only among men with low sperm concentration (34).

REFERENCES:

1. Wein AJ, Kavoussi LR, Novick AC, Partin AW, Peters CA. Campbell-Walsh Urology, Ninth edition, Elsevier, Philadelphia, vol. 1, p:738.
2. Obesity and sexual dysfunction, male and female. Esposito K, Giugliano F, Ciotola M, De Sio M, D'Armiento M, Giugliano D. Int J Impot Res. 2008 Jul-Aug;20(4):358-65.
3. Knoblovits P, Costanzo PR, Rey Valzacchi GJ, Gueglio MG, Layus AO, Kozak AE, Balzaretti MI, Litwak LE. Erectile Dysfunction, Obesity, Insulin Resistance, and Their Relationship with Testosterone Levels in Eugonadal Patients in an Andrology Clinic Setting. J Androl. 2009 Oct 15.
4. Traish AM, Feeley RJ, Guay A. Mechanisms of obesity and related pathologies: androgen deficiency and endothelial dysfunction may be the link between obesity and erectile dysfunction. 2009 Oct;276(20):5755-67.
5. Kim YW, Park SY, Kim JY, Huh JY, Jeon WS, Yoon CJ, Yun SS, Moon KH. Metformin restores the penile expression of nitric oxide synthase in high-fat-fed obese rats. J Androl. 2007 Jul-Aug; 28(4):555-60.
6. Esposito K, Giugliano D. Obesity, the metabolic syndrome, and sexual dysfunction. Int J Impot Res. 2005 Sep-Oct;17(5):391-8.
7. Ozbek E, Tasci AI, Ilbey YO, Simsek A, Somay A, Metin G. The effect of regular exercise on penile nitric oxide synthase expression in rats. Int J Androl. 2009 Sep 28.
8. Hannan JL, Maio MT, Komolova M, Adams MA. Beneficial impact of exercise and obesity interventions on erectile function and its risk factors. J Sex Med. 2009 Mar;6 Suppl 3:254-61.
9. Esposito K, Giugliano F, Ciotola M, De Sio M, D'Armiento M, Giugliano D. Obesity and sexual dysfunction, male and female. Int J Impot Res. 2008 Jul-Aug;20(4):358-65.
10. Ozbek E, Ilbey Y, Simsek A, SomayA. Caloric Restriction Increases Penile And Internal Iliac Arter Endothelial Nitric Oxide Synthase and Neuronal and Endothelial Nitric Oxide Synthase Activities In Rat Cavernousal Tissues. American Urological Association Annual Meeting 25 – 30 April 2009 Chicago, illinois, USA.
11. Cornely CM, Schade RR, Van Thiel DH, Gavaler JS. Chronic advanced liver disease and impotence: cause and effect? Hepatology. 1984 Nov-Dec;4(6):1227-30.
12. Aydinoglu F, Yilmaz SN, Coskun B, Daglioglu N, Ogulener N. Effects of ethanol treatment on the neurogenic and endothelium-dependent relaxation of corpus cavernosum smooth muscle in the mouse. Pharmacol Rep. 2008 Sep-Oct;60(5):725-34.
13. Gan XG, An RH, Wang YQ. Relationship between ethanol intake and sexual function in rats. Zhonghua Nan Ke Xue. 2006 Dec;12(12):1099-101.
14. Tostes RC, Carneiro FS, Lee AJ, Giachini FR, Leite R, Osawa Y, Webb RC. Cigarette smoking and erectile dysfunction: focus on NO bioavailability and ROS generation. J Sex Med. 2008 Jun;5(6):1284-95.
15. Saso L. Effects of drug abuse on sexual response. Ann Ist Super Sanita. 2002;38(3):289-96.
16. Xiao F, Bai WJ, Wang XF. Environment and erectile dysfunction. Zhonghua Nan Ke Xue. 2009 Mar;15(3):265-70.
17. Hsieh FI, Hwang TS, Hsieh YC, Lo HC, Su CT, Hsu HS, Chiou HY, Chen CJ. Risk of erectile dysfunction induced by arsenic exposure through well water consumption in Taiwan. Environ Health Perspect. 2008 Apr;116(4):532-6.
18. Burnett AL. Environmental erectile dysfunction: can the environment really be hazardous to your erectile health? J Androl. 2008 May-Jun;29(3):229-36.
19. Brien SE, Heaton JP, Racz WJ, Adams MA. Effects of an environmental anti-androgen on erectile function in an animal penile erection model. J Urol. 2000 Apr;163(4):1315-21.
20. Morokoff PJ, Baum A, McKinnon WR, Gillilland R. Effects of chronic unemployment and acute psychological stress on sexual arousal in men. Health Psychol. 1987;6(6):545-60.
21. Stewart TM, Liu DY, Garrett C, Jørgensen N, Brown EH, Baker HW. Associations between andrological measures, hormones and semen quality in fertile Australian men: inverse relationship between obesity and sperm output. Hum Reprod. 2009 Jul;24(7):1561-8.
22. Hammoud AO, Gibson M, Peterson CM, Meikle AW, Carrell DT. Impact of male obesity on infertility: a critical review of the current literature. Fertil Steril. 2008 Oct;90(4):897-904.
23. Aggerholm AS, Thulstrup AM, Toft G, Ramlau-Hansen CH, Bonde JP. Is overweight a risk factor for reduced semen quality and altered serum sex hormone profile? Fertil Steril. 2008 Sep;90(3):619-26.
24. Emanuele MA, Emanuele NV. Alcohol's effects on male reproduction. Alcohol Health Res World. 1998;22(3):195-201.
25. Eid NA, Shibata MA, Ito Y, Kusakabe K, Hammad H, Otsuki Y. Involvement of Fas system and active caspases in apoptotic

signalling in testicular germ cells of ethanol-treated rats. Int J Androl. 2002 Jun;25(3):159-67.
26. Sepaniak S, Forges T, Fontaine B, Gerard H, Foliguet B, Guillet-May F, Zaccabri A, Monnier-Barbarino P. Negative impact of cigarette smoking on male fertility: from spermatozoa to the offspring. J Gynecol Obstet Biol Reprod (Paris). 2004 Sep;33(5):384-90.
27. Al-Bader A, Omu AE, Dashti H.Chronic cadmium toxicity to sperm of heavy cigarette smokers: immunomodulation by zinc. Arch Androl. 1999 Sep-Oct;43(2):135-40.
28. Mendiola J, Torres-Cantero AM, Moreno-Grau JM, Ten J, Roca M, Moreno-Grau S, Bernabeu R. Exposure to environmental toxins in males seeking infertility treatment: a case-controlled study. Reprod Biomed Online. 2008 Jun;16(6):842-50.
29. Kenkel S, Rolf C, Nieschlag E. Occupational risks for male fertility: an analysis of patients attending a tertiary referral centre. Int J Androl. 2001 Dec;24(6):318-26.
30. Agarwal A, Deepinder F, Sharma RK, Ranga G, Li J. Effect of cell phone usage on semen analysis in men attending infertility clinic: an observational study. Fertil Steril. 2008 Jan;89(1):124-8.
31. Agarwal A, Desai NR, Makker K, Varghese A, Mouradi R, Sabanegh E, Sharma R.Effects of radiofrequency electromagnetic waves (RF-EMW) from cellular phones on human ejaculated semen: an in vitro pilot study. Fertil Steril. 2009 Oct;92(4):1318-25.
32. Collodel G, Moretti E, Fontani V, Rinaldi S, Aravagli L, Saragò G, Capitani S, Anichini C. Effect of emotional stress on sperm quality. Indian J Med Res. 2008 Sep;128(3):254-61.
33. Clarke RN, Klock SC, Geoghegan A, Travassos DE. Relationship between psychological stress and semen quality among in-vitro fertilization patients. Hum Reprod. 1999 Mar;14(3):753-8.
34. Hjollund NH, Bonde JP, Henriksen TB, Giwercman A, Olsen J; Danish First Pregnancy Planner Study Team. Reproductive effects of male psychologic stress. Epidemiology. 2004 Jan;15(1):21-7.

FUTURE TREATMENT FOR ERECTILE DYSFUNCTION

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Penile erection, the end results of a chain of event that causes vascular and trabecular smooth muscle relaxation of the corpora cavernosa of the penis, is a complex phenomenon regulated by neural, vascular, hormonal, and structural factors. The vascular endothelium of the penis plays a pivotal role in modulating vascular tone and blood flow into the penis in response to neural, humoral, and mechanical stimuli. In endothelial dysfunction, the regulatory role of the endothelium is hindered, resulting in decreased responsiveness to vasodilatory mediators and/or increased sensitivity to various vasoconstricting agents.

Well-recognized disease states and vascular risk factors, such as diabetes mellitus, coronary artery disease, atherosclerosis, hypertension, and smoking, have long been known to impair penile endothelial function, resulting in a decrease in endothelial-dependent corpora cavernosal smooth muscle relaxation through decreased expression and activity of neuronal and endothelial NO synthase (nNOS and eNOS), impaired NO release, and/or increased destruction or total loss of NO bioactivity in the penis (1). Studies have demonstrated that the presence and number of vascular risk factor is correlated with impaired penile hemodynamics as evidenced by penile Doppler duplex ultrasound in more than a thousand subjects (2).

Unless contraindicated, oral phosphodiesterase-5 (PDE-5) inhibitors, such as sildenafil, tadalafil, or vardenafil, are currently first-line treatments of erectile dysfunction (ED). These agents have been showed to be safe and effective in broad population of men with ED. Evidence-based multicenter studies have revealed the success rate with PDE-5 inhibitors ranging between 50 to 70 % in general ED population, but ED men with severe pathologies, such as diabetes mellitus, post-prostatectomy ED, severe cavernosal insufficiency, and age-related ED, should be expected to respond to PDE-5 inhibitors between 30 to 50% (3,4). Although some ED cases can be salvaged by using intracavernosal injection of vasoactive agents and vacuum erection devices, difficulties in using these treatments and their side affects may limit the usage of these approaches at least in some of ED cases. Implantation of a penile prosthesis should recognize as the last resort in cases who failed to respond to first- and second-line treatments.

Recently, a number of new PDE-5 inhibitors have been released by different part of the world including Korea, Brazil, Japan, and the US. The safety and efficacy of these new PDE-5 inhibitors, namely udenafil, avanafil, SLx-2101, Mirodenafil, and lodenafil, have been studied in a number of multi-center, placebo-controlled trials and found to have similar outcomes as seen in conventional PDE-5 inhibitors, possibly due to the comparable pharmacokinetic and pharmacodynamic profiles (5).

Bremelanotide (PT-141) is a synthetic peptide analogue of ?-melanocyte stimulating hormone (?-MSH) activating melanocortin receptors 3 and 4 (MC3R and MC4R). Its effects on sexual behavior and penile erection have been demonstrated in laboratory animals [6]. Bremelanotide has been reported to initiate penile erection in both normal men and men with psychogenic and organic ED as well as increase sexual desire [7]. Although clinical trials have been undertaken to assess the potential use of an intranasal formulation of this compound for the treatment of men with ED [8], it has not yet been licensed, and at the time of writing, development of bremelanotide for men with ED appears to have ceased.

Peripheral mechanisms of penile erection may be the targets for future treatment of ED, such as activation of pro-erectile pathways (prostanoids, cholinergic receptor agonists, vasoactive peptides, potassium channel openers, soluble guanylate cyclase activators, and NO-releasing PDE-5 inhibitors) and inhibition of anti-erectile mechanisms (selective ?-adrenoceptor antagonists, rho-kinase inhibitors, endothelin-receptor antagonists, and angiotensin-II receptor antagonists). Although the importance of these pathways have been shown in animal models of ED, clinical relevance of these possible molecules needs to be elucidated.

The long-term goal for the treatment of any disease process is to identify molecular correlates involved in the pathophysiology of disease and to use this information to develop novel and more effective therapeutics, either with pharmacologic agents or through gene or peptide therapy and cell-based approaches. A major hurdle in this regard is ensuring that the molecular targets of interest are indeed relevant to the physiology or pathophysiology of ED. The penis, as the target organ for managing ED, seems to be convenient for peptide/gene therapy or cell-based treatments due to its external location, suitability for periodic injections, engraftment of the potential molecules by penile sinusoids, and lack of systemic side effects of applications (4,9). Experimental studies in a number of ED model in animals have demonstrated promise in restoring erectile function by the application of gene/peptide treatment and stem cells. Recent studies have also shown the safety of gene therapy in a number of ED men (10).

REFERENCES:

1. Kendirci M, Hellstrom WJ. Role of Endothelium in Erectile Function and Dysfunction. In: Aird WC, editor. Endothelial Biomedicine: A Comprehensive Reference. Cambridge, New York: Cambridge University Press; 2007. p1541–8.
2. Kendirci M, Trost L, Sikka SC, Hellstrom WJG. The effect of vascular risk factors on penile vascular status in men with erectile dysfunction. J Urol 2007; 178: 2516-20.
3. Kendirci M, Tanriverdi O, Trost L, Hellstrom WJG. Management of sildenafil treatment failures. Curr Opin Urol 2006; 16: 449-59.
4. Kendirci M, Gur S, Sikka SG. Gene therapy for erectile dysfunction. Front Biosci 2005; 10: 2758-69.
5. Eardley I, Donatucci C, Corbin J, El-Meliegy A, Hatzimouratidis K, McVary K, Munarriz R, Lee SW. Pharmacotherapy of erectile dysfunction. J Sex Med 2010; 7: 524-40.
6. Kendirci M, Walls M, Hellstrom WJG. Central nervous system agents in the treatment of erectile dysfunction. Urol Clin North Am 2005; 32: 487-501.
7. Rosen RC, Diamond LE, Earle DC, Shadiack AM, Molinoff PB. Evaluation of the safety, pharmacokinetics and pharmacodynamic effects of subcutaneously administered PT-141, a melanocortin receptor agonist, in healthy male subjects and in patients with an inadequate response to Viagra. Int J Impot Res 2004; 16: 135-42.
8. Diamond LE, Earle DC, Rosen RC, Willett MS, Molinoff PB. Double-blind, placebo-controlled evaluation of the safety, pharmacokinetic properties and pharmacodynamic effects of intranasal PT-141, a melanocortin receptor agonist, in healthy males and patients with mild-to-moderate erectile dysfunction. Int J Impot Res 2004; 16: 51-9
9. Kendirci M, Teloken PE, Champion HC, Hellstrom WJ, Bivalacqua TJ. Gene therapy for erectile dysfunction: fact or fiction? Eur Urol 2006; 50: 1208-22
10. Melman A. Gene therapy for male erectile dysfunction. Urol Clin North Am 2007; 34: 619-30.

EFFECT OF SEXUALLY TRANSMITTED INFECTIONS ON SEXUAL AND REPRODUCTIVE HEALTHS

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Introduction and objectives: Sexual transmitted diseases (STD), caused by C. trachomatis, Tr. vaginalis, U. urealiticum, M. genitalium, N. gonorrhea and large group of viruses (HSV, CMV, HPV) and ect., are wide spread in the humans population(1).

Character property of these diseases at this period of time is the minimal clinical manifestation, multifocal lesion of the genital and extragenital organs, difficulties in the diagnostic and treatment (2). Additional problems provides by negative attitude of many west specialist to the etiological role of these microorganisms as in the inflammatory diseases of the males genital system as in the appearance of complications, that limit the elaboration of international standards for the diagnostic and treatment of these diseases (3, 4).

The goal of our work was to asses the possible role of STD in the etiology and pathogenesis of the males infertility.

Materials and methods: We observed 68 men aged 21 to 43 years (average age was 31.3 + - 4.2 years) who were treated for infertility for a long time in various centers. The hormonal and genetic causes of infertility were excluded.

Program survey consisted of anamnesis, general inspection, fill out the forms, the analysis of seminal fluid (at least twice), microscopic and bacteriological study of the scraping of the urethra, prostate fluid, urine, identification of microorganisms by PCR, RIF.

Ultrasound investigation of the urogenital system. In order to avoid false results, verification of the microorganism was considered positive when it is confirmed at least by two methods, and the detection of nonspecific infection taken into account diagnostically significant titer.

Results and discussion: According to a survey of all patients showed varying degrees of astenooligozoospermiya. However, in 22 (32,4%) patients, the concentration of spermatozoa in 1 ml of ejaculate was less than 20 million, and in 28 (41%) patients progressive active forms (categories a + b) does not exceed 50%.

By the signs of the presence or absence of inflammatory changes in genital organs (prostaticic fluid, sperm) patients were divided into two groups.

The first group consisted of 38 patients with microscopical signs of inflammation in the genital organs (number of leukocytes in the prostatic fluid (ejaculate)> 15 and the second group consisted of 30 patients without such signs, though often in patients of second group identified STD pathogens.

All patients of the second group was performed drainage of prostatic acinusis by our original method (the use of proteolytic enzymes, complex physiotherapy, massage of the prostate), resulting in 17 (55%) of them during the control study prostatic fluid showed microscopical signs of inflammation.
Du to microbiological analysis of the patients of both groups, mixed infection was diagnosed in 72% of patients, and monoinfection only at 12%. In 16% of patients to identify the causative agent was not possible.
As the frequency of occurrence the leading role belonged Tr.vaginalis (72%) and mycoplasms (Ur. urealiticum, Mycoplasma genitalium) - 60%. C. Trachomatis had place (58%) cases. Given the above facts, sexual partners were also investigated by gynecologists and treated by medical or (and) epidemiological indications.

All men with a verified diagnosis of STD were treated by our own original technique, which in addition to the traditional treatment include a comprehensive application of physiotherapy procedures aimed to provide the drainage of prostatic acinusis and the local administration of antibiotics into the prostate, using phonophoresis and electrophoresis.

The need for the latter due to poor penetration of nitroimidazole with their classic use in the prostate tissue - the main reservoir of Tr.vaginalis. Latter is known, has the so-called "tank function", absorbing and protecting others microorganisms from etiotropical drugs action.

As a result of treatment was achieved microbiological sanitation of the sex glands in 90% of patients. A monitoring study of ejaculate was observed restoration of spermatozoid concentration > 20 million / ml in 14 out of 22 patients (63%), and progressively increase the number of active forms of spermatozoids (categories a + b) > 50% in 22 out of 28 men (78%).

During subsequent observation for two years in 35 of 68 patients (51%) have been instances of sexual partners, pregnancy and birth of healthy children.

Conclusions:

1. STD causing inflammation in the genital organs may be one of the possible causes of male infertility (excretory – toxic type).
2. Normal levels of leucocytes in the prostatic fluid (sperm) during primary examination do not exclude inflammatory processes of male's genital organs.
3. Combination therapy of inflammatory processes of the reproductive system of men suffering from infertility in most cases leads to the normalization of semen parameters and causes the possibility of pregnancy of sexual partners.

REFERENCES:

1. Schneede P, Tenke P, Hofstetter AG; Urinary Tract Infection Working Group of the Health Care Office of the European Association of Urology. Eur Urol. 2003 Jul;44(1):1-7. Review.
2. Naber KG, Widner G. Chronic prostatitis – an infection disease? J Antimicrob Chemoter 2000;46: 157-161.
3. Weidner W. Schiefer HG, Krauss H at other. Chronic prostatitis: a thought search for etiology involved microorganisms in 1, 461 patients. Infection 1991;19 (Suppl 3):S119-S125
4. World Health Organization. WHO manual for the standardized investigation, diagnosis and management of the infertile male. Cambridge; Cambridge university press, 2000.

EFFECT OF MEDICAL AND SURGICAL TREATMENT FOR BENIGN PROSTATIC HYPERPLASIA ON SEXUAL FUNCTIONS IN MEN WITH LOWER URINARY TRACT SYMPTOMS

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Lower urinary tract symptoms (LUTS) due to Benign Prostatic Hyperplasia (BPH) is found in 75% of men older 50 years and about 35% of them probably have a neccessity to undergo any kind of treatment for LUTS/BPH (1, 2). The aims of BPH treatment are to relieve the LUTS and to decrease bladder outlet obstruction. However, in the recent years, quality of life (QoL) has also gained an importance as well as two aims mentioned above. One of the important parameters of QoL is sexual life following treatment of LUTS/BPH (3). There is an interrelation between sexual life and QoL. Anxiety, depression, lose of self-esteem and lastly lose of QoL is a rule, when a man has erectile dysfunction (4) When erectile function is corrected, it is well-known that patient feells well and QoL improves (5). Ejaculatory function is also important for QoL. In a new study, among sexually active men, 70% indicated that they would not agree to continue using BPH treatment that provided complete relief of urinary symptoms if ejaculatory side effects occured (6). QoL deteriorates due to LUTS as well and sexual dysfunction may occur due to lose of QoL. Improvement of QoL is an important component for the return of sexual function (7). Sexual activity is always important in men's life regardless of their age. A survey including men between 50-88 years of age showed that sex was very important in 13%, sex is important in 29%, sex is occasionally enjoyable in 41% of them. Only 17% of them reported that they could live without a sex life (8). MSAM-7 (Multinational Survey of the Aging Male-7) study included about 14.000 men aged between 50-80 years. Of those men, 83% have sexual activity and 71% reported at least one sexual intercourse during last 4 weeks (9). Therefore, we should consider sexual functions while the patients are treated for LUTS/BPH.

There are many options for treatment of LUTS/BPH including medical treatments [Alpha-1 receptor blockers (alfuzosin, tamsulosin, doxazosin, terazosin), 5-alpha reductase inhibitors (finasteride, dutasteride), Phytotherapy], minimal invazive treatments [Transurethral Needle Ablation (TUNA), Transurethral Microwave Therapy (TUMT), Lasers] and surgical treatments [Transurethral Incision of Prostate (TUIP), Transurethral Resection of Prostate (TUR-P), Transurethral Vaporisation of Prostate (TUV-P), open surgery (OP)]. Sexual dysfunctions after LUTS/BPH treatment are erectile dysfunction (ED), ejaculatory dysfunction (EjD) (retrograde ejaculation, anejaculation, painful ejaculation), decreased libido (DL) and overall decreased sexual satisfaction (10, 11). Effects on sexual functions of treatments for LUTS/BPH are variable. While some studies have shown some improvement after the treatment, most indicated impairment after the treatment.

Alpha-1 receptor blockers: Alpha receptor blockers lower blood pressure. When the blood pressure is lowered, blood flow to penis decreases and ED may occur. ED due to alpha-1 blockers is generally less than 5% (12). The main problem after usage of alpha-1 receptor blockers is EjD. Retrograde ejaculation for all the alpha blockers are about 6% (13). Retrograde ejaculation for Tamsulosin are reported between 10% and 30% (12, 14, 15). EjD due to tamsulosin is not only retrograde ejaculation related to bladder neck relaxation and also anejaculation due to central effect (10). There are also some studies indicating that sexual functions significantly improved after using alpha-1 receptor blockers (16-19). Improvement for sexual functions after alpha-1 receptor blocker treatment may be due to two factors. Alpha-1 receptor blockers provide smooth muscle relaxation in corpus cavernosum and symptomatic improvement has a positive effect on sexual functions (8, 10).

5-alpha reductase inhibitors: There are two 5-alpha reductase inhibitors (Finasteride-Type 2 inhibitor; Dutasteride-Type 1 and 2 inhibitor). These drugs decrease intraprostatic DHT. Their effect on sexual functions is probably related to decreased DHT level. It is well-known that NO and NOS are very important for erection physiology (20). NOS expression in corpus cavernosum is affected by androgens (21). DHT has more potent efficacy on NOS expression in comparison to testosterone (22). There are negative effects on sexual functions of Finasteride. In PROSPECT (proscar safety plus efficacy) study, ED, EjD and DL were 16% and 8% and 10%, respectively (23). Another study also showed that Finasteride treatment caused 6.6% ED, 4.0% decreased libido and 2.1% ejaculatory disorders (24). AUA Practice Guideline Committee has reported that ED and EjD were about 10% and 5%, respectively (12). Same side effects on sexual functions are also seen after dutasteride treatment. A study by Roehborn et al showed that ED, EjD and DL were 7.3%, 2.2% and 4.2%, respectively (25). In our study, ED and DL due to dutasteride treatment were 7.4% and 11.1%, respectively (26).

Phytotherapy: Mostly, Serenoa repens (saw palmetto), derived from berry of American dwarf palm tree, is used as phytotherapy. Although it is not clear how Serenoa repens is effective in the treatment of LUTS/BPH, 5-alpha reductase inhibition is an accepted mechanism of their efficacy (27). Although some studies indicated that there is no significant deletorious effect on sexual functions (28, 29), we found that Serenoa repens caused ED in 3.7% and DL in 7.4% of the patients (26).

TUNA: Sexual dysfunction is very rare after TUNA (30). Multicentered American Study showed retrograde ejaculation less than 1% and 2% ED (31).

TUMT: Sexual dysfunction due to TUMT is very rare as for TUNA. ED related to TUMT occurs in less than 5% of men (32). In a study comparing TUMT to TUR-P, normal antegrade ejaculation at 1 year after treatment were 74% for TUMT and 27% for TURP.

Satisfying sex for TUMT and TUR-P were 55% and 27%, respectively. This study indicated that TUMT is superior to TUR-P in terms of sexual functions (33).

Laser prostatectomy: After interstitial laser coagulation, retrograde ejaculation was between 0-12% and ED was not seen (34, 35). Another study compared TUR-P to holmium laser enucleation. There was no significant difference between TUR-P and holmium laser enucleation in terms of ED (36).

Surgical treatment: The results of surgical treatments in terms of sexual dysfunction are variable. Although ED is not common after surgical treatment, retrograde ejaculation is main problem.

1. TUR-P: A study including 280 patients who underwent TUR-P was evaluated sexual functions after surgery. Pre-operatively, 73 men were sexually active. Six months after surgery, these 73 men were still sexually active. 17% of the patients who had sexual dysfunction pre-operatively improved sexual activity and erectile quality (37). Another study found that ED and painful ejaculation decreased after TUR-P (3). A recent study found that TUR-P very effectively alleviates bothersome LUTS due to BPH. Erectile function in 81% of the men treated remained unchanged or improved. Ejaculatory function worsened in 45% of the patients and remained improved or unchanged in 55% of the patients (38) AUA Cooperative study reported a 13% incidence of ED in about 3000 patients following TUR-P (39). Kassabian found that ED after TUR-P was between %4% and 40% and retrograde ejaculation was the most common complication after TUR-P, detecting in more than 50% of the patients (40). AUA Practice Guideline Committee reported 10% ED and 65% EjD after TURP (12)

2. Open prostatectomy: Gacci et al showed that severe LUTS decreases sexual desire and overall satisfaction. After OP, improved LUTS provides better social and physical performance. As a result of these, sexual desire and overall satisfaction improve (41). In our study comparing OP to TUR-P, no significant difference was found between two methods in terms of sexual dysfunctions. DL, ED, EjD, decreased sexual intercourse were 32%, 42%, 46% and 52%, respectively (42). Retropubic and suprapubic prostatectomy are most invasive surgical treatments for LUTS/BPH. ED occurs in 3-5% of patients and retrograde ejaculation in almost 100% (28).

3. TUI-P: ED is very rare after TUIP. Retrograde ejaculation is less than 40% after TUIP (28).

4. TUV-P: ED and retrograde ejaculation after TUV-P were reported 17% and 72%, respectively (43). Preoperative criteria to predict ED after prostate surgery are diabetes mellitus, erectile dysfunction before surgery, high anxiety level, small prostate and advanced age (over 65 years) (44-47). Peroperative criteria to predict ED after prostate surgery are capsular perforation and excess bleeding (48). ED after prostate surgery depens on organic and psycogenic factors (44, 49). Organic factors are cavernosal nerve injury, cavernosal artery injury and neuropraxia due to thermal injury. Psycogenic factors include emotional stress due to surgery and decreased ejaculate volume. ED due to neuropraxia and psycogenic factors is temporary. In early period, temporary ED may be found more because of psycogenic factors and neuropraxia. Therefore, erectile function should be evaluated 2-3 months after surgery (45). To avoid emotional stress due to surgery, preoperative counseling is very important. Patients, especially younger ones, should be informed about sexual adverse effects of the treatments.

In conclusion, treatments for LUTS/BPH may cause some adverse effects on sexual functions. Especially young men could be effected more by ejaculation disorders. Sexually active men should be informed about this issue before deciding on any kind of treatment for LUTS/BPH.

REFERENCES:

1. Da Silva FC. Benign prostatic hyperlasia: natural evolution versus medical treatment. Eur Urol 1997; 32 (suppl 2): 34-37
2. Oesterling JE. Benign prostatic hyperplasia. A review of its histogenesis and natural history. Prostate1996; Suppl 6: 67-73
3. Brooks ST, Donovan JL, Peters TJ et al. Sexual dysfunction in men after treatment for lower urinary tract symptoms: evidence from randomized controlled trial. BMJ 2002; 324: 1059-1064
4. Sadovsky R. Integrating erectile dysfunction treatment into primary care practice. Am J Med 109 (suppl 9a): 22-28, 2000
5. Paige NM et al. Improvement in emotional well-being and relationship of user of silenafil. J Urol 2001; 166: 1774-1778
6. Fourcade RO, Theret N, Taleb C. Sexual function and opinion of patients treated for the first time for LUTS/BPH (abstract). Eur Urol 2008; Suppl 7: 169
7. Bargawi AB, Myres JB, O'Donnell C, Crawford ED. The effect of alpha-blocker and 5 alpha-reductase inhibitor intake on sexual health in men with lower urinary tract symptoms. BJU Int 2007; 100:853-857
8. Burger B, Weidner W, Altwein JE. Prostate and sexuality: an overview. Eur Urol 1999; 35: 177-184
9. Rosen R, Altwein J, Boyle P, Kirby RS, Lukacs B, Meuleman E, et al. Lower urinary tract symtomps and male dysfunction: the multinational survey of the aging male (MSAM-7). Eur Urol 2003; 44:637-649

10. Larson TR. Current treatment options for benign prostatic hyperplasia and their impact on sexual life. Urology 2003; 61: 692-698
11. Zlotta AR, Teillac P, Raynaud JP et al. Evaluation of male sexual function in patients with lower urinary tract symptoms associated with benign prostatic hyperplasia treated with a phytotherapeutic agent (permixon), tamsulosin or finasteride. Eur Urol 2005, 48: 269-276
12. AUA Guideline on management of benign prostatic hyperplasia (2003). Chapter 1: diagnosis and treatment recommandations. AUA Practice Guideline Committee. J Urol 2003; 170: 530-547
13. Roehrborn CG. The agency for health care policy and research. clinical guidelines for the diagnosis and treatment of benign prostate hyperplasia. Urol Clin North Am 22:445-453,1995.
14. Lepor H, for the Tamsulosin Investigator Group. Phase III multicenter palcebo-controlled study of Tamsulosin in benign prostatic hyperplasia. Urology 1998; 51: 892-900
15. Narayan P and LeporH. Long-term, open-label, phase III multicenter study of tamsulosin in benign prostatic hyperplasia. Urology 2001; 57: 466-470
16. Höfner K, Claes H, De Reijke TM et al for the European Tamsulosin Study Group. Tamsulosin 0.4 mg once daily: effect on sexual function in patients with lower urinary tract symptoms suggestive of benign prostatic hyperplasia. Eur Urol 1999; 36: 335-341
17. van Kerrebroeck, Jardin A, Laval KU, et al. Efficacy and safety of a new prolonged release formulation of alfuzosin 10 mg once daily versus alfuzosin 2.5 mg twice daily and placebo in patients with symptomatic benign prostatic hyperplasia. ALFORTI Study Group. Eur Urol 2000, 37: 306-313
18. Kirby RS, Andersen M, Gratze P et al. A combined analysis of double-blind trials of the efficacy and tolerability of doxazosin-gastrointestinal therapeutic system, doxazosin standart and placebo in patients with benign prostatic hyperplasia. BJU Int 2001; 87. 192-200
19. Van Moorelaar RJ, Hartung R, Emberton M et al. Alfuzosin 10 mg once daily improves sexual function in menwith lower urinary tract symptoms and concomittatnt sexual dysfunction. BJU Int 2005; 95: 603-608
20. Burnett AL. Role of nitric oxide in the pysiology of erection. Biol Reprod 1995; 52: 485-489
21. Hellstrom WJ, Giuliano F, Rosen RC. Ejaculatory dysfunction and its association witt lower urinary tract symptoms of benign prostatic hyperplasia and BPH treatment. Urology 2009; 74: 15-21
22. Park KH, Kim SW, Kim KD et al. Effects of androgens on the expression of nitric oxide synthase mRNA in rat corpus cavernosum. BJU Int 1999; 83: 327-333
23. Nickel JC, Fradet Y, Boake RC et al. Effifcacy and safety of finasteride therapy for beign prostatic hyperplasi: results of a year randomized controlled tria (the PROSPECT study). PROscar Safety Plus Canadian Two year Study. Can Med Assoc J 1999; 155: 1251-1259
24. Marberger MJ. Long-term effects of finasteride in patients with benign prostatic hyperplasia: a double-blind, placebo-controlled, multicenter study. Urology 1998; 51: 677-686
25. Roehrborn CG, Boyle P, Nickel JP et al. Efficacy and safety of a dual inhibitor of 5-alpha reductase types 1 and 2 (dutasteride) in men with benign prostatic hyperplasia. Urology 2002;60: 434-441
26. Tuncel A, Ener K, Nalcacioglu V, et al. Effects of short term dutasteride and serenoa repens on perioperative bleeding and microvessel density in patients undergoing transurethral resection of the prostate. Scan J Urol Nephrol 2009; 43:377-382
27. Weisser H, Tunn S, Behnke B, Krieg M. Effects of the Sabal serrulata extract IDS 89 and its subfractions on 5 alpha reductase activity in human benign prostatic hyperplasia. Prostate 1996; 28: 300-306
28. Martin DJ and Mulhall JP. Enlarging the scope of managing benign prostatic hyperplasia: addressing sexual function and quality of life. Int J Clin Pract 2005; 59: 579-590
29. Dedhia RC and McVary KT. Phytotherapy for lower urinary tract symtoms secondary to benign prostatic hyperplasia. J Urol 2008; 179: 2119-2125
30. Bruskewitz R, Issa MM, Roehrborn CG, et al. A prospective, randomized 1-year clinical trial comparing transurethral needle ablation to transurethral resection of the prostate for the treatment of symptomatic benign prostatic hyperplasia. J Urol 1998; 159: 1588-1593
31. Roehborn CG. Issa M, Bruskewitz RC, et al. Transurethral needle ablation for benign prostatic hyperplasia:12-month results of a prospective, multicenter U.S. study. Urology 1998; 51: 415-421
32. Tsai YS, Lin JS, Tong YC, et al. Transurethral microwave thermotherapy for symptomatic benign prostatic hyperplasia: long term durability with Proscare. Eur Urol 2001; 39: 688-692
33. Francisca EAE, d'Ancona FCH, Meuleman EJH et al. Sexual function following high energy microwave thermotherapy: results of a randomized controlled study comparing transurethral microwave thermotherapy to transurethral prostatic resection. J Urol 1999; 161: 486-480
34. de la Rosetta JJMCH, Muscher R, Lopez MA, Gilliatt D. Interstitial laser laser coagulation in the treatment of benign prostatic hyperplasia using a diode-laser system with temperature feedback. Br J Urol 80: 433-438, 1997
35. Arai Y. Interstitial laser coagulationfor management of benign prostatic hyperplasia: a Japanese experience. J Urol 1998; 159: 1961-1965
36. Gilling PJ, Kennet KM, Fraundorfer MR. Holmium laser enucleation of the prostate for glands larger than 100 gr: am

endourologic alternative to open surgery. J Endourol 2000; 14: 529-531
37. Mishriki SF, Cohen NP, Mawas A, Gibbons B. TURP can improve your sexual life. J Urol 2001; 165: 366 (abs 1501)
38. Muntener M, Aelling S, Kuettel R, et al. Sexual function after transurethral prostate of the prostate (TURP): results of an independent prospective multicentre assessment of outcome. Eur Urol 2007; 52: 510-516
39. Mebust WK, Holtgrewe HL, Cockett AT, et al. Transurethral prostatectomy: immediate and postoperative complications. A cooperative study of thirteen participating institutions evaluating 3885 patients. J Urol 1989; 141: 243-247
40. Kassabian VS. Sexual function in patients treated for benign prostatic hyperplasia. Lancet 2003; 361: 60-62
41. Gacci M, Bartoletti R, Figloi S et al. Urinary symptoms, quality of life and sexual function in patients with benign prostatic hypertrophy beforeand after prostatectomy: a prospective study. BJU Int 2003; 91: 196-200
42. Aslan Y, Tuncel A, Aksut H, et al. Are sexual functions affected by prostatectomy in patients with benign prostate hyperplasia? Turk J Geriatrics 2004; 7: 62-65
43. Hammadeh MY, Madaan S, Singh M, Philp T. Two-year follow-up of prospective randomised trial of electorvaporization versus resection of the prostate. Eur Urol 1998; 34: 188-192
44. Tscholl R, Largo M, Poppinghaus E et al. Incidence of erectile impotence secondary to transurethral resection of benign prostatic hyperplasia, assessed by preoperative and posroperative Snap Gauge test. J Urol 1995; 153: 1491-1493
45. Taher A. Erectile dysfunction after transurethral resection of the prostate: incidence and risk factors. World J Urol 2004; 22: 457-460
46. Poulakis V, Ferakis N, Witzsch U et al. Erectile dysfunction after transurethral prostatectomy for lower urinary tract symtoms: results from a center with over 500 patients. Asian J Androl 2006; 8: 69-74
47. Zohar J, Meiraz D, Maoz B, Durst N. Factors influencing sexual activity after prostatectomy: a prospective study. J Urol 1976; 116: 332-334
48. Bieri S, Iselin CE, Rohner S. Capsuler perforation localization and adenoma size as prognostic indicators of erectile dysfunctional after transurethral prostatectomy. Scan J Urol Nephrol 1997, 31: 545-548
49. Soderdahl DW, Knight RW, Hansberry KL. Erectile dysfunction following transurethral resection of the prostate. J Urol 1996; 156: 1354-1456

EFFECTS OF RADIOTHERAPY AND CHEMOTHERAPY ON MALE INFERTILITY

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Introduction

Considerable advances in cancer therapy during last two decades have led to a high proportion of cure, an a majority of patients becoming long-term survivors, especially children. In fact, about 1 in 1,000 young adults is estimated to be a survivor of childhood malignancy according to a recent review. In the United States, testicular cancer, Hodgkin's diseases, lymphoma, an leukemia are diagnosed each year in 9,100 males aged 15 to 35. Approximately 1,400 of these patients are subjected to polychemotherapy and irradiation at doses sufficient to induce prolonged azoospermia. The cure rate of these malignancies is approaching 90% with an upward tendency, and most of these patients receive polychemotherapy and/or irradiation, leading to a rapidly increasing incidence of post-therapy reproductive dysfunction. An estimated 1,372,910 people were diagnosed with cancer in 2005, of whom 4% (approximately 55,000) are under the age of 35. Moreover, cancer is diagnosed and managed by chemotherapy in 4,000 children under age of 15 each year in the United States.

Factors affecting fertility of men with cancer can be summarized as follows; 1.Cancer itself, 2.Chemotherapy related factors, 3. Radiotherapy related factors, 3. Hormone therapy related factors, 4. Surgery related factors, and 5. Psychological factors (1-6).

Does infertility in cancer patients originate from the treatment, the tumor, or the testis?
Important alterations of spermatogenesis, unrelated to cytotoxic chemotherapy, can be detected prior to treatment in the majority of young patients with testicular germ cell tumors (TGCT) or lymphoma. The changes are hard to predict and thus make it difficult to assess the impact of cytotoxic chemotherapy and radiotherapy on fertility of affected men. Although mechanisms underlying this phenomenon are still poorly understood, some possible causes include disorders of urogenitel development and/or primary endocrine dysfunction and presence of contralateral testicular pathology (atrophy or unclassified intratubular germ cell neoplasia) were known. The other possible causes can be summarized as raised serum ß-hCG levels, tumor-mediated cytokine production, antisperm antibodies, and emotional stres (2).

In this proceedins, only effects of chemotherapy and radiotherapy on male fertility are reviewed and discussed.

Cytotoxic treatment and gametogenesis

The majority of patients develop azoospermia about 8 to 12 weeks after the initiation of cytotoxic chemotherapy. Most cytostatics target only cells outside the G0 phase and thus destroy mainly the rapidly proliferating type B spermatogonia. Type A dark spermatogonia, which show no proliferative activity under normal condition, and type A pale spermatogonia, which divide at 16-day intervals, are less responsive to cytostatics than the rapidly destroyed type B spermatogonia because these other cells have little or no mitotic activity. If threshold cumulative cytostatic doses are not surpassed, type A spermatogonia survive and spermatogenesis can be reiniciated. At low cytostatic doses, recovery of spermatogenesis may be expected around 12 weeks after polychemotherapy. The destruction of type A spermatogonia at higher doses leads to a sustained or irreversible loss of sperm cell production. It took up to three years for the majority of patients to reach pretreatment fertility parameters, but it showed that, in individual cases, it took patients with TGCTs as long as nine years to achieve recovery after therapy.

Standart doses of chemotherapy do not lead to a significant deterioration of Leydig cell function in long term survivors of TGCT. In contrast, high doses of chemotherapy cause a significant and persistent impairment of Leydig cell function leading to testosterone deficiency and sexual dysfunction (3,4).

Estimating the risk of infertility after treatment for cancer

Rates of permanent infertility after cancer treatment vary depend on many factors. The effects of chemotherapy and radiotherapy depend on the drug or size/location of the radiation field, dose, age, sex, and pretreatment fertility of the patient. The measurable effects of chemotherapy or radiotherapy include compromised sperm number, motility, morphology, and DNA integrity. Because traditional gold Standard of randomized, contolled, and blinded therapeutic studies may not possible in this area, available data are poor and heterogenous, so summarization was felt to be beyond the scope of guidelines. However, Table 1 illustrate the range of risks associated with several cancer therapies. ***Total-body irradiation as used in myeloablative stem-cell transplantation*** is highly associated with infertility, while lesser doses or limited radiation fields have less gonadal toxicity. Several agents such as ***methotrexate, fluorouracil, vincristine, bleomycin,*** and ***dactinomycin*** are associated with a low or no risk of infertility. There are little human data available for the newer agents such as taxanes (1,6).

Radiation therapy can cause infertility in two distinct ways: **Primary testicular** damage occurs from radiation aimed directly at or near the testicles. Spermatogonia cells are extremely sensitive to the effects of radiation therapy. Doses as low as 600 cGy cause irreversible damage to the sperm forming cells. Doses less than this may cause a temporary drop in the number and quality of sperm produced (Gonad doses > 50 cGy and cumulative doses > 200 cGy may lead to permanent injury). The type

and dimensions of cancer determine the area of the body to be radiated and how much radiation will be given. For example, radiation may be delivered directly to the testicles, as is used for treatment of testicular leukemia and as part of the total body irradiation used in bone marrow transplant.

Scatter radiation is the term used to describe radiation that occurs in areas not directly within the treatment field, but near to it. Examples of radiation sites that may result in scatter radiation to the testis include: radiation to the lymph nodes in the lower abdomen used for treatment of higher stage Hodgkin's Disease or testicular cancer, or radiation delivered to the upper thigh for a tumor located in this area. Lead shields are used to protect the testis when the treatment field is nearby, but small amounts of radiation exposure may still occur.

Leydig cells are relatively resistant to the damaging effects of radiation therapy. Normal function remains following exposure or treatment with doses less than 2400 cGy.

Secondary or indirect testicular failure may occur following radiation therapy to the brain. Radiation may damage the pituitary gland, located in the brain, which is responsible for secreting hormones needed for normal sexual function. Pituitary damage may result in low doses of the hormones (FSH and LH) needed to stimulate the sperm forming cells and Leydig cells (4,5).

Options for fertility preservation in the male

Sperm collection and banking. Important progress in minimizing the unwanted side effects of oncological therapies has been achieved by constantly modifying and optimizing the therapeutic regimens. The most reliable and time-tested options for fertility preservation in adult patients following oncological therapy are to cryopreserve gametes and embryos. Cryopreservation of semen has been used in the past, and the succes rates improved after the introduction of ICSI. However, these techniques are available only for post-pubertal patients who can provide functional germ cells. Also, a retrospective study of 115 Hodgkin patients who cryopreserved sperm before receiving treatment revealed that only 33 had used the stored gametes and only 11 of these cases culminated in live births (1,6).

Table 1. Effects of different antitumor agents on sperm production in men (1).

Agents (Cumulative dose for effect)	Effects
Radiation (2.5 Gy to testis) **Chlorambucil (1.4 g/m^2)** **Cyclophosphamide (19 g/m^2)** **Procarbazine (4 g/m^2)** **Melphalan (140 mg/m^2)** **Cisplatin (500 mg/m^2)**	**Prolonged azoospermia**
BCNU (1 g/m^2) CCNU (500 mg/m^2)	Azoospermia in adulthood after treatment before puberty
Busulfan (600 mg/kg) **Ifosfamide (42 g/m^2)** **BCNU (300 mg/m^2)** **Nitrogen mustard** **Actionomycin D**	**Azoospermia likely, but always given with other highly sterilizing agents**
Carboplatin (2 g/m^2) Doxorubicin, Adriamycin (770 mg/m^2)	Prolonged azoospermia not often observed at indicated doses
Thiotepa (400 mg/m2) **Cytosine arabinoside (1g/m2)** **Vinblastine (50 g/m2)** **Vincristine (8 g/m2)**	**Can be additive with above agents in causing prolonged azoospermia, but cause only temporary reductions in sperm count when not combined with other agents**
Amsacrine, bleomycin, dacarbazine, Epirubicin, etoposide, fludarabine, Fluorouracil, 6-mercaptopurine, Methotrexate, mitoxantrone, thioguanine	Only temporary reductions in sperm count at doses used in conventional regiments
Prednisone Interferone-?	**Unlikely to affect sperm production** No effect on sperm production
New Agents: **Oxaliplatin, irinotecan,** **Bevacizumab, imatinib,** **Taxanes**	**Unknown effects on sperm production**

Since the patients can be embarrassed and uncomfortable about producing sperm or too ill to do so, alternative measures used at some centers include harvesting sperm by means of testicular biopsy, testicular extraction, electroejaculation, or epididymal sperm aspiration (6).

Drug strategies to protect/stimulate spermatogenesis. Hormonal protection from chemotherapy-induced testicular damage by pretreatment with GnRH agonists combined with nonsteroidal antiandrogens or with testosterone plus 17ß-estradiol has thus far only succeeded in animal models. However, clinical studies have not yet been performed in men. The protective mechanism of these hormonal therapy for spermatogenesis is not entirely clear (1,6).

Testicular shield for abdominal and/or pelvic radiotherapy. For abdominal and pelvic irradiations of male patients in the reproductive age groups, adequate shielding is necessary to preserve testicular functioning. It was reported that surface doses were as high as 20 and 15% for 2 cm distance and 8 and 5% for 10 and 12 cm distances of the central axis dose from the beam edge. Therefore, careful shielding of male gonads to < 2% of prescribed dose is recommended to reduce the absorbed dose to this sensitive organs. Thanks to new two semi-spherical half shields, this ratio could be decreased as low as 0.8% of prescribed doses (5).

In vitro maturation of gametes. The technical complexity of the cell culture system required to maintain the development of spermatozoa in vitro means that this option is not yet clinically useful in males (6).

Xenotransplantation. This method has been used to initiate spermatogenesis not only in postpubertal males from several different species, but also in prepubertal testicular tissue, thereby opening the door to fertility preservation for prepubertal boys. However this approach raises the safety issues as all forms of xenotransplatation, since it could result in the transfer of nonhuman DNA or viruses to humans. Because this method have some medical and ethical concerns, it seems unlikely to enter into accepted use (6).

Artificial gametes. The possibility of generating gametes from adult somatic cells by means of stem cell and cloning techniques or through the differentation of induced pluripotent stem cells is currently under investigation. Sperm-like cells have been generated from Mouse embryonic stem cells cultured in the laboratory. The applicability of such methods to humans is currently only theoretical. If this avenue of fertility preservation ultimately were to prove safe and efficacious, it could eliminate the need to use any of the methods described above to preserve fertility in those who face cancer treatment. However, this is a highly speculative possibility at present (1,3,6).

REFERENCES:

1. Lee SJ, Schover LR, Partridge AH, Patrizio P, Wallace WH, Hagerty K, et al. American Society of Clinical Oncology recommendations on fertility preservation in cancer patients. J Clin Oncol. 2006 Jun 20;24(18):2917-31.
2. Wohlfahrt-Veje C, Main KM, Skakkebaek NE. Testicular dysgenesis syndrome: foetal origin of adult reproductive problems. Clin Endocrinol (Oxf). 2009 Oct;71(4):459-65.
3. Schrader M, Heicappell R, Müler M, Straub B, Miller K. Impact of chemotherapy on male fertility, Onkologie 2001;24:326-30.
4. Gerl A, Mühlbayer D, Hansmann G, .Mraz W, Hiddeman W. The impact of chemotherapy on Leydig cell function in long term survivors of germ cell tumors, Cancer 2001;91:1297-303.
5. Ravichandran R, Binukumar JP, Kannadhasan S, Shariff MH, Ghamrawy KE. Testicular shield for para-aortic radiotherapy and estimation of gonad doses. J Med Phys. 2008 Oct;33(4):158-61.
6. Gosden RG. Fertility preservation: Definition, history, and prospect. Semin Reprod Med, 2009; 27: 433-37.

10 YEARS EXPERIENCE OF THE ORGANISATION WORK IN CHILDREN'S UROLOGISTS-ANDROLOGIST'S IN RUSSIA

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In our country Illnesses of urinal and sexual system at children was in fild of interests a pediatric surgeons. However, researches of last years was show, that reproductive health is a field of interdisciplinary interaction We have 5500 children's surgeons, 900 medical genetics, 3500 children's endocrinologists' now in Russi?. Successes in each of directions are present, but the global result is not reached - reproductive health of boys and men worsens.

In 1996 experts recognized necessity of allocation of the specialty separated from children's surgery - children's urology-andrology. As a whole, it is the doctor with the pediatric formation, prepared in the field of children's surgery, the general urology, endocrinology, genetics, sexology, ultrasonic diagnostics, rehabilitation and differentiation of a sex questions.

It seems that it is dream? No, in our country it is an objective reality!

Today in Russia more than 600 experts having such preparation. Many of them are members of professional association andrologyst's of Russia, professional associations of children's urologists-andrologist's of Russia, the European society of children's urologists and other professional associations.

The state regulators enter rules of carrying out of preventive work, the order of treatment and rehabilitation of boys and the young men, Some government programs receive financing.

More than 10 years children's doctors take part in conferences on andrology. More than 30 meetings with the international participation are spent for discussion of pressing questions of reproductive health of boys, adolescents and young men's .

Collective discussion has allowed to reconsider for 10 years the relation and tactics to such diseases, as varicocele, illnesses processus vaginalis, epididimal cyst's, hypospadia, a problem cryptorhidism, intersex, hypogonadism, urgent testicular surgery.

We hope that our experience will be interesting to you.

SEX TRANSFORMING IN CHILDREN

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The problem of sex transforming in children is difficult and dramatic, and it began to be solved in Russia thanks to works performed in 1970-1993 by famous gynecologist and endocrinologist I.V. Golubeva, developer of branch of science about human sex; by pediatric endocrinologists A.N. Mestkova, E.P. Kasatkina, M.A. Zhukovsky, by pediatric surgeons S.Ya. Doletsky and W.A. Reino.

Phraseology

Our research works permit to determine content and borderlines of branch of science about human sex and to show its multicomponent and interdiscipline character; difficult, expensive and individual education of specialists in this problem. But expenses of professional training and of child's examination and treatment are repaid by patient's relative wellbeing at the age of social maturity and by his/her satisfactory adaptation, including good life quality.

Branch of science about human sex *is study of men and women on a par with each other, and its parts are such disciplines as andrology, gynecology, psychology, clinical genetics, part of endocrinology studying hormonal regulation of reproductive function and genital system; part of surgery which corrects anatomic malformations of genital system. It includes also some oncological problems connected first of all with hormone-dependent neoplasms of breast and prostate gland due to disorders of gonads function. Peculiarities of evolution (puberty) and involution (climacteric period) are studied from the same pint of view.*

Naturally, branch of science about human sex must include pediatric part.

Pediatric androgynecology *is specific region of pediatric knowledge about age- depended anatomic and physiological peculiarities of normal reproductive system and about its pathology in males and females. It also studies different aspects of some sexual disorders forming in present and in future which influence upon all procreationary and recreationary* capacity of adult individual.*

Pediatric part of branch of science about human sex we call "Pediatric androgynecology". Is corresponds with peculiarities of pediatric surgery service in Russia.

Idea of sex is not clearly determined neither in Russian no in foreign medical literature. But accuracy in this problem is very important, because its absence complicates outwork of laws about sex transforming. In past 3 signatures of specialists were enough for juristical change of sex, now court decision is necessary, and this practice brings us nearer to jural state.

We determine term "sex" as integrated multicomponent idea presenting totality of biological and social peculiarities determining appointed role of individual in society.

Material and methods

Organization of diagnostic and therapeutic process is difficult and important part of our work. The most important part is the decision about sex transforming: of cause, collective decision.

All disorders leaded to surgical sex transforming are part of so called complicated or "classic" variants of reproductive system disorders. Present data are based on results of examination of more than 10 thousands of children, in prevalence at the age of 1-10 years. It is important to mention that correct diagnosis was late (at the age 13-18 years and later) in more than 500 cases, and it testifies that work quality of diagnostic institutions was insufficient.

Surgical sex transforming was performed in 54 cases from more than 1000. This group included in prevalence children with adrenogenital syndrome and with syndrome of incomplete testicular feminization, and also 9 children with micropenis and male and female young people with transsexualism.

Naturally, special plan of examination was outworked for this category of patients. This plan is not original, but screening program notices attention. It is not need in expensive diagnostic equipment; but can direct thoughts and efforts of specialist on the only true way. A number of simple techniques and tests permit to obtain important information for diagnosis.

Surgical sex transformation was performed before complete forming of patient's psychosexual orientation.

Treatment

Masculinizing or feminizing genitalia plasty is choused in dependence of sex choice of patient. *Masculinizing* plasty includes surgical removal of breast and derivates of Mullerian ductus; reconstruction of artificial penis, plasty of urethra, scrotum; testicular endoprosthesis. Replacement hormonal therapy is prescribed according to routine protocols.

Feminizing plasty includes resection of cavernous bodies with forming of clitoris, big and small vulvar lips; intrpitoplasty of vaginoplasty. The last one provides for usage of peritoneum leaf of colonic segment under laparoscopic control. Breast endoprosthesis is performed if it is indicated.

Prospects of plastic urogenital surgery development

- Reconstructive and plastic surgery with bioengineering cellular techniques usage
- Usage of autodermal cellular cultures in reconstruction of neovagina, neophallus, neourethra.
- Renewal of long-term follow up system during reproductive period of patient

REFERENCES:

1. Golubeva I.V. Hermaphroditism. Moscow, 1980
2. Okulov A.B., Negmajanov B.B. Surgical pathology of reproductive system and sex- transforming surgery. Moscow, 2000

STANDARD AND FURTHER EVALUATION OF INFERTILE MEN

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The questions of diagnosis and treatment of male infertility are the important problems in the modern andrology. The World Health Organization has developed the manual on standardized examination, diagnosis and management of man infertile (2000). Among the variety of the causes of male infertility varicocele is one of the widespread diseases, which frequency achieves up to 15 %. Thus, the specific gravity of subclinical varicocele is rather great in development of infertility. Taking into account above-stated, we have defined the purpose of research as The efforts to improve the results of treatment of the patients with male infertility associated with subclinical varicocele by perfection of the therapeutic-diagnostic algorithm at the given pathology, in particular.

Material and methods of researches. There were analyzed the results of treatment of 78 patients admitted with the symptoms of male infertility to the stationary treatment in the First Clinical Hospital in Tashkent-city at the clinical base of the Chair of operative urology and nephrology of Tashkent Medical Institute of Postgraduate Education, at who were diagnosed subclinical varicocele after examination.

The age of the patients fluctuated from 19 till 27 years. Duration of disease to the moment of the admission was 19,4 3,2 months.

The main instrumental method of diagnosis of subclinical varicocele was colour ultrasonic dopplerography (CUSDG). During investigation the measurement of the vein maximal diameter, the sum of varicose vein plexuses, blood flow velocity changes in Valsalva test were in the focus of attention. Using the technique manual compression of C.Trombett in modification of E.B.Mazo we defined hemodynamic types of varicocele by Coolsaet. Depending on a type of venous reflux there was defined renospermatic (type 1), ileospermatic (type 2) and mixed (type 3) types.

The therapeutic algorithm was determined in relation to the CUSDG results. During identification of type 1 varicocele the ligation of spermatic veins was carried out by Ivanisevich. At minimal percent of changes in the sperm analyses and in hemodynamic type 2 we abstained from operative intervention. These patients were under dynamic supervision with periodic performance of the analysis of sperm. In marked changes in spermogram there was performed ligation of the iliac collaterals, formation of testiculo-epigastral anastomoses.

At presence in the patient of hemodynamic type 3 varicocele the first was the performance of operation by Ivanisevich for liquidation of renospermatic reflux. Taking into account an opportunity of domination of ileospermatic reflux in the postoperative period there was performed control sperm analysis. At normalization of the ejaculate analysis the patients were under dynamic supervision. At preservation of changes in the analyses of sperm that indicated about prevalence of ileospermatic reflux there was carried out ligation of ileocollaterals or formation of testiculo-epigastral anastomosis.

Results

The performance of CUSDG allowed to diagnose hemodynamic type 1 of reflux in 67 (85,9 %) patients, the second type in 7 (8,9 %) patients, and type 3 in 3 (5,2 %) patients. The maximal diameter of veins was 3,5 mm, the sum of varicose vein plexuses - 3,0 mm, the blood flow speed at performance of Valsalva test was 12,4 cm/sec.

The analysis of spermograms revealed that the quantity of spermatozoons fluctuated from 20 up to 108 mln/ml (on the average 55,4 6,1), the quantity of active movable- 0 - 57 % (31,9 4,0), weakly movable - 0 - 40 % (20,3 3,9), immovable - 21 - 100 % (47,8 4,5), alive - 20 - 66 % (46,8 4,1), dead - 34 - 80 % (53,2 4,1). It is necessary to note, that the greatest changes in the spermogram were found at presence of the first hemodynamic type.

At type 1 in 67 cases the operation of Ivanisevich was performed. IN the patients with the 2d type in 2 cases there was carried out ligation of iliac collaterals and in 2 cases there was formed testiculo-epigastral anastomosis, in the rest 3 patients the change in the analyses of spermogram were not significant and they were taken on monitoring. At type 3 at the first stage all patients were performed operation of Ivanisevich. After operation only in one case there were no changes in spermogram, this patient was performed ligation of the iliac collaterals.

The study of spermograms of the patients in the postoperative period showed that in 45 (57,7 %) patients there was found normalization of the partameters during the period from 2 to 5 months.

Conclusions

1. The color ultrasound dopplerography seems to be the most informative method of diagnosis of the subclinical varicocele which allows identification of the hemodynamic types of the reflux.
2. The analysis of spermogram in subclinical varicocele allowed to reveal on the basis of the results of CUSDG that the most marked changes were noted in renospermatic type of the reflux.
3. The use of the therapeutic-diagnosis algorithm developed by us for male infertility associated with subclinical varicocele allows restoration of the reproductive function in 57,7% of cases.

ROLE OF HORMONAL TREATMENT IN MALE INFERTILITY

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Male factor is inolved in 50% of infertility of cases. Especially genetic, obstructive factors, varicocele, undescended testis and genito-urinary infections are main factors (1). Hormonal factors are less common in infertile men. However, in some specific cases with correct endocrinological evaluation and treatment , successful results can be achieved. Despite the advancements in diagnostic technology, still, idiopathic male infertility is a great concern (2).

Spermatogenesis is initiated and regulated by the hypothalamo-pituitary-gonadal axis Gonadotropin-releasing hormone (GnRH) is released in a pulsatile manner and acts on the pituitary to stimulate secretion of luteinizing hormone (LH) and follicle stimulating hormone (FSH). FSH acts on Sertoli cells and LH acts on Leydig cells in the testis. They are both required to initiate and maintain spermatogenesis (3)

Hypogonadotropic hypogonadism accounts less than 1% of all cases of male infertility

Primary hypogonadism (FSH ve LH increased, T low)

- Anorchia, maldescended testis,
- Testicular trauma or tumor
- Gonadotoxins,varicocele
- Orchitis
- Klinefelter syndrome
- Systemic diseses (Hepatic or renal failure)

Secondary hypogonadism (FSH, LH, T in low levels)

- Kalmann syndrome,
- Prader Willi syndrome
- Isolated LH deficiency
- Isolated FSH deficiency
- Pituitary and hypothalamic tumors
- Hemochromatosis
- Hormonal reasons: hyperprolactinemia, overdose testosterone, cortisone or oestrogen use or anti-pyschotic drugs and obesity

Gonadotropin replacement is the rational treatment and is the only clearly accepted and effective management of associated infetility. Gonadotropins have proven highly effective in inducing fertility. Spermatogenesis can be inducted with pulsatile GnRH or hCG/hMG combinations and %60-80 sperm recovery is reported. Initial management consists of hCG, until adequate serum testosterone levels are detected. If sperm undetected after 6 months concomitant treatment with hMG treatment or FSH ensues and therapy may be needed up to 2 years. Also in infertile patients with isolated either luteinizing or follicle-stimulating hormone deficieny, replacement of hCG and recombinant FSH containg drugs are preferred for therapy (4).

Antiestrogens were commonly instructed for idiopathic male infertility. Clomiphene citrate and Tamoxifen are the most commonly used drugs in the treatment of idiopathic oligospermia. Increasing GnRH, LH, and FSH secretion and stimulating testosterone production and spermatogenesis are the theoretical aspects of these drugs (5-6). Self-limited, common side effects are weight gain, blurred vision, hypertension, gastrointestinal disturbances and insomnia. They should not be given in increased levels of FSH (7). Aromatase inhibitors have been used to block the conversion of androgens to estrogen and therefore increase testosterone with the hopes of improving male infertility. They have an effect of FSH and LH increase with inhibiting oestrogen. Side effects are on bone mineral density with long term use and low tromboembolism risk. They are in steroidal structure (eg, testolactone) or in non-steroidal (eg, anastrazole). Testolactone and anastrozole (Arimidex) has similiar effects, but testolactone has a steroid structure and can inhibit adrenal streoidal production.Before starting aromatase inhibitors, testosterone and estradiol levels should be examined (8). For the treatment of idiopathic infertility, randomized controlled trials have observed no significant effect of clomiphene, tamoxifen, hCG, hMG, or rhFSH on pregnancy rates or seminal parameters (9).

Klinefelter syndrome is 11% detected in azoospermic patients and TESE success rate was reported as 30% in various series. In order to increase the sperm retrieval rate, patients who underwent testosterone replacement therapy, treatment should be stopped and at least 6 months wash-out period should be planned before TESE. Aromatase inhibitors with or without hCG combination therapy protocols are also reported to stimulate intratesticular testsosterone production in patients with Klinefelter syndrome and the sperm retrieval rate was increased up to 70% in Schlegel's series (10).

Hyperprolactinoma is a very rare cause of etiology. Prolactin inhibits the hypothalamic secretion of GnRH and both gonadotrpins and testosteron are suppressed. Hyperprolactinemia may be caused by pituitary adenomas, stress or drugs contaning antidepressants, phenothiazines. Dopaminergic agonists (cabergolin or bromocriptine) are used to treat hyperprolactinemia.

Side-effects of hormonal treatment should be kept in mind that hormonal treatments should be followed for any detrimental side effects, such as irreversible azoospermia or damage to the germinal epithelium (11). Rebound testosterone therapy has been discouraged, because it leads to azoospermia and tamoxifen use in idiopathic male infetility caused disruption of the testicular seminiferous epithelium and induced the formation of multinucleated cells in the testis. Hormonal treatment of infetile men with normal hormonal levels might not be overestimated for increasing pregnancy rates. However, therapies using specific hormones for particular endocrine deficiencies should be encouraged. Not only gonadotropins, but also various locally secreted peptides and proteins such as cytokines, activin, inhibin, follistatin, and estrogen have autocrine and paracrine control over spermatogenesis. Other hormones, such as growth hormone leptin , insulin-like growth factor-1 , and thyroid hormone have also been implicated in spermatogenesis. Experimental studies related with these hormones will explain the unanswered questions abouth male infertility (12).

REFERENCES:

1. Jarow JP. Endocrine causes of male infertility. Urol Clin North Am. 30:83–90,2003.
2. Madhukar D, Rajender S. Hormonal Treatment of Male Review Infertility: Promises and Pitfalls. Journal of Andrology, 30(2):95-112, 2009.
3. Finkel DM, Phillips JL, Snyder PJ. Stimulation of spermatogenesis by gonadotropins in men with hypogonadotropic hypogonadism. N Engl J Med. 12:651–655,1985.
4. Moudgal NR, Sairam MR. Is there a true requirement for follicle stimulating hormone in promoting spermatogenesis and fertility in primates? Hum Reprod. 13:916–919,1998.
5. Adamopoulos DA, Pappa A, Billa E, Nicopoulou S, Koukkou E, Michopoulos J. Effectiveness of combined tamoxifen citrate and testosterone undecanoate treatment in men with idiopathic oligozoospermia. Fertil Steril. 80, 914–920, 1997
6. Hampl R, Heresova´ J, Lachman M, Sulcova´ J, Sta´rka L. Hormonal changes in tamoxifen treated men with idiopathic oligozoospermia. Exp Clin Endocrinol. 92:211–216, 1988.
7. Newton R, Schinfeld JS, Schiff I. Clomiphene treatment of infertile men: failure of response with idiopathic oligospermia. Fertil Steril. 34:399–400,1980.
8. Raman JD, Schlegel PN. Aromatase inhibitors for male infertilty. J Urol 167(2): 624-9, 2002.
9. Foresta C, Bettella A, Garolla A, Ambrosini G, Ferlin A. Treatment of male idiopathic infertility with recombinant human follicle stimulating hormone: a prospective, controlled, randomized clinical study. Fertil Steril. 84:654–661, 2005.
10. Ramasamy R, Ricci JA, Palermo GD, Gosden LV, Rosenwaks Z, Schlegel PN. Successful fertility treatment for Klinefelter's syndrome. J Urol. 182(3):1108-13, 2009.
11. Paradisi R, Busacchi P, Seracchioli R, Porcu E, Venturoli S. Effects of high doses of recombinant human follicle-stimulating hormone in the treatment of male factor infertility: results of a pilot study. Fertil Steril. 86:728–731, 2006.
12. Liu PY, Handelsman DJ. The present and future state of hormonal treatment for male infertility. Hum Reprod Update. 9:9–23, 2003.

NOVEL MANAGEMENT OF INFERTILE MEN WITH AZOOSPERMIA

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Azoospermia incidence of infertile men is between 5% and 20%, while in the general population, it is about 2% [1]. "Azoospermia" is defined as the absence of sperm in a centrifuged semen sample. Azoospermia is classified as either nonobstructive (NOA) or obstructive (OA).

Azoospermia due to low sperm production (NOA) affects approximately 1% of the male population and 10% of men who seek fertility evaluation. NOA is caused by severely reduced sperm production, resulting in the absence of sperm in the semen. Testis biopsy reveals that these men have Sertoli cell-only pattern, maturation arrest, or hypospermatogenesis. Low level of sperm production may be present in the testes of men with azoospermia, but the sperm do not survive epididymal transit and ejaculation [2].

Although there are many causes of azoospermia, obstruction of the ductal system is responsible for approximately 40% of case. OA is characterized by a testis biopsy demonstrating sufficient spermatogenesis and a physical occlusion of the repro¬ductive tract distal to the testis that prevents sperm from entering the semen. Obstructive azoospermia following inflammation includes ejaculatory duct obstruction in 1-3%, intratesticular obstruction in 15% and epididimal obstruction in 30-67% of cases. Vas deference obstruction are, as rule, non inflammatory origin. Although testicular sperm have dramatically lower motility than those that have transited the male reproductive tract, these sperm can be used for intracytoplasmic sperm injection (ICSI) during in vitro fertilization (IVF). Such observations led investigators to perform testicular sperm extraction (TESE) with ICSI for men with non-obstructive azoospermia. Low pregnancy rates of 20 to 21% per attempt have been reported [3].

Even if sperm retrieval and ICSI are being employed, distinction between by these two types of disease is still important for 2 reasons. First, successful sperm retrieval is far more likely with obstructive azoospermia. Second, the potential un¬derlying genetic defects is different in the 2 types of azoospermia [4].

Management of NOA. Endocrine abnormality associated with azoospermia can be corrected with pharmacologic management. Azoospermia secondary to anabolic steroid use may be reversed with withdrawal of the offending drug. The most common correctable endocrine deficiency associated with infertility is hypogonadotropic hypogonadism. In these men, pituitary magnetic resonance imaging should be performed to rule out a mass lesion. If this is negative, then therapy with gonadotropins can initiate spermatogenesis. When no specific therapy is available – TESE/ICSI may allow the patient to have his own biological children. TESE/ICSI has been applied to NOA and represents an extraordinary treatment advance for one of the most severe forms of male factor infertility. The TESE procedure involves extracting sperm from testis tissue removed with open or percutaneous biopsy or by percutaneous aspiration. Successful sperm retrieval has been achieved in large series in as many as 77% of cases [5]. Even men with nonmosaic Klinefelter syndrome and severe testis atrophy have fathered children with TESE/ICSI [6]. Most reports of TESE in NOA describe an open approach [5]. Direct comparisons of open and percutaneous TESE approaches have generally demonstrated that the open approach has a higher chance for successful sperm retrieval [7].

Men with NOA can now be treated by using intra-oocyte round spermatid injection (ROSI) or elongated spermatid injection (ELSI) in cases for which no mature sperm are available, sperm precursors, obtained from either the ejaculate or the testis. But the rates of fertilization and pregnancy with spermatids have been disappointing.

Two innovative techniques have been developed to improve chances for successful sperm retrieval and limit the amount of testis tissue removed in TESE. A fine needle aspiration mapping procedure has been described by Turek. This mapping procedure can be used to identify pockets of spermatogenesis within the testis that can be sampled at the time of TESE. In a recent small cohort of patients, this technique enabled successful sperm retrieval in 95% of cases (20 of 21) [8]. The second sperm retrieval procedure recently introduced is the microdissection technique developed by Schlegel [9]. In this procedure, the tunica albuginea is opened widely to expose the testis parenchyma. Under the operating microscope, dilated tubules bearing sperm can be identified and differentiated from the sclerotic ones that do not contain sperm. The dilated tubules are then sampled, limiting the amount of tissue removed and improving chances for successful retrieval [9]. Clinical pregnancy rates between 11% and 49% per cycle have been reported for TESE/ICSI in NOA. It is possible to perform ICSI with cryopreserved testicular sperm, and several studies suggest that pregnancy rates are not compromised [10].

Management of OA. The introduction of ICSI with epididymal and testicular sperm has revolutionized the management of men with **CBAVD** and other forms of uncorrectable obstruction. Clinical or ongoing pregnancy rates for ICSI and obstructive azoospermia range from 17% to 56%. Prior to the sperm retrieval procedure, the patient and his partner should be tested for CF mutations [11]. Microepididymal sperm aspiration (MESA) reliably provides adequate numbers of sperm that can also be

cryopreserved for future cycles but is also the most invasive retrieval technique. Percutaneous epididymal sperm aspiration (PESA) is an alternative to open epididymal sperm aspiration and can be performed in the office with local anesthesia. Testicular sperm can also be reliably obtained percutaneously or with an open biopsy in men with obstructive azoospermia. Cryopreserved sperm, either epididymal or testicular, can be used with ICSI.

Epididymal obstruction can be secondary to vasectomy, congenital, inflammatory, or idiopathic. In an azoospermic man with normal semen volume, normal size testes, bilateral palpable vasa, and a testis biopsy that demonstrates sufficient spermatogenesis, the most likely site of obstruction is the epididymis. Prior to performing VE, vasography should be performed to document vasal patency. Vasography should only be performed at the time of a planned surgical reconstructive procedure. If vasography is performed as a separate procedure, then an additional site of obstruction can be created. Vasography can be performed with either an open or a puncture technique. The puncture technique eliminates the need for closure of the vas deferens. Radiographic contrast can be injected distally toward the abdomen, and a plain x-ray is taken to define the anatomy of the vas deferens. A Foley catheter with air in the balloon on gentle traction can eliminate contrast reflux into the bladder and provide a better quality film. Alternatively, the bladder can be catheterized following injection of a mixture of saline and methylene blue. If blue fluid is noted, then patency of the vas deferens is confirmed. Patency of the vas deferens can also be verified by simply injecting saline distally. If it flows easily, then the vas deferens is assumed to be patent. Injection should not be performed toward the epididymis, as this could cause injury.

Vasal obstruction can occur secondary to vasectomy and other scrotal surgery besides vasectomy, or lower abdominal or inguinal surgery, such as renal transplantation or herniorrhaphy. Reconstruction after renal transplantation is usually not feasible, as the abdominal end of the vas deferens retracts proximally in the retroperitoneum. Obstruction caused by hernia repair may be correctable, though these repairs are technically challenging. Crossover transseptal procedures (VV or VE) are possible when a normal testis with unreconstructable obstruction is present on one side and an atrophic testis and patent ductal system are present on the contralateral side.

Vasal obstruction secondary vasectomy can be corrected with microsurgical vasovasostomy (VV). When a secondary epididymal obstruction occurs after vasectomy, vasoepididymostomy (VE) is required. Patency and pregnancy rates for VV range from 75% to 93% and from 46% to 82%, respectively [12]. VE is more technically demanding and less successful than VV. Patency rates range from 67% to 85%, and pregnancy rates range from 27% to 49% [13]. Patency can take as long as 6 months for VV [14] and as long as 1 year following VE [15]. The average time to achieve pregnancy was 1 year for VV.

Azoospermic men with low semen volume, a normal FSH, and at least 1 palpable vas deferens should be evaluated for **ejaculatory duct obstruction** with TRUS. Endorectal coil magnetic resonance imaging can also be useful in making the diagnosis. Causes of ejaculatory duct obstruction include trauma, infection, congenital atresia or stenosis, and utricular, Mullerian, or Wolffian duct cysts. A seminal vesicle greater than 1,5 cm in greatest diameter is suggestive of ejaculatory duct obstruction, though there is no definite threshold for making the diagnosis. TRUS may also demonstrate a midline cyst or visible dilation of the ejaculatory ducts. Traditionally, ejaculatory duct obstruction has been diagnosed by vasography following a testis biopsy demonstrating normal spermatogenesis. Recently, seminal vesiculography, either via a transrectal or transperineal approach, has been developed as an alternative to vasography. The potential advantage is that it does not risk creating an additional site of obstruction at the vasogram site. Ejaculatory duct obstruction treatment has traditionally been accomplished with transurethral resection of the ejaculatory ducts (TURED). A limited resection of the prostate is performed at the level of the verumontanum, either to unroof a cyst or to open a narrowed ejaculatory duct. A mixture of saline and methylene blue is simultaneously injected distally in the vas deferens. Endoscopic visualization of blue fluid confirms opening of the ejaculatory duct. A new alternative to TURED is balloon dilation of the ejaculatory duct at the time of seminal vesiculography. The patency rate for TURED is about 50%, and the overall pregnancy rate is about 25% [16]. Alternatively, sperm retrieval and ICSI can be employed if surgical correction is not possible or not desired by the couple. The average time to achieve pregnancy was 1 year. Success rates for repeat reversals are lower than for first-time procedures. Patency rates for repeat reversals range from 64% to 79%, and pregnancy rates range from 27% to 44% [17].

Recent modifications address one of the main technical difficulties encountered in VE, that is, suture placement in an open collapsed epididymal tubule. These newer intussusception techniques involve placement of sutures in a distended epididymal tubule before it is opened. The technique reported by Berger uses three 10-0 sutures and that by Marmar uses 2. The main theoretical advantage of these newer intussusception techniques is that the resultant invagination of the epididymis may reduce leakage from the anastomosis. Whether these modifications will translate into improved pregnancy rates is not known [18]. Patency may occur earlier, however. In the small series by Marmar, 6 of 9 (67%) patients had sperm in the semen at 3 months.

Despite the recent technological advances outlined above, some couples may not wish to pursue treatment with assisted reproductive techniques. Reasons for this may include financial limitations or religious objections. These couples may pursue other alternatives, including therapeutic insemination with donor sperm (TID), adoption, or child-free living.

Recent advances have dramatically changed the evaluation and treatment of the azoospermic man. Two innovative techniques have been developed to improve chances for successful sperm retrieval and limit the amount of testis tissue removed in TESE and modifications of VE that addressed to main technical difficulties encountered in , that is, suture placement in an open collapsed epididymal tubule. Several investigators have attempted to use fewer sutures, augmented by fibrin glue or laser soldering for both vasovasostomy and vasoepididymostomy procedures, allowing for a shorter operative time. In addition, robotics have been used for both vasovasostomies and vasoepididymostomies, with the hope that it may help with microsurgical technical issues, including eliminating tremor and improving dexterity with microsurgical instruments. While these techniques are not the current clinical standard, they appear to yield similar patentcy rates and may represent alternatives for the surgeon who performs only an occasional vasectomy reversal.

REFERENCES:

1. Jarow JP. Evaluation and treatment of the azoospermic patient. Curr Probl Urol. Jan/Feb 1992:4–30.
2. Silber SJ; Nagy Z; Devroey P; Tournaye H; Van Steirteghem AC. Distribution of spermatogenesis in the testicles of azoospermic men: the presence or absence of spermatids in the testes of men with germinal. Hum Reprod Nov; 12(11):2422-8, 1997.
3. Peter N. Schlegel, M.D.What's New in Male Infertility Treatment at Cornell. Management of Men with Non-obstructive Azoospermia. 2005 http://www.maleinfertility.org/new-noa.html
4. Kolettis PN. The Evaluation and Management of the Azoospermic Patient. Journal of Andrology, Vol. 23, No. 3, May/June 2002
5. Amer M, Ateyah A, Hany R, Zohdy W. Prospective comparative study between microsurgical and conventional testicular sperm extraction in non-obstructive azoospermia: follow-up by serial ultrasound examinations. Hum Reprod. 2000;15:653–656.
6. Palermo GD, Schlegel PN, Sillis ES, Veeck LL, Zaninovic N, Menendez S, Rosenwaks Z. Births after intracytoplasmic sperm injection of sperm obtained by testicular extraction from men with nonmosaic Klinefelter's syndrome. N Engl J Med. 1999;338:588–590.
7. Mercan R, Urman B, Alatas C, Aksoy S, Nuhoglu A, Isiklar A, Balaban B. Outcome of testicular sperm retrieval procedures in nonobstructive azoospermia: percutaneous aspiration versus open biopsy. Hum Reprod. 2000;15:1548–1551.
8. Turek PJ, Givens CR, Schriock ED, Meng MV, Pedersen RA, Conaghan J. Testis sperm extraction and intracytoplasmic sperm injection guided by prior fine-needle aspiration mapping in patients with nonobstructive azoospermia. Fertil Steril. 1999;71:552–557.
9. Schlegel PN. Testicular sperm extraction: microdissection improves sperm yield with minimal tissue excision. Hum Reprod. 1999;14:131–135.
10. Kupker W, Schlegel PN, Al-Hasani S, et al. Use of frozen-thawed testicular sperm for intracytoplasmic sperm injection. Fertil Steril. 2000; 73:453–458.
11. Prins GS, Dolgina R, Studney P, Kaplan B, Ross L, Niederberger C. Quality of cryopreserved testicular sperm in patients with obstructive and nonobstructive azoospermia. J Urol. 1999;161:1504–1508.
12. Fox M. Vasectomy reversal-microsurgery for best results. Br J Urol. 1994;73:449–453.
13. Takihara H. The treatment of obstructive azoospermia in male infertility - past, present and future. Urology. 1998;51 (suppl 5A) :150–155.
14. Belker AM, Thomas AJ Jr, Fuchs EF, Konnak JW, Sharlip ID. Results of 1,469 microsurgical vasectomy reversals by the Vasovasostomy Study Group. J Urol. 1991;145:505–511.
15. Jarow JP, Sigman M, Buch JP, Oates RD. Delayed appearance of sperm after end-to-side vasoepididymostomy. J Urol. 1995;153:1156–1158.
16. Schlegel PN. Management of ejaculatory duct obstruction. In: Lipshultz LI, Howards SS, eds. Infertility in the Male. 3rd ed. St Louis, Mo: Mosby; 1997:385–394.
17. Hernandez J, Sabanegh ES. Repeat vasectomy reversal after initial failure: overall results and predictors for success. J Urol. 1999;161:1153–1156.
18. Berger RE. Triangulation end to side vasoepididymostomy. J Urol. 1998; 159:1951–1953.

TRANSURETHRAL EJACULATORY DUCT RESECTION FOR OBSTRUCTIVE INFERTILITY

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Infertility currently affects 15% of all couples, with an anticipated increase over the next 20 years (1). Although azoospermia has many causes, approximately 40% of cases result from obstruction in ductal system (2). Men with obstructive infertility may father children in one of two ways: 1)surgical correction of the obstruction or 2) retrieval of sperm by assisted reproductive technics.

Ejaculatory Duct Obstruction

Ejaculator duct obstruction is reported to be the cause of azoospermia in up to 5% of patients (3). Ejaculatory duct obstruction, although rare, is a surgically correctable cause of male infertility (4-6). Ejaculatory duct obstruction can be either congenital or acquired [13,15]. Congenital causes include congenital atresia or stenosis of the ejaculatory ducts and utricular, mullerian, and wolfian duct cysts. Acquired causes may be secondary to trauma, either iatrogenic or otherwise, or infectious or in ammatory etiologies (7,8,9). Calculus formation secondary to infection may also cause obstruction (10). Cyst formation from prior instrumentation or infection may also occur (11). In many cases, patients with ejaculatory duct obstruction have no significant antecedent history (12).

Diagnosis

Complete ejaculatory duct obstruction should be suspected in patients with azoospermia and decreased ejaculatory volume (<1.0 mL) in the presence of acidic semen lacking fructose. Serum testosterone and gonadotropin levels are usually within normal limits. On occasion, rectal examination will reveal a palpable midline mass or dilated seminal vesicles. Jarow et al reported that 37% of infertile patients with azoospermia have some form of ductal obstruction and that 6% of azoospermic men have ejaculatory duct obstruction.

Partial ejaculatory duct obstruction has highly variable signs and symptoms and can be found in infertile patients who have significantly low sperm motility and oligospermia despite normal testicular size and normal hormone profile (FSH, luteinizing hormone, testosterone) (13,14). In some men with partial ejaculatory duct obstruction, some of the semen parameters approach normal (15). Partial ejaculatory duct obstruction leads to entrapment of sperm at the point of obstruction, and the increased body temperature at this location as well as sperm stasis is thought to cause unique impairment in sperm motility.

Transrectal ultrasonography should be used to evaluate infertile patients with low ejaculatory volume (<1.0 mL), low sperm motility (<30%), or oligospermia (<20 million sperm/mL) when findings on physical examination are normal and serum gonadotropin and testosterone are within normal ranges.

The many methods used to diagnose ejaculatory duct obstruction can be subdivided into static tests and dynamic tests (16). Static tests include transrectal ultrasonography, magnetic resonance imaging, and seminal vesicle aspiration (17); dynamic tests include vasography and seminal vesiculography. In a comparative study of dynamic and static tests for the diagnosis of ejaculatory duct obstruction, Purohit et al found that transrectal ultrasonography used alone had a poor specificity for diagnosis of ejaculatory duct obstruction (16). When dynamic tests were incorporated into the diagnostic evaluation, the rate of unnecessary duct resections was significantly decreased.

Transrectal Ultrasonography

Transrectal ultrasonography has become the standard modality for diagnosis of ejaculatory duct obstruction. Ejaculatory duct obstruction is suspected in the presence of a cystic midline structure within the prostate as well as dilated seminal vesicles. Seminal vesicles are considered dilated when their axial diameters are greater than 1.5 cm (18,19). However, it is possible that partial ejaculatory duct obstruction can exist when the axial diameters of seminal vesicles are normal (19).

Vasography and Seminal Vesicle Aspiration

Historically, vasography was the gold standard for diagnosis of ejaculatory duct obstruction (19,20,21). However, the risk of vasal injury and subsequent vasal occlusion has limited its use. Vasography is now used to help confirm equivocaltransrectal ultrasonography findings. Vasography is also necessary if no sperm are found on seminal vesicle aspiration. Vasography, with instillation of methylene blue dye or indigo carmine, can be used instead of seminal vesiculography to guide in the resection of the ejaculatory ducts. It is important to document sperm production as well as patency of the seminal vesicles, especially in patients with partial ejaculatory duct obstruction, before initiating surgical correction. Therefore, transrectal ultrasonography–guided aspiration of the seminal vesicles should be performed before surgery.

Treatment

Transurethral Resection of the Ejaculatory Ducts

Transurethral resection of the ejaculatory duct, first described by Farley and Barnes in 1973 , is the primary treatment of ejaculatory duct obstruction. A 24 French resectoscope is placed into the urethra, and resection is carried out at the level of the verumontanum. An O'Connor drape is used with a finger in the rectum to allow better depth perception and visualization of the posterior prostate. If an ejaculatory duct cyst is present, it is usually deep and just posterior to the verumontanum. Therefore, the verumontanum is deeply resected with care not to injure the rectum. Real-time ultrasonography can be used concurrently to visualize the resection of the ejaculatory cyst. Once efflux from the ejaculatory ducts of copious cloudy material or indigo carmine, if present, is identified, the resection is complete. If the cyst still is not unroofed, a Collings knife is used to make bilateral incisions just lateral to the base of the resected verumontanum. These incisions make it possible to open obstructed ejaculatory ducts that may have been missed during the initial midline incision. Electrocautery is used judiciously to avoid occlusion of the newly opened ejaculatory ducts. Care is taken at all times to protect the bladder neck and external sphincter from injury that might result in retrograde ejaculation and urinary incontinence. A urethral catheter is left in place overnight and removed the next day.

Complications

A common complication of transurethral resection of the ejaculatory duct is the reflux of urine into the ejaculatory ducts and subsequently into the seminal vesicles, vas deferens, or even the epididymis. This reflux into the epididymis can lead to acute or chronic epididymitis. Other complications include retrograde ejaculation secondary to bladder neck injury, incontinence secondary to external sphincter injury, and, although rare, rectourethral fistula secondary to rectal injury (22,23,24). Postoperative bleeding, bladder neck contractures, and erectile dysfunction are also known complications. Large defects within the prostate can allow mixing of semen and urine, which can further impair sperm quality.

Outcomes

Results of studies treating infertile men with ejaculatory duct obstruction are shown in Table1. Overall results from surgical correction of ejaculatory duct obstruction show a 55% improvement in semen parameters and a 27% pregnancy rate.

Table1: Results of Treatment of Ejaculatory Duct Obstruction in Infertile Men

Date	Author	No. of Patients	No. of Surgical Procedures	Improved Semen Quality	No. of Pregnancies
1978	Hassler and Weber	1	1	1	1
1978	Porch	1	1	1	1
1980	Weintraub	4	4	2	1
1980	Silber	4	4	1	0
1982	Amelar and Dubin	6	6	2	1
1983	Vicente et al	9	9	3	1
1984	Carson	4	4	3	1
1985	Goldwasser et al	1	1	1	1
1986	Dunetez and Krane	1	1	1	1
1991	Pryor and Hendry	87	31	18	8
1992	Hellerstein et al	2	2	2	2
1992	Hendry and Pryor	26	26	12	7
1993	Meacham et al	24	26	12	7
1998	Netto et al	14	14	10	5
1998	Popken et al	8	8	6	0
2001	Ozgök et al	24	24	15	6
2003	Fuse et al	10	10	7	3
Total		202	148	82 (55%)	40 (27%)

The type (partial versus complete), location, and etiology of ejaculatory duct obstruction can have an impact on surgical outcomes. Kadioglu et al reported that after surgical treatment of ejaculatory duct obstruction, improvement of semen parameters was greater in patients with partial obstruction (94%) than in patients with complete obstruction (59%) (25). Others have shown that patients with midline cysts treated by transurethral resection tend to have better outcomes than do patients with other causes of ejaculatory duct obstruction (26). Finally, Netto et al demonstrated in their series that after treatment, 83% of patients with congenital ejaculatory duct obstruction had an improved sperm count, and pregnancy was achieved through sexual intercourse by 66% of the patients. Of those with acquired ejaculatory duct obstruction, 37.5% had improved semen quality after transurethral resection of the ejaculatory duct, and 12.5% achieved pregnancy by sexual intercourse (27). Thus, patients with partial, congenital, and midline cystic causes of ejaculatory duct obstruction tend to have the best surgical outcomes.

REFERENCES:

1. Thonneau P, Marchand S, Tallec A, Ferial M, Ducot B, Lansac J, Lopes P,Tabaste J, Spira A. Incidence and main causes of infertility in a resident population of three French regions. Hum Reprod 1991; 6:811-16.
2. Jarow JP, Espeland MA, Liphultz. Evaluation of the azoospermic patient. J Urol 1989; 142:62-5.
3. Turek PJ, Mgana JO, Lipshultz LI. Semen parameyers before and after transurethral surgery for ejacultaory duct obstruction. J Urol 1996; 155:1291-93.
4. Meacham RB, Hellerstein DK, Lipshultz LI. Evaluation and treatment of ejaculatory duct obstruction in the infertile male. Fertil Steril 1993; 59:393-97
5. Weintraub MP, De Mouy E, Hellstrom WJ. Newer modalities in the diagnosis and treatment of ejaculatory duct obstruction. J Urol 1993; 150:1150-54.
6. Nagler HM, Rotman M, Zoltan E, Fisch H. The natural history of partial ejaculatory duct obstruction. J Urol 2002; 167:253-54.
7. Pryor JP, Hendry WF. Ejaculatory duct obstruction in subfertile males: analysis of 87 patients. Fertil Steril 1991; 56:725-730.
8. Goldwasser BZ, Weinerth JL, Carson CC III. Ejaculatory duct obstruction: the case for aggressive diagnosis and treatment. J Urol 1985; 134:964-966.
9. Ozgök Y, Kilciler M, Aydur E, Saglam M, Irkılata HC, Erduran D: Endoscopic seminal vesicle stone removal. Urology 2005; 65(3):591.
10. Hellerstein DK, Meacham RB, Lipshultz LI. Transrectal ultrasound and partial ejaculatory duct obstruction in male infertility. Urology 1992; 39:449-452.
11. Mayersak JS. Urogenital sinus-ejaculatory duct cyst: a case report with a proposed clinical classification and review of the literature. J Urol 1989; 142:1330-1332.
12. Fisch H. Transurethral resection of the ejaculatory ducts. Curr Surg Techn Urol 1992; 5:2-7.
13. Hellerstein DK, Meacham RB, Lipshultz LI: Transrectal ultrasound and partial ejaculatory duct obstruction in male infertility. Urology 1992; 39:449-452.
14. Ozgok Y, Tan MO, Kilciler M, Tahmaz L, Kibar Y: Diagnosis and treatment of ejaculatory duct obstruction in male infertility. Eur Urol 2001; 39(1):24-9.
15. Meacham RB, Hellerstein DK, Lipshultz LI: Evaluation and treatment of ejaculatory duct obstruction in the infertile male. Fertil Steril 1993; 59:393-397.
16. Purohit RS, Wu DS, Shinohara K, Turek PJ: A prospective comparison of 3 diagnostic methods to evaluate ejaculatory duct obstruction. J Urol 2004; 171:232-235.
17. Orhan I, Onur R, Cayan S, et al: Seminal vesicle sperm aspiration in the diagnosis of ejaculatory duct obstruction. BJU Int 1999; 84:1050-1053.
18. Littrup PJ, Lee F, McLeary RD, et al: Transrectal US of the seminal vesicles and ejaculatory ducts: Clinical correlation. Radiology 1988; 168:625-628.
19. Jarow JP: Transrectal ultrasonography of infertile men. Fertil Steril 1993; 60:1035-1039.
20. Ford K, Carson III CC, Dunnick NR, et al: The role of seminal vesiculography in the evaluation of male infertility. Fertil Steril 1982; 37:552-556.
21. Pryor JP, Hendry WF: Ejaculatory duct obstruction in subfertile males: Analysis of 87 patients. Fertil Steril 1991; 56:725-730.
22. Vazquez-Levin MH, Dressler KP, Nagler HM: Urine contamination of seminal fluid after transurethral resection of the ejaculatory ducts. J Urol 1994; 152(pt 1):2049-2052.
23. Goluboff ET, Kaplan SA, Fisch H: Seminal vesicle urinary reflux as a complication of transurethral resection of ejaculatory ducts. J Urol 1995; 153:1234-1235.
24. Goluboff ET, Stifelman MD, Fisch H: Ejaculatory duct obstruction in the infertile male. Urology 1995; 45:925-931.
25. Kadioglu A, Cayan S, Tefekli A, et al: Does response to treatment of ejaculatory duct obstruction in infertile men vary with pathology?. Fertil Steril 2001; 76:138-142.
26. Kendirci M, Sanli O, Celtik M, et al: The pathology causing distal ejaculatory duct obstruction predicts the successful outcome of TUR-ED [abstract], San Francisco, American Urologic Association, 2004.
27. Netto Jr NR, Esteves SC, Neves PA: Transurethral resection of partially obstructed ejaculatory ducts: Seminal parameters and pregnancy outcomes according to the etiology of obstruction. J Urol 1998; 159:2048-2053.

COMPARISON OF EMBRIOLOGICAL DATA IN PATIENTS WITH ASTENO - AND TERATOZOOSPERMIA IN IVF/ICSI PROGRAM

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Infertility is a common problem affecting 10% - 15% of all couples [1,2]. In 50% of the cases it is attributed to reduced sperm quality of the male partner [3]. Semen quality is a measure of the ability of semen to accomplish fertilization. Asthenozoospermia (AZS) is a common cause of male infertility characterized by reduced forward motility [A+B sperm motility <50% or A < 25%, World Health Organization (WHO) criteria (WHO, 1999)] or absent sperm motility in fresh ejaculate. AZS may exist as an isolated disorder, in combination with other sperm anomalies or as part of a syndromic association. AZS as an isolated disorder is found in as many as 24% of patients presenting for the evaluation of male subfertility and may be a significant factor in another 55% of patients with combined defects in sperm concentration, motility and morphology [4]. Decreased sperm motility may be caused by sperm dysfunction, prolonged periods of sexual abstinence, partial blockage of seminal tract, varicocele, infection or genetic factors [5, 6, 7].

Presence of AZS can be a very subtle, 'early indicator' of reduction in the semen quality, which many a times gets overlooked, if the semen sample shows adequate sperm count and normal morphology. Abnormal morphology (i.e. malformed sperm) appears to play a lesser role in male infertility. While there are many theories about what causes these conditions, it is not always possible for the infertility due to severe male factor. The introduction of intracytoplasmic sperm injection (ICSI) in 1992 by Palermo et al. [8] has made it possible to treat infertility due to severe male factor. With this technique even spermatozoa from men with an extremely low sperm count and with poor semen motility and morphology can be successfully used to fertilize the oocyte. However, the use of ICSI in severe male infertility treatment may give good fertilization rate, but not always good quality of embryos and pregnancy.

The aim of this study is understanding the influence of sperm parameters to the quality of embryos and pregnancy rate in ART programs and tray to understand the possible cause.

MATERIALS AND METHODS: We performed a retrospective review of 51 consecutive infertile couples in whom the man presented with clinical astenozoospermia, teratozoospermia, and ICSI programs was made. Control group was 19 couple in whom ART programs with donor sperm was made.

Ovarian stimulation was performed using gonadotropin releasing hormone agonist, human menopausal gonadotropin, and human FSH. Human chorionic gonadotropin was administered when optimal follicle development was achieved, as evaluated by serial transvaginal ultrasound and estrogen determinations. Oocyte retrieval was performed via a transvaginal approach with sonographic guidance 34 hours after human chorionic gonadotropin injection. The ICSI procedure was performed with oocytes in metaphase II according to the technique described by Palermo et al. [8]. Twenty-four hours later, cleavage of fertilized oocytes was assessed. Embryo transfer was performed 120 hours after fertilization.

Table 1. Comparison of the embryos quality in ICSI program in tree clinical groups

	Astenozoospermia (n = 23)	**Teratozoospermia (n = 28)**	**Sperm of donor (n = 19)**
Sperm count	10,6 mln/ml	14,3 mln/ml	34,2 mln/ml
Motility (A)	6,5 %	12,3%	26 %
Abnormal	67 %	82 %	46 %
Oocytes / egg collection	11,4	12.2	9,7
Fertilization rate	68 %	67 %	77 %
Blastocysts formation rate	14,6 %	22,2 %	49 %
Pregnency	27%	33 %	68 %

RESULTS: In either IVF or ICSI, the fertilization rate did not show dramatic correlation with the morphology and motility of sperm. We found the lowest quality of embryos (low rate of blastocysts formation) and decreased pregnancy rate in group of patients with severe astenozoospermia.

The exploration of sperm DNA stability and integrity are being used to evaluate fertility disorders and to increase the predictive value of sperm analysis [9, 10]. For understanding the cause of negative influence of severe astenozoospermia to embryos quality, we compared sperm parameter in patients with high sperm DNA fragmentation level (more, than 60%) and with low sperm DNA fragmentation level (less, than 30%).

Tab. 2 Comparison of some sperm parameters in patients with high and low DNA fragmentation level

	DNA fragmentation level (more, than 60%) n = 24	**DNA fragmentation level (less, than 30%) n = 32**
Sperm count	7,9 mln/ml	16,4 mln/ml
Motility (A)	4,6 %	15,5%
Abnormal	67,7 %	62,8%
Sperm DNA fragmentation rate	75,3 %	21,2%

In group of patients with high sperm DNA fragmentation level the most important difference was in progressive sperm motility. There was also negative correlation with sperm count. We don't found the correlation of high sperm DNA fragmentation level with sperm morphology.

DISCISSION: abnormalities in spermatogenesis and/or spermiogenesis due to disturbance of breakdown in cell system regulation, apoptosis, DNA chromatin remodeling may give the changes in routine parameters of semen analysis. The percentage of sperm cells with progressive motility seems to be the most sensible and the most predictable parameter of their functional capability. The oxidative stress is one of the most important factors of sperm DNA fragmentation, so antioxidant treatment prior to ART (IVF - ICSI) may minimize quantity of sperm with DNA fragmentation. The quality of sperm even in IVF-ICSI programs influence dramatically embryos quality and success rate.

REFERENCES:

1. Ryu HM, Lin WW, Lamb DJ, Chuang W, Lipshultz LI, Bischoff FZ. Increased chromosome X, Y, and 18 nondisjunction in sperm from infertile patients that were identified as normal by strict morphology: implication for intracytoplasmic sperm injection. Fertil Steril. 2001;
2. Giorlandino C, Calugi G, Iaconianni L, Santoro M.L., Lippa A. Spermatozoa with chromosomal abnormalities may result in a higher rate of recurrent abortion. Fertil Steril. 1998;
3. Rives N, Clair AS, Mazurier S, Sibert L. at al. Relationship between clinical phenotype semen parameters and aneuploidy frequency in sperm nuclei of 50 infertile males. Hum Genet. 1999;
4. Luconi M, Forti G, Baldi E. Pathophysiology of sperm motility. Front Biosci. 2006;
5. Gaur DS, Talekar M, Pathak VP. Effect of cigarette smoking on semen quality of infertile men. Singapore Med J. 2007;
6. Gdoura R, Kchaou W, Chaari C, Znazen A, Keskes L, Rebai T, Hammami A. Ureaplasma urealyticum, ureaplasma parvum, mycoplasma hominis and mycoplasma genitalium infections and semen quality of infertile men. BMC Infect Dis. 2007;
7. Pasqualotto FF, Sundaram A, Sharma RK, Borges E Jr, Pasqualotto EB, Agarwal A. Semen quality and oxidative stress scores in fertile and infertile patients with varicocele. Fertil Steril. 2008;
8. PalermoG, Joris H, Devroey P, Steirteghem AC. Pregnancies after intracytoplasmic injection of single spermatozoon into an oocyte. Lancet. 1992;
9. Aziz N., Agraval A. Evaluation of sperm damage: beyond the World Health Organization criteria. Fertil Steril. 2008;
10. Zinzi A., Libman J. Sperm DNA damage: clinical significance in the era of assisted reproduction. CMAJ 2006

CORRECTION OF MALE INFERTILITY VERSUS ASSISTED REPRODUCTIVE TECHNOLOGIES

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Infertility is detected in 15% of couples who desire children, however, the ethiology is pure male factor in 20%, and male and female factors in 30-40% of the couples. Therefore, the assessment of male infertility plays important role in approximately 50% of the couples (1,2). Male infertility may occur due to obstructive (ejaculatory duct, vas deferens and epididiymal obstruction) and non-obstructive (varicocele, secondary hypogonadism, gonadotoxins exposure) as correctable pathologies, and may also occur due to testicular atrophy after mumps orchitis as uncorrectable pathology (3-10). The aim of the evaluation of men for infertility is to point out to diagnose correctable pathologies, to detect genetic disease and also to diagnose life threatened disease. Assisted reproductive technologies (ART) should be used in only selected endications. However, it is sometimes not possible to treat men with idiopathic oligospermia or azoospermia, and these men are referred for intrauterin insemination (IUI), in vitro fertilization (IVF) or intracytoplasmic sperm injection (ICSI) as ART based on impaired semen quality. Therefore, the aims of patho-physiologic specific treatment of male infertility are to achieve spontaneous pregnancy, to obviate the need for ART, to downstage the level of ART needed to bypass male factor infertility, and also to increase pregnancy rates with ART in cases who achieved no spontaneous pregnancy. Initial evaluation of male infertility should include careful history, physical examination and semen analysis (2x) based on WHO criteria (11,12).

VARICOCELE

Varicocele is the most commonly seen and correctable cause of male factor infertility (4, 13-22). Varicocele is diagnosed with physical examination, and not necessary to forward radiologic imaging. Here is a case with varicocele. A couple (30 years old man and 29 years old female) has presented with infertility for 2 years. Physical examination revealed grade 3 varicocele on the left side and grade 1 varicocele on the right side with the 16 ml and 18 ml of testicular volume, respectively. Semen analysis showed ejaculate volume of 3 ml and sperm count of 18 million/ml with a 30% motility. The approach in infertile men with varicocele may be observation, treatment of varicocele and the use of assisted reproductive technologies directly. Treatment of varicocele includes surgery (open, laparoscopic) and radiologic embolization, although open surgery is gold standard. The aims of varicocele repair are to ligate all external and internal spermatic veins with the preservation of artery, lymphatic vessels and vas deferens. Varicocele is among a cost effective treatment of infertility. Postvaricocelectomy semen analysis shows any improvement in sperm density for 66% and sperm motility for 70% of patients. Varicocele repair upgrades to normal semen and may allow natural pregnancy. Postopeartive pregnancies occur with a mean duration of 7 months (3-11 months) after surgery. Current treatment modality is microsurgical inguinal or subinguinal varicocelectomy with high improvement in postoperative semen parameters (50% at least 50% increase in total motile sperm count) and pregnancy rates (36-43%) and highly low complication and recurrence rates (0-1%). Genetic screening should be performed in cases who have no improvement in semen parameters.

Varicocele repair has significant potential not only to obviate the need for ART, but also to downstage the level of ART needed to bypass male factor infertility. After varicocelectomy, IUI may be tried again for men who had not achieved pregnancy by natural intercourse. Following varicocelectomy, the results with IUI seem improved or 11-21% pregnancy rates per cycle. The initial sperm concentration is predictive of unassisted pregnancy outcome in this population.

ANEJACULATION

Ejaculatory failure or anejaculation may occur due to diabetes, multipl sclerosis, abdominal-pelvic surgery and spinal cord injury and physchogenic reasons (23). Penile vibration and electroejaculation via rectal prob are commonly used method in the treatment of anejaculation. Sperm obtained with these method can be used for IUI and IVF/ICSI, and therefore cost-effective and easy pregnancies can be achieved instead of more invasive testicular or epididymal sperm extraction.

HYPOGONADOTROPIC HYPOGONADISM

Hypogonadotropic hypogonadism includes idiopathic, execive exercise, trauma, stres, Kalmann syndrome, late puberty and hyperprolactinemia. Novel treatment of male hypogonadotropic hypogonadism includes human chorionic gonadotropin (hCG) 1500 IU 3 times/week for 2-3 months initially, and then plus human recombinant FSH (hrFSH) 100-150 IU 3 times/week for 12-18 months (24-26). Spontaneous pregnancies can be achieved with the treatment of hypogonadotropic hypogonadism, however, in cases who fail therapy, treatment may increase pregancy rates with ART.

Finally, a case with maturation arrest will be presented at the meeting. A 35 years old male presented with primary infertility. Physical examination showed testicular volumes of 20 ml. on the both sides with no pathology. His serum FSH level was 8 mIU/ml, and azoospermia was detected on semen analysis. He had previously testicular biopsy, showing maturation arrest at the spermatid level.

REFERENCES:

1. Mosher WD: Reproductive impairments in the United States, 1965-1982. Demography 1985; 22: 415-30.
2. De Kretser DM: Male infertility. Lancet 1997; 349: 787-90.
3. Stanwell-Smith RE, Hendry WF: The prognosis of male subfertility: a survey of 1025 men referred to a fertility clinic. Br J Urol 1984; 56: 422-8.
4. Çayan S, Erdemir F, Özbey İ, Turek PJ, Kadıoğlu A, Tellaloğlu S: Can varicocelectomy significantly change the way couples use assisted reproductive Technologies?. J Urol 2002; 167: 1749-1752.
5. Çayan S, Hernandez A, Turek PJ: The findings on antisperm antibody testing in an evidence based approach to male infertility. J Urol 2001; 165 (Suppl): 347.
6. Palermo GD, Schlegel PN, Hariprashad JJ, et al: Fertilization and pregnancy outcome with intracytoplasmic sperm injection for azoospermic men. Hum Reprod 1999; 14: 741-8.
7. Kadıoğlu A, Çayan S, Tefekli A, et al: Does response to treatment of ejaculatory duct obstruction in infertile men vary with pathology? Fertil Steril 2001; 76: 138-142.
8. Orhan I, Onur R, Çayan S, Koksal IT, Kadıoğlu A: Seminal vesicle sperm aspiration in the diagnosis of ejaculatory duct obstruction. BJU Int 1999; 84: 1050-3.
9. Çayan S, Lee D, Conaghan J, et al: A comparison of ICSI outcomes with fresh and cryopreserved epididymal spermatozoa from the same couples. Hum Reprod 2001; 16: 495-9.
10. Schlegel PN, Goldstein M: Vasectomy; in Goldstein M (ed): Surgery of male infertility. Philadelphia, Saunders, 1995; pp 35-45.
11. WHO laboratory manual for the examination of human sperm and sperm-cervical mucus interaction, 4th edition: World Health Organization, 1998.
12. Kruger TF, Acosta AA, Simmons KF, Swanson RJ, Matta JF, Oehninger S: Predictive value of abnormal sperm morphology in in vitro fertilization. Fertil Steril 1988; 49: 112-7.
13. Kadıoğlu A, Tefekli A, Çayan S, Kandıralı E, Erdemir F, Tellaloglu S: Microsurgical inguinal varicocele repair in azoospermic men. Urology 2001; 57: 328-33.
14. Çayan S, Kadıoğlu TC, Tefekli A, Kadıoglu A, Tellaloglu S: Comparison of results and complications of high ligation surgery and microsurgical high inguinal varicocelectomy in the treatment of varicocele. Urology 2000; 55: 750-4.
15. Tefekli A, Çayan S, Uluocak N, et al: Is internal spermatic venography necessary in determining recurrence varicocele after varicocele surgery. Eur Urol 2001; 40: 404-8.
16. Çayan S, Kadıoglu A, Orhan I, Kandıralı E, Tefekli A, Tellaloglu S: The effect of microsurgical varicocelectomy on serum follicle stimulating hormone, testosterone and free testosterone levels in infertile men with varicocele. BJU Int 1999; 84: 1046-9.
17. Çayan S, Lee D, Black LD, Reijo Pera RA, Turek PJ: Response to varicocelectomy in oligospermic men with and without defined genetic infertility. Urology 2001; 57: 530-5.
18. Kamal KM, Jarvi KJ, Zini A: Microsurgical varicocelectomy in the era of assisted reproductive technology: influence of initial semen quality on pregnancy rates. Fertil Steril 2001; 75: 1013-1016.
19. Daitch JA, Bedaiwy MA, Pasqualotto EB, Hendin BN, Hallak J, Falcone T, Thomas AJ Jr, Nelson DR, Agarwal A: Varicocelectomy improves intrauterine insemination success rates in men with varicocele. J Urol. 2001;165(5):1510-3.
20. Marmar JL, Corson SL, Batzer FR, Gocial B: Insemination data on men with varicoceles. Fertil Steril. 1992;57(5):1084-90.
21. Penson DF, Paltiel AD, Krumholz HM, Palter S: The cost-effectiveness of treatment for varicocele related infertility. J Urol. 2002;168(6):2490-4.
22. Schlegel PN: Is assisted reproduction the optimal treatment for varicocele-associated male infertility? A cost-effectiveness analysis. Urology. 1997;49(1):83-90.
23. Çayan S, Turek PJ: How useful are the various techniques for sperm retrieval and assisted reproductive technologies in helping couples with an ejaculation?. Fertil Steril 2001; 76(3)(Suppl 1): S244-5.
24. Bouloux P, Warne DW, Loumaye E, FSH Study group in men's infertility: Efficacy and safety of recombinant human follicle-stimulating hormone in men with isolated hypogonadotropic hypogonadism. Fertil Steril 2002; 77(2): 70-73.

25. Selman H, De Santo M, Sterzik K, Cipollone G, Aragona C, El-Danasouri I: Rescue of spermatogenesis arrest in azoospermic men after long-term gonadotropin treatment. Fertil Steril 2006; 86(2): 466-468.
26. Efesoy O, Çayan S, Akbay E. The efficacy of recombinant human follicle-stimulating hormone in the treatment of various types of male factor infertility at a single university hospital. J Androl 2009; 30 (6): 679-684.

CONTEMPORARY MANAGEMENT OF UNDESCENDED TESTIS

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Approximately **1–2%** of boys have an undescended testis, with 80–90% unilateral and **10–20% bilateral**, depending on the clinical series. Although cryptorchidism is one of the most common congenital anomalies of the genitourinary system, its pathogenesis is uncertain. Boys with an undescended testis have an increased risk of **infertility, testicular cancer, testicular torsion, and inguinal hernia**. The goal of therapy is to minimize these risks.

By 6 to 8 months of age, the undescended testis shows delayed germ cell development and maturation, specifically in the transformation of gonocytes into Ad spermatogonia, and delayed appearance of primary spermatocytes. Consequently, orchiopexy by 9 to 12 months is recommended.

The clearest **classification system** divides undescended testis into palpable and non-palpable groups. *A true undescended testis* has had its descent halted somewhere along the path of normal descent. *The ectopic testis* has left the path of normal descent and can be found in the inguinal region, the perineum, the femoral canal, the penopubic area, or even the contralateral hemiscrotum. A *retractile testis* spontaneously assumes a suprascrotal position and can be pulled down into the scrotum, remains in the upper or lower part of the scrotum after the traction is released. In a recent study 22.7% of the patients with retractile testis required operation during 3 year median follow up, because the testis became cryptorchid or decreased in size. *Gliding testis* is defined as a testis which can be manipulated through the scrotal entrance into a high, after release, the testis retracts immediately to the groin region. While most boys with cryptorchidism are diagnosed at birth, an increasing number are being diagnosed at a later age with *an ascending (aquired) testis*. For treatment, orchidopexy is usually recommended. *An iatrogenic undescended testis* is a previously descended testis that has become trapped in scar tissue cephalic to the scrotum after inguinal surgery.

HORMONAL TREATMENT

Treatment of cryptorchidism with human chorionic gonadotropin (hCG) was introduced in 1930. Intranasal treatment with Gonadotrophin releasing hormone (GnRH) was first used in 1975. Since then, these two kinds of hormonal treatment have been advocated with varying enthusiasm over the years. Great variation of the effects of hormonal treatment have been reported, with **success rates** from 0% to 55% and 9% to 78% with hCG and GnRH, respectively, depending on inclusion of different proportions of boys with retractile testes. Cryptorchidism has also been treated with human menopausal gonadotropin, synthetic analogues of GnRH and combined hormonal therapy. Pyorala et al. reviewed thirty-three studies using hormonal therapy for cryptorchidism from 1975 to 1990. In the meta-analysis of the nine randomised controlled trials available, hormonal therapy was effective in only a fifth of the cases GnRH 21%, hCG 19, and placebo 4%. If retractile testes were excluded, the success rate of GnRH was even lower: 12%. Subgroup analysis of results based on the initial position of the testes found a greater success rate the more caudal the position of the testes was before treatment. The authors also mentioned that the age of the boy may play a role in the success rates obtained with hormonal treatment. Ong et al. summarised randomised and nonrandomised trials published subsequent to Pyorala et al.'s metaanalysis from 1991 to 2003. The overall success rates reported by the six randomised controlled trials ranged from 8% to 43%. The studies generally agree with Pyorala et al. in that therapeutic success is greater when the testis is in a lower position and age is not an important determinant for success. Four trials reported that hormonal therapy is more effective in bilateral cases.

Studies assessing long-term outcome of hormonal treatment alone are very few. On the other hand, reports on the **optimal age** for hormonal treatment of undescended testes are not conclusive. De Muinck Keizer-Scrama et al. found the highest success rates with GnRH in the 5–12 year age group. This result was in contrast to other studies in which the highest success rate was achieved in boys aged two to five years. In a more recent study of bilateral cryptorchidism, Christiansen et al. found that both hCG and GnRH were more efficient the younger the boys were. However, in the meta-analysis of the results of pooled data for uni and bilateral cases, there was no significant difference in efficacy between patients older or less than 4 years.

In a preliminary study, Huff et al. reported that GnRH treatment **after orchidopexy** improved total germ cell counts in 75% of patients and Hadziselimovic and Herzog reported that the luteinizing hormone-releasing hormone analogue Buserelin, administered intranasally every other day for 6 months following successful orchiopexy, appears to have a long lasting, positive effect on germ cells. These results have so far not been confirmed by other groups.

It has generally been assumed, that the **adverse affects** of hormonal treatment are few and transient, and only included erections, growth of the penis, pain in the genital region and injections site and psychological changes. However, during recent years, accumulating evidence of deleterious effect on the germ cells has been described and evidence that fetal human chorionic gonadotropin causes irreversible changes in germ cell maturation has been widely acknowledged. Thus, Heiskanen et al. and Kaleva and Toppari reported that hCG treatment before orchiopexy in prepubertal boys induced apoptotic changes in the germ

cells and inflammatory changes in the testes, not seen in those that underwent surgery without prior hCG treatment. Furthermore, Dunkel at al. demonstrated that treatment with hCG for cryptorchidism is followed by an increase in *germ cell apoptosis*. The degree of apoptosis correlated negatively with the testis volume and positively with serum levels of FSH 20 years later, in adulthood. Similarly, Cortes et al. found that hCG or GnRH treatment before surgery in 1–3-year-old boys suppressed the number of germ cells, compared to those undergoing surgery alone. In contrast, Four trial studies that included testicular biopsies18-21 concluded that GnRH treatment increased the germ cell count per tubule. Recently, Hadziselimovic6 demonstrated that infertility in unilateral cryptorchidism can be successfully corrected when suitably treated with a luteinizing hormone-releasing hormone analog. In a recent study Jallouli et al. concluded that neoadjuvant GnRH treatment improves the fertility index in prepubertal cryptorchidism and consequently should improve fertility in adulthood. Preoperative GnRH therapy should be considered in every child with cryptorchidism, regardless of age, for maximal transformation of gonocytes to adult dark spermatogonia to promote the first postnatal maturational step of the germ cells.

SURGICAL TREATMENT

Palpable undescended testis:

The main goal of surgical treatment of cryptorchidism is to establish a scrotal position of the testis without iatrogenic atrophy. Multiple operative techniques have been described and are associated with various success rates. These are;

Classical inguinal orchiopexy

Classical inguinal orchiopexy was first described in 1957 by Lattimer. Inguinal orchiopexy is the most common surgical approach to undescended testes. Through an inguinal incision, the testis is mobilized from within the tunica vaginalis. Typically, there is a patent processus vaginalis
(hernia sac). The limiting factor in moving the testis into the scrotum is the length of the testicular artery and vein. Transecting the hernia sac and separating it from the cord structures often allows significant testicular mobilization.

The overall success rate was 88.6%. In addition, the success rate in studies published after 1985 was 91.2%, although it was not statistically significantly higher than in older studies. Currently, most pediatric urologists expect a success rate >95% for inguinal orchiopexy. It is likely that with subspecialization in pediatric urology, success rates of orchiopexy will improve.

Prescrotal orchiopexy

The prescrotal (Bianchi) orchiopexy involves making an incision along the edge of the scrotum, mobilizing the testis and spermatic cord, repairing the inguinal hernia, if present, and placing the testis in the scrotum. The advantage of this approach is that the testis and spermatic cord often can be mobilized sufficiently for the testis to reach the scrotum through a single incision, with less post-operative pain and shorter operative time. With retraction of the superior aspect of the wound, often the hernia can be repaired also. If mobilization of the spermatic cord is inadequate through this incision, then an inguinal incision can be made. This technique is especially ideal for the ascending or ectopic testis located in the superficial inguinal pouch. It also seems ideal for the obese patient, in whom inguinal orchiopexy must be done through a larger incision.

Following the initial report of this technique, the Bianchi orchiopexy has been performed in an increasing number of centers. Success rates have been high. Only 4-6% needed an inguinal incision in the reports. Dayanc et al reported that the success rate was 96.9% (124 testes of 128), and only 4 patients (four testes) required conversion to a traditional inguinal incision. Operative times generally were 18 to 25 min in these studies.

Nonpalpable undescended testis:

Most of the more contemporary series begin with diagnostic laparoscopy to localize a nonpalpable testis, and then an orchiopexy is attempted with a variety of techniques, both open and laparoscopic. Most probably, some of the patients in these series had peeping testes, which are much easier to mobilize into the scrotum. Some testes are relatively easy to mobilize into the scrotum by dividing the testicular vessels, whereas others have a very short vascular pedicle. Despite this heterogeneity of anatomic settings, most series include patients managed by a single technique.

Transabdominal Orchiopexy (The standard two-stage orchiopexy):

The standard two-stage orchiopexy involves mobilizing the abdominal testis as much as possible, waiting 6 months, and then performing the orchiopexy a second time. Some surgeons wrap the testis in a silastic sheath following the first stage, to make it easier to identify the testis during the second stage. It is possible that mobilizing the testis and vessels stimulates growth factors in the vascular pedicle that allow the testis to reach the scrotum during the second stage. The advantage is that the testicular artery is preserved.

It was reported an 81.3% success rate for transabdominal approach, with a 91% success rate after 1985 (19). More recent series have demonstrated an even higher success rate approaching 100%. Using an inguinal incision and extensive retroperitoneal vascular mobilization, described in detail by Hutcheson et al., Kirsch et al. were able to achieve satisfactory mobilization without

vascular division in most cases. In contrast, transabdominal 2-stage orchiopexy with the testes brought as far distally as possible in the first stage, followed by scrotal positioning in the second stage (without vascular division), were shown to be 71.1% successful in early studies with 64.6% success rates after 1985. Presumably, these testes were quite high, but theoretically could have been mobilized satisfactorily with a Fowler–Stephens approach also.

Fowler–Stephens Orchiopexy

The Fowler–Stephens orchiopexy is utilized for boys in whom the testicular artery and vein are too short to allow the testis to reach the scrotum. Originally described for the abdominal testis with a long-looping vas deferens, the technique involves clamping and transecting the testicular vessels. Ideally, there is sufficient collateral arterial flow through the deferential (vasal) artery to allow the testis to survive. It is generally performed as a single stage procedure. Maintaining a strip of peritoneum on the vessels increases the likelihood of preserving the integrity of the vessels. Unfortunately, the deferential artery is often so small that it goes into vasospasm and the testis atrophies.

The reported success rates for Fowler–Stephens orchiopexy has improved significantly over the years. Docimo reported a 67% success rate for the procedure. Subsequent reports have shown higher success rates. King showed that leaving a strip of peritoneum attached to the lower spermatic cord in patients requiring spermatic vessels division resulted in scrotal position in 21 out of 22 patients, and none of the boys had testicular atrophy. Koff and Sethi also had a high success rate with the modified Fowler–Stephens approach.

The staged Fowler–Stephens procedure, theoretically, should have a higher success rate. Indeed, in Docimo's review the success rate was 77%. In contrast, more recent studies have success rates of 95% or more. Most of these patients underwent laparoscopic clipping of the vessels with open second stage orchiopexy 3 to 6 months later.

Laparoscopic Orchiopexy

Laparoscopy is frequently used for localization and treatment of nonpalpable testes. Laparoscopic orchiopexy has become a procedure of choice for many practitioners. In a series of patients from 10 different centers, Baker et al. reported a 97% success rate with a single stage laparoscopic orchiopexy without division of the testicular vessels. Laparoscopic Fowler–Stephens orchiopexy, both single and two stage, has had high success rates.

Microvascular Orchiopexy

Microvascular orchiopexy had a high success rate of 80.3% in Docimo's review. More recent series from a single institution, using both open and laparoscopic-assisted microvascular anastomosis have demonstrated impressive success, but not higher than contemporary series of Standard abdominal or staged Fowler–Stephens orchiopexy, whether open or laparoscopic.

POSTOPERATIVE FOLLOW UP

Traditionally, the success rate in relation to operative treatment of cryptorchidism is defined as the percentage of testes that remains in the scrotum and does not atrophy. In adulthood estimation of the fertility potential is an additional parameter, especially when comparing the results of earlier and later surgery. Irkilata et al showed an increase in inhibin B level after successful orchiopexy.

REFERENCES

1. Taran I, Elder JS. Results of orchiopexy for the undescended testis. World J Urol. 2006 Aug;24(3):231-9.
2. Thorup J, Haugen S, Kollin C, Lindahl S, Läckgren G, Nordenskjold A, Taskinen S. Surgical treatment of undescended testes. Acta Paediatr. 2007 May;96(5):631-7.
3. Adult and Pediatric Urology, edited by Jay Y. Gillenwater, John T. Grayhack, Stuart S. Howards, and Michael E. Mitchell. Chapter 53;Pediatric Andrology, written by Kogan SJ, Hadziselimovic F, Howards SS, Huff D, Synder third HM. 4th ed, ISBN 0-7817-3220-4, Philadelphia, Pa, Lippincott Williams & Wilkins, 2001.
4. Jallouli M, Rebai T, Abid N, Bendhaou M, Kassis M, Mhiri R. Neoadjuvant gonadotropin-releasing hormone therapy before surgery and effect on fertility index in unilateral undescended testes: a prospective randomized trial. Urology. 2009 Jun;73(6):1251-4.
5. Dayanc M, Kibar Y, Irkilata HC, Demir E, Tahmaz L, Peker AF. Long-term outcome of scrotal incision orchiopexy for undescended testis. Urology. 2007 Oct;70(4):786-8.
6. Dayanç M, Kibar Y, Tahmaz L, Yildirim I, Peker AF. Scrotal incision orchiopexy for undescended testis. Urology. 2004 Dec;64(6):1216-8.
7. Irkilata HC, Dayanc M, Kibar Y, Musabak U, Yesilkaya E, Oral E, Ors O. Effect of scrotal incision orchiopexy on serum inhibin B levels and comparison with classic inguinal orchiopexy. Urology. 2008 Sep;72(3):525-9.
8. Irkilata HC, Yildirim I, Onguru O, Aydur E, Musabak U, Dayanc M. The influence of orchiopexy on serum inhibin B level: relationship with histology. J Urol. 2004 Dec;172(6 Pt 1):2402-5.

CONTEMPORARY MANAGEMENT OF ADOLESCENT VARICOCELE

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Varicocele is defined as an abnormal dilatation of testicular veins in the pampiniformis plexus caused by venous reflux.The absence of varicocele before the age 11 suggest that puberty must play a part in their initiation. **Prevalence of varicocele** is 6-8% in 11-14 years and 11-19% in 15-19 years old(1).Studies show that between 80% and 90% of varicoceles occur on the left side. Right-sided varicoceles are uncommon, are usually noted only when bilateral varicoceles are present(2).
Many mechanisms have been proposed in **the physiopathology of varicocele**, such as hypoxia, hyperthermia, renal-adrenal reflux, hormonal dysfunction,autoimmunity, oxidative stress, and apoptosis. Countercurrent heat-exchange disruption seems to be the most plausible theory, and it readily explains other aspects of the varicocele effect. Ipsilateral testis growth arrest(time-dependent) is noted in 25% to 75% of boys with varicocele. Published studies are at variance regarding the risk of growth arrest related to varicocele grade, some indicating that it occurs with equal frequency in each grade and others demonstrating an increased frequency with increasing varicocele grade. Larger varicoceles may also be associated with volume loss of the right testicle as well as the left(2). Growth arrest is often associated with a softer testis as well. Varicocele was associated with reduced motility and an increased number of abnormal forms and more DNA fragmentation(1). **Histological changes** may affect all cellular compartments: germ cell maturational arrest and sloughing, ultrastructural changes in the Sertoli cells, and alterations in the Leydig cells ranging from atrophy to hyperplasia have been described(2). It is imperative that **the examination** to detect a varicocele be done with the patient in an upright standing position, A Valsalva maneuver should be requested (cough or abdominal straining or both); this will produce a "tapping" sensation, representing transmission of increased abdominal pressure in the scrotally palpated dilated veins.

Varicoceles have been graded according to physical characteristics: grade III (large, visible through the scrotal skin), grade II (moderately sized, easily palpable without a Valsalva maneuver), and grade I (small, palpable only with a Valsalva maneuver). Bilateral varicoceles are palpable in less than 2% of males.Subclinical varicoceles (grade 0) are not recognized in general in adolescence, because there is no reason to consider their presence unless an otherwise unexplained small testis is present(3). **Diagnostic measures**, such as scrotal ultrasonography, thermography, Doppler examination, radionuclide scanning and spermatic venography, should not be used for the detection of subclinical varicoceles in patients without a palpable.(4). When a varicocele is detected, the testis size (volume) and consistency should be noted. Orchidometry using the Prader or Takihara models should be performed, or ultrasonography may be used to more precisely define differences in size.Testis volume, a much less precise and more end-stage manifestation of orchiopathy, is used to guide therapy. Testis size (volume) should be approximately equal bilaterally, with the differential normally not greater than 2 mL or 20% of volume(3). Varicocele size, age, and serum testosterone levels were not significantly different between those with normal and those with abnormal GnRH responses. Most importantly, a significant number of boys with normal-size or growth-arrested testes had abnormal GnRH tests(2). These data suggest that hormonal testing used in this manner is clinically unhelpful.
Direct relation exists between patient age, pubertal stage, and varicocele size, and an inverse relation occurs between varicocele size and testis size. Selected studies in adolescents have also indicated that observant therapy is associated with deterioration of semen parameters in some adolescent boys with varicocele. By contrast, arguments in favor of observant (nonoperative) treatment exist, indicating that not all adolescents with varicocele suffer growth arrest of the ipsilateral testis and that not all ultimately become subfertile(2). Currently, it appears that multiple different techniques are applied clinically, with the choice of technique guided by the experience of the surgeon and by taking into account the age, body habitus, and peculiarities of the patient and varicocele in question.

Retroperitoneal ligation of the internal spermatic vein, described by Palomo in 1949 , remains a commonly used technique for varicocele ablation in adolescents, in part because of a relatively short operative time and quick recovery. Retroperitoneal ligation may be performed by mass ligation of the spermatic vessels or by an artery-sparing technique (7.2% hydrocele,0-2% recurrence with the mass ligation ,7.2% hydrocele, 11% recurrence when testicular artery sparing was attempted.)(3).

Laparoscopic varicocele ligation is a technique that is easily mastered by surgeons familiar with laparoscopic technique and is in many ways and complication similar to open retroperitoneal ligation of the internal spermatic vein. Lymphatic-sparing varicocelectomy is preferred to prevent hydrocele formation and an outpatient procedure with rapid ecovery(3). When using **the inguinal or subinguinal** approach for varicocele ablation, several adjunctive techniques may be considered that have been reported to improve results in several series. Classic open inguinal, subinguinal technique has 3-9% hydrocele and 15% recurrence rate. Doppler identification of the testicular artery is an important adjunct. In addition to delivering the testis for ligation of the cremasteric and gubernacular vessels, performed **microsurgical ligation of the spermatic veins**, a technique that has become standard in the practice of many adult fertility specialists and that seems to minimize the potential for recurrence.(<1% hydrocele,1-3%recurrence rate)(3). Intraoperative spermatic venography has been reported to improve the success of varicocele ablation in adolescents (2). Angiographic occlusion of the internal spermatic veins is less invasive, it appears to have a higher failure rate(0% hydrocele,10-25% recurrence). Experience indicates that persisting unrecognized veins

adhering to the wall of the internal spermatic artery are the most common cause for varicocele recurrence. **Reoperation** is indicated, because the original goals of surgery are not fulfilled, and the original risks associated with nonoperative treatment remain. Microsurgical repair is effective for recurrences resulting from initial varicocelectomy performed by either route. Reversal of testicular growth arrest occurs in 50% to 75% of adolescents undergoing successful varicocele repair and also improved semen analysis(2). **The only absolute indication universally agreed on is a significantly smaller ipsilateral testis(<2 ml or <20%)**. The implications of other indications : additional testicular condition affecting fertility,pathological sperm quality (in older adolescents),bilateral palpable varicocele,large size(grade),softer ipsilateral testis,pain, varicocele associated with a supranormal response to LHRH stimulation test,Patient or parental anxiety,abnormal scrotal appearance, symptomatic varicocele should be discussed fully with the parents and, when appropriate, with the patient, so that a fully informed decision regarding the benefits and risks of surgery may be arrived at(2,5).

REFERENCES:

1. Woodhouse CRJ.Adolescent Varicocele.In Carlson,Kirby,Goldstein,Wyllie. Textbook of Erectile Dysfunction. Second edition.Informa Healtycare 2009,pp378-379
2. Paul.Zelkovic, Stanley J.Kogan.Pediatric Varicocele.In:Gearhart JP,Rink RC,Mouriquand PDE.Pediatric urology. Second edition.WB Saunders,2010,pp 585-594
3. Francis X. Schneck, Mark F. Bellinger.Varicocele. Chapter 127 – Abnormalities of the Testes and Scrotum and their Surgical Management In Campbell-Walsh Urology 9th.ed. 2007 Saunder elsevier, pp3794-3797
4. Male Infertility Best Practice Policy Committee of the American Urological Association; Practice Committee of the American Society for reproductive Medicine: Report on varicocele and infertility. Fertil Steril, suppl., 2004; 82:S142.
5. S. Tekgül, H. Riedmiller, E. Gerharz, P. Hoebeke, R. Kocvara, R. Nijman, Chr. Radmayr, R. Stein. Guidelines on Paediatric Urology In: European Association of Urology Guidelines. Arnhem, TheNetherlands: European Association of Urology 2008; pp.23-25.

PRINCIPLES AND RULES OF URETHRAL SURGERY

Peter A. Scheplev, MD
President of the Professional Association of Andrologists of Russia

The surgeon who is dealing with urethral surgery should master at least 10-12 variants of urethroplasty. In 1920, French surgeon Marion suggested an operation – "resection of the stricture and "end-to end" anastomosis". It is now called "the gold standard of reconstructive urethal surgery". However, as early as 1926, American surgeons Young and Davis wrote: "Total resection of the urethra with end-to end anastomasis is a failure and it has no place in perineal surgery".

There are 4 different groups of methods of urethral lumen restoration:

- Regenerative methods (reepithelisation after the urethrotomy, stenting or bouging)
- Anastomotic plasty (urethral resection and direct anastomosis)
- Substitution plasty (reconstruction with using genital and extragenital flaps and grafts)
- Perineostomy (temporary or life-long)

Dealing with tissue.

The sensitiveness of urethral tissue is similar to that of the eye-lid. We recommend to adhere to the following rules:

- To maintain the constant moisture of the tissue (especially, transplantat) by means of constant irrigation with normal saline
- To control the time of ishemy
- To minimize the time elapsed from harvesting the flap/graft to its replantation
- To make perforations of the graft after its fixation in order to avoid haematoma formation
- To use specials set of sophisticated instruments
- To make the haemostasis meticulously

"When dealing with the urethral tissue, the surgeon should be so delicate as the lioness who is holding its child". (2)

Haemostasis.

Inadequate haemostasis will contribute to haematoma formation and infection development. Excessive coagulation leads to tissue necrosis with subsequent failure of the urethroplasty.

The rule No.1:

Bipolar diathermy should be used for the coagulation, because of less area of the necrosis.

The rule No.2:

When operating the distal urethra, an elastic tourniquet should be applied at the base of the penis intermittently for 30-40 min.

The rule No.3:

The only method to control bleeding from spongious or cavernous tissue is suturing.

The rule No.4:

To reduce bleeding, subcutaneous infiltration of penile shaft or glance with 1% lidocain and epinephrine (diluted in proportion 1:100000) may be used.

The rule No.5:

After transecting corpus spongiosus, the distal and proximal ends of the urethra should be clipped with "bulldog" forceps.

Suturing material.

Monofilament threads: monosyn, monocryl, PDS. Their advantages are smooth surface, significant elasticity and small reactogenuity. The urethra and adjacent tissue will regain their strength within 7-10 days, therefore, it is necessary to use only degrading suturing material.

Knots.

The type of thread that necessitate less knots should always be chosen. It is necessary to tie minimally sufficient number of knots. The length of ends of the monofilament thread should be 3 mm, polyfilament threads – 5mm.

The number of knots for various types of threads:

- Polyfilament – 3 knots
- Polyfilament with coating – 4 knots
- Monofilament – 4 knots
- Monofilament (PDS) – 6 knots

How to open the urethra at the level of the stricture?

If its lumen is not completely obliterated, the optimum is the longitudinal cut above the catheter. If the urethra is completely obliterated, it is reasonable to insert a catheter in the posterior urethra through the cystostoma (if present). If the cystostoma is absent, corpus spongiosus should be cut step by step in transverse direction until the lumen is visualized.

The technicque of suturing and anastomosing.

1. The sutures should not be placed above each other.
2. The strength of the thread should not be much than that of the tissue.
3. The diameter of the thread should be as less as possible.

The ideal anastomosis is watertight.

The first raw consists of extraluminal knots fixing the mucous layer. The second raw consists of the knots fixing spongious tissue. The most difficult is performing an anastomosis at the level of membranous part.

The types of proximal urethra suturing.

1. Running extraluminal sutures.
2. Interrupted intraluminal sutures.
3. Single sutures.
4. Special mattress sutures for sututing the glance.

Flap or graft.

The graft is "dead" tissue that needs to be "revived", and the flap is "live" tissue that needs not to be "killed".(2)

There is no "ideal material" for urethroplasty. Both flaps and grafts are associated with high percentage of relapses (up to 12% within the first year and 30% after 5 year).

There is following algorithm in choosing the proper method:

- Posterior urethra – anastomotic plasty
- Bulbar urethra - anastomotic plasty if the defect is less than 2,5 sm; substitution plasty if defect is more than 2,5 sm
- Anterior urethra - substitution plasty.

Transplants have some advantages. Their harvesting is more quick and easy. Patch application is more preferable than tubularization.

Scrotal skin is not recommended as substitution material because of the risk of contact dermatitis development and stone formation.

If using the flap is inevitable, genital flaps are preferable.

Indications for using flaps.

- The absence of the urethral ground
- Infection or inflammation at the site of reconstruction
- Significant scarring with subsequent impairment of blood supply
- Alterations after radiotherapy
- The necessity to perform one-step tubularizaton procedure. (3)

Contradictions for using flaps.

The absolute contradiction for using penile or prepucial skin is balanitis xerotica because the disease involves not only the anterior urethra but also penile skin.

How to choose the plastic material?

The graft is recommended for using in all cases except those when the flap is the only available material.

The shortages of the grafts are following:

- less reliability due to poor blood supply
- high demands to the recipient area
- they may not be tubularized in one-step fashion

The recommended transplants (only full-thick):

- buccal (preferable)
- penile or preputial skin (if the buccal one is not available)
- post-auricular Wolf graft (an alternative to the penile skin graft)
- bladder mucosa (extremely rare)

Contraindications for using buccal skin.

- Oral infections (candida, Herpes, and so on)
- Previous traumas or operations in the oral area restricting opening the mouth
- Not recommended in musicians who play aerophone

REFERENCES:

1. Scrreiter, Jordan. Reconstructive Urethral Surgery, Springer, 2006
2. Hadidi, Azmy. Hepospadias Surgery, Springer, 2006
3. Scheplev P.A. Reconstructive urethral surgery, Moscow, 2006.

MANAGEMENT OF DIFFICULT CASES IN ANDROLOGY

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PANELISTS

M. Boiko *(Ukraine)*
I. Ahmedov *(Azerbaijan)*
B. Rispaev *(Kyrgyztan)*
E. Uçaner *(Northern Cyprus)*
S. Shavakhabov *(Uzbekistan)*
M. Usta *(Turkey)*

Case-1

- 36 years old
- Priapism lasting for 24 hours
- No trauma
- Physical Examination
  - Full rigid erection
- Normal CBC
- No medication

Blood Gas Analysis

- P_{O2} = 22
- P_{co2} = 71
- pH= 7.2

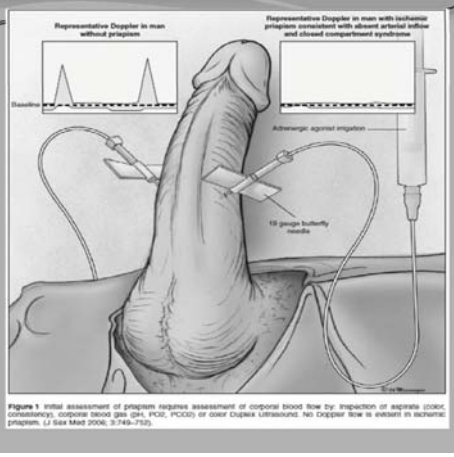
Blood Gas Analysis

	P_{O2}	P_{co2}	pH
Ischemic priapism	**<30**	**>60**	**<7.25**
Normal arterial value	**>90**	**<40**	**7.40**
Normal venous value	**40**	**50**	**7.35**

If P_{O2} >70 mmHg, high flow priapism
If P_{O2} <40 mmHg, ischemic priapism

What is the first approach?

- Aspiration and alfa adrenergic drug
- Distal shunt
- Immediate implantation of penile prosthesis



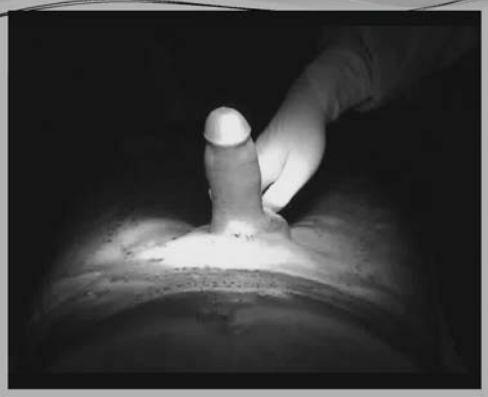
- Aspiration and alfa adrenergic drug (phenylephrine)

  Priapism still persists

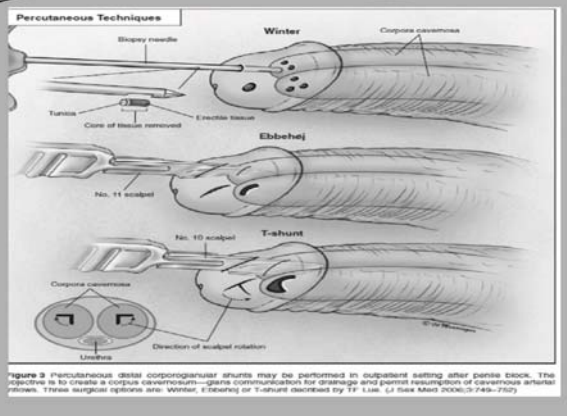
Second step?

- Distal shunt Percutaneous:
  - Winter
  - Ebbehoj
  - T-shunt

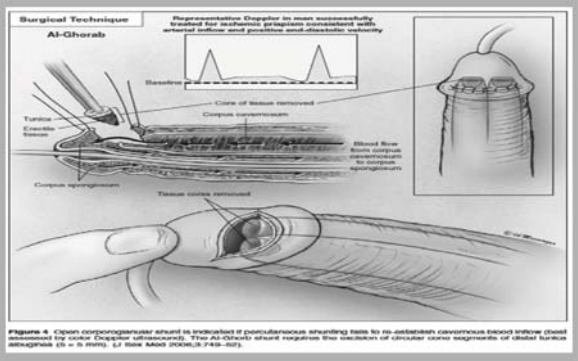
  Open:
  - Al-Ghorab
- Proximal shunt
- Immediate implantation of penile prosthesis



Percutaneous techniques



Open technique



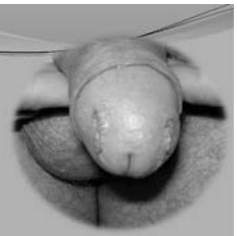
T shunt at prolonged priapism

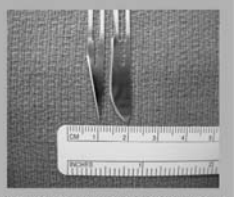
- N:13, >24 hours priapism
- Unsuccesful irrigation and/or intracorporeal administration of sympathomimetics in 12/13 patient
- Unsuccesful cavernous-glandular shunts surgery in 6/13 patient

Brant WO, Lue TF
J Urol. 2009 Apr;181(4):1699-705

T shunt- Surcigal tecnique

- No:10 blade is placed vertically through the glans until it is fully within the cavernosum, staying at least 4mm away from the opening of the meatus and thereby preventing urethral injury.
- The blade is rotated 90 degrees away from the urethra and then removed.
- No: 10 blade from edge to rotational axis is 4mm, this should create a nominal shunt surface area of 50 mm2 after scalpel rotation and removal





Difference in size between number 10 and number 11

Brant WO, Lue TF,
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In ischemic priapism of >3 days duration a T-shunt alone might be insufficient to restore penile circulation and consideration must be given to placing a bilateral T-shunt with tunnelling of each corpus cavernosum, using a rigid straight *20-24f urethral sound or dilator*.

Maurice M.Garcia, Alan W. Shindel and Tom F. Lue
The Jornual Of Urology April 2009,1699-1705

T shunt at prolonged priapism

Pt Age	Days Priapism	Procedure(s) Before Presentation	Procedure	Mos to Followup	Postop SHIM Score	Postop SHIM Question 2 Score*	Postop SHIM Question 3 Score†
44	2	Aspiration/adrenergic	T-shunt (unilat)	14	25	5	5
26	0.75	Aspiration	Bilat T-shunt	12	Not available	4	5
32	1.5	Aspiration/adrenergic	Bilat T-shunt	9	25	5	5
52	1.5	Aspiration	Bilat T-shunt	14	25	5	5
32	3.5	Aspiration/adrenergic, Winter shunt	Bilat T-shunt	10	11	2	1
50	3.5	Aspiration, Winter shunt	Bilat T-shunt	9	22	5	4
54	2	Aspiration/adrenergic	Bilat T-shunt + intracorporeal tunneling	26	171	3	3
36	2	Aspiration/adrenergic, Ebbehoj shunt, Winter shunt	Bilat T-shunt + intracorporeal tunneling	5	151	2	2
39	2.75	Aspiration/adrenergic	Bilat T-shunt + intracorporeal tunneling	14	23	5	4
55	4	Aspiration	Bilat T-shunt + intracorporeal tunneling	16	24	5	5
26	4	Aspiration	Bilat T-shunt + intracorporeal tunneling	15	103	2	2
44	4.5	Al-Ghorab shunt, Quackels shunt	Bilat T-shunt + intracorporeal tunneling	9	19	4	4
50	14	Aspiration, Quackels shunt	Bilat T-shunt + intracorporeal tunneling	25	11	1	1

6/13 patient had normal erectil function (post-op SHIM score)
5/13 patient →→→ post-op question-3 score is 5

Brant WO, Lue TF, J Urol. 2009 Apr;181(4):1699-705

Prolonged priapism-ED

- 39 cases of venooclusive priapism
- 8% of men had priapism for <12 hours
- 59% of men had priapism for 12-24 hours
- 22% of men had priapism for 24-36 hours
- 11% of men had priapism for >36 hours

Bennett and Mulhall J Sex Med. 2008 May;5(5) 1244-50. Epub 2008 Feb 25

- A standard protocol of aspiration and phenylephrine was performed
- Shunting for failure of medical management was performed in 28%.

Bennett and Mulhall
J Sex Med 2008;5:1244–1250

- **Spontaneous erections (+)**

➢ **100%** of men with priapism reversed <12 hours
➢ **78%** of men with priapism reversed by 12-24 hours
➢ **44%** of men with priapism reversed by 24-36 hours
➢ **0%** of men with priapism reversed by >36 hours

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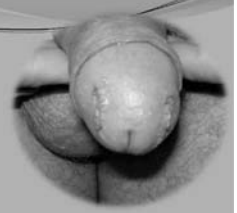

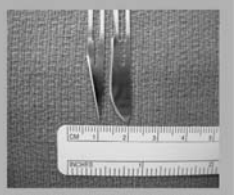

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Bennett and Mulhall
J Sex Med 2008;5:1244–1250

Educational aspect of the case -1

- After 4-6 hours of priapism, ischemia and asidosis occur in corporal blood sample
- Phenylephrine effect will reduce after 48 hours of priapism(asidosis and ischemia decrease the effect of sympathomimetics)

Educational aspect of the case -1

- Percutaneous shunts may be prefered because of the less invasiveness
- Among them (Winter, Ebbohoj, T-shunt), T-shunt can be prefered because of the larger surface shunt created between corpus cavernosum and corpus spongiosum
- T shunt can be used under local anesthesia and ultrasound guidance.

Guideline

- The ISSM Standards have stated that shunting is to be considered for priapism events lasting 72 hours; consideration should be given to foregoing shunting in priapism events lasting longer, in particular, where cavernous thrombosis is evident and no blood can be aspirated from the corporal bodies.
- İmmediate implantation of penile prosthesis can be performed for ischemic priapism

Gregory A. Broderick, Ates Kadioglu, Trinity J. Bivalacqua
Hussein Ghanem, Ajay Nehra, Rany Shamloul
J Sex Med 2010;7:476–500

Case-2

- 33 y old male
- Primary infertile
- Wife: 32 y old, normal fertile capacity
- No medical history
- Normal secondary sex characteristics

- Semen Analysis:
  - SA1: 0,7 cc/azoospermia/pellet(-)
  - SA2: 0,6 cc/azoospermia/pellet(-)
- FSH:5,8mIU/ml (1,5-12,4mIU/ml)
- Testosterone: 550ng/dl (300-900ng/dl)

Preliminary Diagnosis?

- Retrograd ejaculation? ⇨ Post-ejeculatory urine sperm (-)
- Distal ejaculatory duct obstruction?
- Proximal ejaculatory duct obstruction?
- CBAVD?

- FE
  - Testis volume
    R: 15cc, L: 12cc
- Bilateral vasa deferentia: nonpalpable

Which additional tests should be done?

- CFTR gene mutation → Female→→ Mutation (-)
  → Male→→ F508del mutation (+)
- Transrectal ultrasound → Normal
- Abdominal ultrasound → Normal

CFTR gene mutation-CBAVD

- CBAVD is associated with CFTR mutations and was found in approximately 2% of men with OA
  Donat R, McNeill AS, Fitzpatrick DR, Hargreave TB. Br J Urol 1997;79(1):74-7.
- Approximately two-thirds of men with CBAVD have mutations of the CFTR gene.
  AUA Guideline 2001
- 1500 mutations are listed on the CFTR database
  EAU Guideline 2009
- Men with CBAVD often have mild clinical stigmata of CF (e.g. history of chest infections).
  EAU Guideline 2009

Recommendations

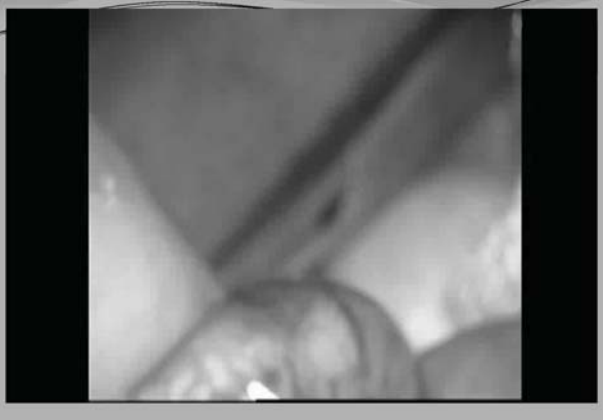
Genetic testing for CFTR mutations in the female partner should be offered before proceeding with treatments that utilize the sperm of a man with CBAVD.

- *If the female partner tests positive for a CFTR mutation, the male should be tested as well.*
- *If the female partner has a negative test for CFTR mutations, testing of the male partner is optional.*

AUA Guideline 2001

Treatment

- MESA?
- TESA?
- TESE?



- MESA is successful for sperm retrieval in >90% of the cases.

Belker et all,1994, J.Urol151,1255-59
Chen et all,1995, Hum. Reprod., 10,1104-08
Collins et all,1996,Br.J.Urol,78,437-39
Oates et all,1996,Hum.Reprod.,11,133-38
Holden et all,1997,Fertil. Steril.,67,81-87
Silber et all,1997,Hum. Reprod.,12,2693-700

- Initially, try to obtain sperm by way of MESA in the treatment of CBAVD
- Otherwise, TESA or TESE can be used to harvest sperm

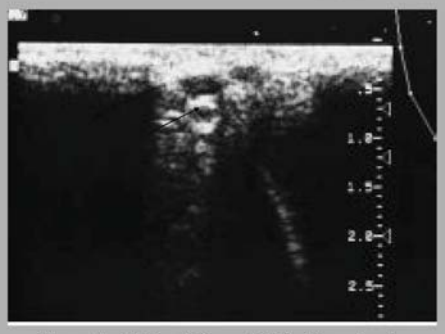
Case -3

- 38 years old, male
- 5 years married
- He complains about a mass like spaghetti for the last month
- No medical history
- CBC: N
- SMA-4 : N

- FE:
  - Scrotum and testes are normal
  - Palpable vascular structure at proximal and dorsal area of the penis

Which test should we done?

- Penil Doppler USG
- Protrombin time: 3sec (10-15)
- aPTT: 25,6sec(19,5-29,1)
- INR: 1,08 (0,85-1,20)
- Fibrinogen: 216,62(180-350)
- Protein C: 89,9% (70-140)
- Protein S: 86% (59-130)
- ATIII: 80,2(75-125)
- Factor V Leiden mutation (-)
- Homosistein:15,7(5-12)ug/ml



Superficial Penil Dorsal Vein Trombosis

Diagnosis ?

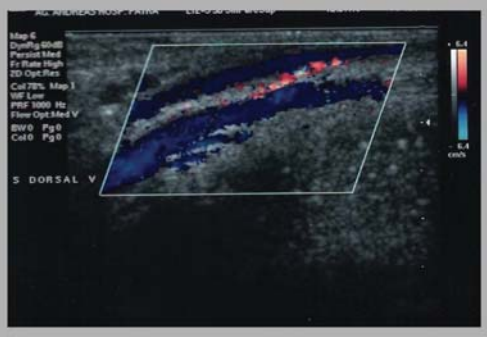
Superficial penil dorsal vein trombosis

(PENILE MONDOR DISEASE)

Treatment

- Antibiotics
- Acetylsalicylic acid
- Refrain from sexual activity for 4-6 weeks

- Symptoms relieve after 2 weeks of the medical treatment



Penil Doppler USG: N after 1 month

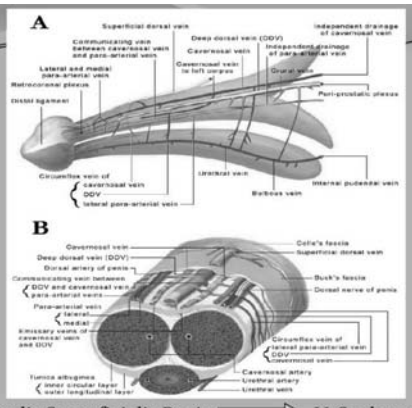
Educational aspect of the case -3

MONDOR Henri (1885 - 1962

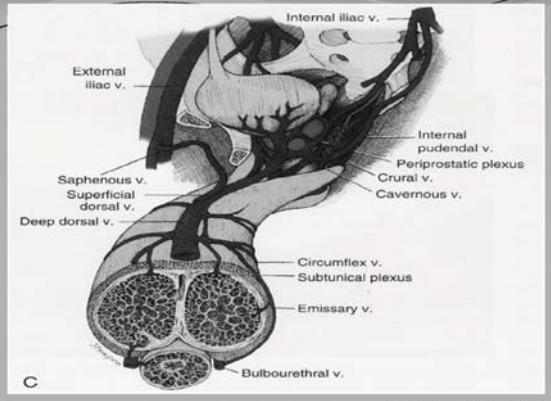
- At the anterior wall of the chest, firstly defined by Mondor (1939)

- In 1955, trombosis was shown at the superficial dorsal vein of the penis by Braun-Falco

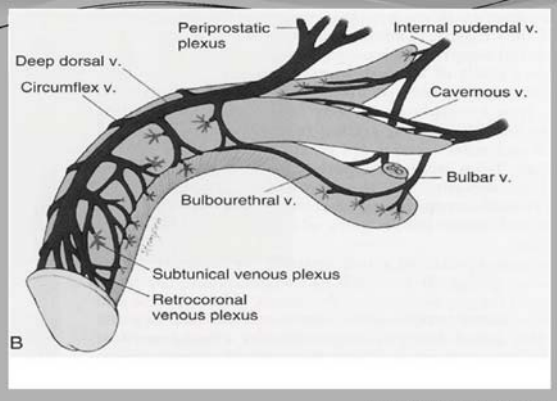
Mondor Henri, Mem Acad Chir 1939, 65: 1271.



V. Dorsalis Superficialis Penis ⟹ V. Saphena Magna



Campbell-Walsh UROLOGY
9th Edition



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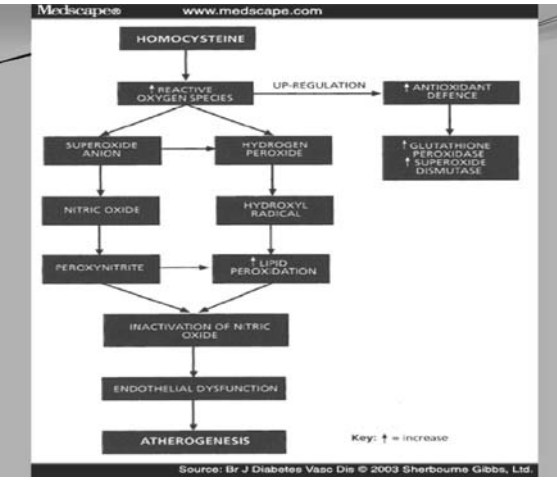
- Etiology is still unknown but some clinical factors related with Virchow triad may play a role in etiology
  - Venous stasis (immobilisation, postoperative period, postpartum, pregnancy)
  - Endothelial damage (trauma, burn, lower extremity surgery, sepsis, cancer)
  - Hypercoagulation (oral contraceptive, infection, ABO)



- Homocysteine is a sulphur-containing amino acid
- Approximately 80% of plasma homocysteine is protein bound.

- Homocysteine is readily oxidized when added to plasma, principally as a consequence of auto-oxidation leading to the formation of **homocystine, homocysteine-mixed disulfides**, and **homocysteine thiolactone**.
- During oxidation of the sulfhydryl group, superoxide anion radical and hydrogen peroxide are generated, and these oxygen-derived molecules are believed to account for the endothelial cytotoxicity of homocyst(e)ine.

Homocysteine and atherothrombosis -mechanisms for injury
J. Thambyrajah and J. N. Townend
Division of Medical Sciences (Cardiology), University of Birmingham, U.K.
European Heart Journal (2000) 21, 967–974

- Genetic anomalies that cause thrombosis
  - Protein C, protein S and antithrombinIII deficiency
  - F V Leiden mutation
  - Hyperhomosisteinemi

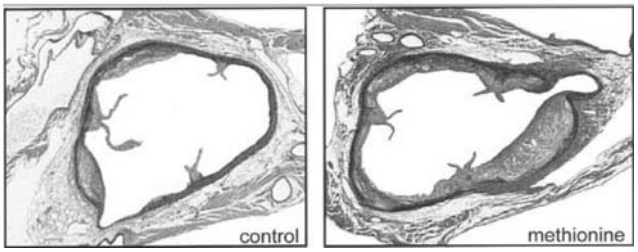
Cell Death and Differentiation (2004) 11, S56–S64

www.nature.com/cdd

Review

Role of hyperhomocysteinemia in endothelial dysfunction and atherothrombotic disease

RC Austin*,1, SR Lentz2 and GH Werstuck3



Result

- Doppler US for differential diagnosis
- Differentiate from Peyronie disease
- Improvement with medical treatment in 6-8 weeks
- Low molecular weight heparin can be used for recurrent Mondor attack
- Surgical trombectomy and superficial vein resection is done in cases who can't be healed with medical treatment

Case-4

- 27 y old male, 25y female
- İnfertility for 4 years
- Female factor (-)

- FE
  - Testicular volume
    - R: 16cc, L: 14cc
  - Bilateral vasa deferentia palpable
  - Epididiym is normal
  - L: grade 2 varicocele
  - R: grade 1 varicocele

Which test should be done?

- Semen analysis (x2)

- Semen analysis
  - SA1: 3,0 cc/17.000.000/a+b 32% (a:15%, b:17%)
  - SA2: 3,2 cc/15.000.000/a+b 25% (a:18%, b:7%)
- FSH: 6,1 mIU/ml
- T: 420ng/dl

→ Obtained outside of our center

Treatment

- Microscopic varicocelectomy

Recommendations: *Varicocele treatment should be offered to the male partner of a couple attempting to conceive, when all of the following are present: 1) a varicocele is palpable; 2) the couple has documented infertility; 3) the female has normal fertility or potentially correctable infertility; and 4) the male partner has one or more abnormal semen parameters or sperm function test results.*

Adult men who have a palpable varicocele and abnormal semen analyses but are not currently attempting to conceive should also be offered varicocele repair.

Young men who have a varicocele and normal semen analyses should be followed with semen analyses every one to two years.

Adolescents who have a varicocele and objective evidence of reduced ipsilateral testicular size should be offered varicocele repair. Adolescents who have a varicocele but normal ipsilateral testicular size should be offered follow-up monitoring with annual objective measurements of testicular size and/or semen analyses.

AUA Guideline 2009

AUTHORS