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### SAFETY OF TESTOSTERONE TREATMENT ON ENDOMETRIAL PROLIFERATION

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**Introduction:** In recent years the interest in treating post menopausal women with androgens has increased, due to their beneficial effects on libido, bone mass and well-being. At present, our knowledge on the safety of Testosterone (T) administration on endometrium is limited. Aim of this study is to evaluate the effects on endometrial proliferation of high dose T administered for an extended period.

#### Materials and methods:

30 Female to Male (FtM) transsexuals treated with T (i.m. injection of 100mg Testoviron Depot/10 days for at least one year), 30 Post Menopausal women (PM) and 13 Pre Menopausal women (PrM) in the proliferative phase of their cycle undergoing hysterectomy or endometrial biopsy were enrolled. Endometrial proliferation was evaluated on the basis of histology and expression of the proliferation marker Ki-67. Both PM and PrM women had not received any hormonal treatment for at least one year.

**Results:** In FtM, T levels were increased above normal female levels. At histological analysis, FtM and PM had atrophic endometrium and PrM women had proliferative endometrium. The percentage of cells that expressed Ki-67 is shown in the table:

|     | Total         | Glands        | Stroma      |
|-----|---------------|---------------|-------------|
| FtM | 1.79±2.71     | 1.28±2.05     | 0.51±0.78   |
| PM  | 0.64±0.93     | 0.41±0.53     | 0.23±0.54   |
| PrM | 28.95±16.13*§ | 24.88±12.20*§ | 4.07±7.39*§ |

\*= P<0.05 vs. FtM

§= P<0.05 vs. PM

**Conclusions:** Our data suggest that long term, high dose T treatment does not stimulate endometrial proliferation in FtM subjects. Exogenous T administration appears to have no adverse effects on the endometrium.

### ALTERATION OF FLOW-MEDIATED DILATATION IN PATIENTS WITH KLINEFELTER SYNDROME

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Epidemiological data suggest there is an increased risk of heart disease among patients with Klinefelter syndrome (KS). A recent study showed subclinical alteration of left ventricular function in KS, probably related to high prevalence of hypogonadism and metabolic syndrome. Nevertheless, there are no data on endothelial reactivity, an important component of the metabolic or insulin resistance syndrome, implicated in the pathophysiology of atherosclerosis, essential hypertension and congestive cardiac failure in patients with KS. We aimed at evaluating vascular reactivity of the brachial artery in patients with KS. We enrolled into the study patients with KS (n=9, age 29.4±9 yrs) and subclinical hypogonadism before starting replacement therapy with testosterone. Nine age-matched males served as controls. **Results:** Patients with KS, compared to controls showed a reduction of flow-mediated dilatation (FMD). In particular three out of nine patients presented FMD values lower than 2SD under the mean of the control group (<9%). **Conclusion:** Patients with KS showed preclinical alteration of vascular function that could be related to the higher prevalence of cardiovascular risk. Moreover our data suggest that testosterone replacement therapy should be considered also in patients with KS with subclinical hypogonadism to prevent cardiovascular risk. In fact recent clinical studies have reported that testosterone therapy reduces myocardial ischaemia in men with coronary artery disease, and the beneficial modulation of coronary vascular tone by testosterone has been proposed as an effector mechanism.

### ROLE OF MICROSURGERY FOR CHRONIC ORCHALGIA : EXPERIENCE AT FATIMA MEMORIAL HOSPITAL LAHORE

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Chronic orchalgia is a relatively uncommon but a miserable condition for the patient. In severe cases patients are unable to tolerate the touch of routine dress garments. These patients are difficult to treat and there are reports that severe cases may not improve even with orchietomy.

We are presenting our experience of managing these patients at our andrology clinic. Since August 2003, thirty nine 39 patients have reported at our center with chronic orchalgia. Out of them, 27 patients presented with dull pain, 5 with moderate pain and 7 with severe pain. Patients were managed according to their disease. Varicocele was the commonest etiology in our patients. Other causes were past epididymoorchitis, mumps orchitis, scrotal injury and chronic prostatitis. Two patients had idiopathic orchalgia. We managed our patients with analgesics, spermatic cord block, high inguinal nerve block, caudal epidural block, microsurgical varicocelectomy and microsurgical inguinal denervation of spermatic cord. Microsurgical denervation was reserved for patients who responded to cord block but had recurrent pain after repeated blocks. We performed denervation of the cord in 7 patients with complete relief in all of them. Blood flow of the testes was determined before and after surgery with doppler ultrasonography. No significant difference was seen after surgery in peak systolic velocity of the subcapsular arteries of testes.

In summary patients having mild to moderate pain unrelated to varicocele, responded well to analgesics and spermatic cord block and occasionally to high ilioinguinal nerve block or caudal epidural block. Patients with mild pain and varicocele were relieved of pain with microsurgical subinguinal varicocelectomy, but patients with severe chronic orchalgia required microsurgical denervation of the spermatic cord. In our practice microsurgical inguinal denervation of the spermatic cord has proved to be safe and effective for selective patients

### RELATIONSHIP BETWEEN DEGREE OF NEUROPATHY AND POST-EJACULATORY SEMINAL VESICLES VOIDING AND SEMINAL LEUKOCYTE CONCENTRATIONS IN DIABETIC PATIENTS

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We have already reported that the seminal vesicles may represent a target for neuropathy secondary to diabetes mellitus. This study was undertaken to evaluate the relationship, if any, between the degree of diabetic neuropathy and post-ejaculatory seminal vesicle voiding and seminal leukocyte concentration. To accomplish this, 12 infertile diabetic patients, aged 19-36 years, with a different degree of neuropathy damage, evaluated by the Dick criteria, were enrolled. Each patient underwent sperm analysis and seminal leukocyte determination, according to the WHO (1999) criteria, and transrectal ultrasonography of the prostatic-vesicular region before and after ejaculation to estimate the seminal vesicle antero-posterior diameter (APD). Patients were divided in 3 groups according to the neuropathy severity: Dick 0 (absent), Dick 1 (mild) and Dick 2 (severe) and the APD, the difference between pre- and post-ejaculatory ADP (delta APD) and seminal leukocyte concentration were analyzed by 1 way ANOVA followed by the DUNCAN test. A statistical significant difference was accepted when the p value was lower than 0.05. The results (mean±SEM) are shown in the following table:

| Dick score | Pre-ejaculatory APD (mm) | Post-ejaculatory APD (mm) | Delta APD (mm) | Seminal WBC (mil/ml) |
|------------|--------------------------|---------------------------|----------------|----------------------|
| 0 (n=6)    | 10.7±1.6                 | 7.0±2.0                   | 3.7±0.6        | 0.38±0.21            |
| 1 (n=3)    | 10.7±4.2                 | 9.3±4.3                   | 1.3±0.3*       | 0.39±0.31            |
| 2 (n=3)    | 18±3.2                   | 17.7±3.2                  | 0.3±0.3*       | 2.05±0.58*^          |

WBC: leukocytes; \*p<0.05 vs. Dick 0; ^p<0.05 vs. Dick 1

Diabetic patients with the most severe degree of neuropathy had pre- and post-ejaculatory seminal vesicle APD bigger than patients with less severe neuropathy. Accordingly, they had a significantly lower delta-APD and a significantly higher seminal leukocytes concentration. These findings showed that diabetic patients with the most severe neuropathy damage have an altered dynamic of seminal vesicle voiding. We hypothesize that this may explain the tendency to develop male genital tract chronic inflammation as suggested by the increased seminal leukocyte concentration.