

## Faculty Abstracts

### F1

#### ED TREATMENTS: CURRENT AND FUTURE

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The aim of successful management of erectile dysfunction (ED) is restoration of quality of life and sexual health in couples. The advent of phosphodiesterase type-5 (PDE-5) inhibition as oral therapy has significantly revolutionised both clinical and basic research in this area, and much of this progress is due to better understanding in the last two to three decades of the various pathophysiological and cellular mechanisms leading to ED. All the three currently available PDE-5 inhibitors, namely, sildenafil, tadalafil and vardenafil, have provided good safety profiles and have widened the horizon in patient choice, selectivity and efficacy. The newer PDE Is, udenafil and avanafil may also meet the specific needs of selected patients. With the ease of self administration and better patient compliance these drugs may relegate the other measures for ED including intracavernosal injections and non-pharmacological treatments to second-line therapy. In some refractory and resistant cases, vasoactive agents such as prostaglandin E<sub>1</sub>, papaverine, and phentolamine and their combinations, and even the increasing number of other agents in the pipeline including nitric oxide donors, guanylate cyclase activators, potassium channel openers and Rho-kinase inhibitors, may offer significant promise of clinical application.

In some patients with mild to moderate ED, L-arginine analogs, cAMP activators, melanocortin-stimulating hormone analogs, endothelin antagonists and others may also be useful. In a severe pathophysiological state of ED, a combination pharmacotherapy may ensure greater success rate. Once commonly used, penile prostheses have a limited role now in the management of ED, being reserved for patients with severe organic ED in whom all other therapeutic measures have failed. Silencing of PDE-5 isoenzyme and cloning of iNOS have opened a new era in the use of gene therapy and stem cells may also offer better prospects for the future in ED management.

Together with the drug management for ED and FSD (sexual arousal, desire and pain disorders), the co-existent conditions in males such as ejaculatory problems, desire, arousal and orgasmic dysfunctions and interpersonal conflicts have to be recognised and managed for a holistic couple care. In the aging male, late-onset hypogonadism (LOH) is seen together with other physical changes such as increase in abdominal fat, loss of libido, decrease in strength, lean body mass, bone density and cognitive function, similar to symptoms of androgen deficiency in younger men. Androgen supplements may be useful in this group of ED patients (also improve the PDE I efficacy). Since hyperoestrogenemia caused loss of libido and ED in men, its delicate balance with testosterone may be considered important in patients, particularly with LOH for successful management outcome. Studies have also established the causative roles of high lipid (cholesterol and triglyceride), hypertension, diabetes mellitus and chronic alcoholism in ED in addition to endothelial dysfunction and aging. Therefore, the timely inception of

preventive measures including lifestyle modifications in overcoming sexual problems may hold promise for the future.

### F2

#### PROSTATE CANCER AND TESTOSTERONE THERAPY – IS THERE AN EXPECTATION OF PARADIGM SHIFT?

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**Objectives:** Prostate safety is a primary concern when aging men receive testosterone therapy (TT), but little information is available regarding the effects of TT on prostate tissue in men with a major concern: DHT levels. History of prostate cancer has been an absolute contraindication for testosterone therapy. We want to review the historical origins and current evidence for the belief that testosterone (T) causes prostate cancer (PCa) growth.

**Methods:** Review of the historical literature regarding testosterone administration and PCa, as well as more recent studies investigating the relationship of T and PCa. Hypogonadal patients treated with radical retropubic prostatectomy (RRP), or even radiotherapy for organ confined prostate cancer to determine if testosterone therapy (TT) could be efficacious and administered safely without causing recurrent prostate tumour. Dihydrotestosterone (DHT) levels show no alteration under testosterone therapy, also no DHT overexpression in prostate tissues in placebo controlled studies.

**Results:** According to Morgenthaler, in 1941 Huggins and Hodges reported that marked reductions in T by castration or oestrogen treatment caused metastatic PCa to regress, and administration of exogenous T caused PCa to grow. Remarkably, this latter conclusion was based on results from only one patient. Multiple subsequent reports revealed no PCa progression with T administration, and some men even experienced subjective improvement, such as resolution of bone pain. More recent data have shown no apparent increase in PCa rates in clinical trials of T supplementation in normal men or men at increased risk for PCa, no relationship of PCa risk with serum T levels in multiple longitudinal studies, and no reduced risk of PCa in men with low T. The apparent paradox in which castration causes PCa to regress yet higher T fails to cause PCa to grow is resolved by a saturation model, in which maximal stimulation of PCa is reached at relatively low levels of T. Dihydrotestosterone (DHT) levels show no alteration under testosterone therapy, also no DHT overexpression in prostate tissues in placebo controlled studies.

**Conclusions:** This historical perspective reveals that there is not now — nor has there ever been — a scientific basis for the belief that T causes PCa to grow. Discarding this modern myth will allow exploration of alternative hypotheses regarding the relationship of T and PCa that may be clinically and scientifically rewarding.

## F3

**ERECTILE DYSFUNCTION, METABOLIC SYNDROME, AND TESTOSTERONE DEFICIENCY – IS THERE A LINK?**F. Saad<sup>1</sup>, A.A. Yassin<sup>2</sup>, R. Shabsigh<sup>3</sup>

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**Objective:** To evaluate associations between erectile dysfunction (ED), metabolic syndrome, and testosterone deficiency.

**Methods:** Review of the current literature.

**Results:** Metabolic syndrome is a complex of risk factors which progressively leads to the manifestation of diabetes mellitus type 2 and cardiovascular diseases. Erectile dysfunction may appear as the first symptom.

Cross-sectional and longitudinal epidemiological studies show associations between testosterone levels and features of metabolic syndrome. Low testosterone levels are more common in patients with metabolic syndrome, cardiovascular diseases, or diabetes type 2 than in the normal population. Recent studies have shown that the prevalence of hypogonadism in male patients with angina or diabetes type 2 can be approximately 50%.

Observations in prostate cancer patients receiving androgen deprivation therapy show an increased risk of unfavourable changes in body composition, lipid pattern, and insulin resistance.

Studies in obese men reveal that obese men in good or impaired health have lower testosterone levels than non-obese controls. Waist circumference as an indicator for visceral obesity is inversely associated with testosterone. The risk of obese men to develop metabolic syndrome and consequently diabetes and cardiovascular diseases is significantly higher than in normal-weight controls.

Studies in diabetic men demonstrate that many of the risk factors for diabetes correlate negatively with testosterone levels.

Several intervention studies in patients with visceral obesity, cardiovascular diseases, and diabetes type 2 suggest that the normalisation of testosterone levels reduces fat mass, increases lean body mass and shows an overall improvement of the risk factors for metabolic syndrome and the consecutive diseases.

**Conclusion:** Erectile dysfunction may be the first symptom driving men to seek medical help. It is therefore an opportunity but also a responsibility for physicians seeing patients with erectile dysfunction to look for concomitant risk factors and diseases.

## F4

**RELAXATION EFFECT OF PDE INHIBITOR ON COPD PENILE SMOOTH MUSCLE IN VITRO**

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Sexual function, especially erectile function, is deteriorated in COPD patients. We conducted a study to evaluate the effect COPD in the relaxation of corpus cavernosum smooth muscle as a physiological process in erectile function.

**Material and methods:** To determine the relaxation effect of PDE5 inhibitor COPD penile smooth muscle, we studied strips of corpus cavernosum tissue obtained from 24 rabbits divided into two groups: 12 as control; and to make the COPD group, 12 rabbits exposed with SO<sub>2</sub> in a biochamber for 4–5 weeks. Contraction was induced on isolated strips of corporal smooth muscle by norepinephrine; then relaxation was assessed with the administration of three agents: selective phosphodiesterase type 5 (PDE-5) inhibitor (sildenafil citrate)

and zaprinast and acetylcholine Neurotransmitter. Analysis of variance was used to compare the responses to the different agents.

**Results:** Contraction of penile smooth muscle in control group was higher compared with COPD groups in all doses of norepinephrine but there was no statistical difference.

Relaxation of COPD penile smooth muscle was decreased by sildenafil, zaprinast and acetylcholine, and there was statistical difference by zaprinast and acetylcholine but no statistical difference by sildenafil.

**Conclusion:** COPD decreased capability of penile smooth muscle in contraction on relaxation.

## F5

**TESTOSTERONE MAY RECOVER PENILE VENOUS LEAKAGE IN PATIENTS WITH HYPOGONADISM AND ERECTILE DYSFUNCTION**A.A. Yassin<sup>1</sup>, F. Saad<sup>2</sup>

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**Introduction:** Venous leakage is often a factor in erectile dysfunction (ED) in elderly men. It has been traditionally considered as a mechanical lesion of the structure of the corpora cavernosa. This study demonstrates that treatment with testosterone in a number of cases is capable of restoring venous leakage.

**Patients and methods:** A total of 23 hypogonadal patients were studied. They suffered from severe ED associated metabolic syndrome/diabetes mellitus and had not responded to either PDE-5 inhibitors or to intracavernosal injection with Alprostadil 20 µg. Their mean age was 57 years (47–72). Two subjects had diabetes mellitus (DM) Type I and three DM Type II. Other co-morbidities were metabolic syndrome and hypertension. Their testosterone levels were in the hypogonadal range at 1.07–3.3 ng/ml or 3.7–11.4 nmol/L (normal range 4–8.6 ng/ml or 13–28 nmol/L). In 12 cases penile cavernosography was performed and showed venous leakage. This study focuses on these men with proven venous leakage. They received IM injections of long-acting testosterone undecanoate 1000 mg at day 1, again after six weeks and thereafter three-monthly. Re-evaluation cavernosography followed in these 12 patients after 3–6 months.

**Results:** 6 weeks after the first injection plasma testosterone had increased to 4.3 ± 0.31 ng/ml, or 14.8 ± 1.0 nmol/L. Three patients with DM type 2 and/or metabolic syndrome, reported improvement of their sexual function within 9 weeks of testosterone treatment. Another patient with severe hypogonadism and Peyronie's disease reported similar results. The repeated cavernosography showed also considerable improvement of the venous leakage. A fifth patient whose primary testosterone level was at 1.07 ng/ml, reported partial but still considerable improvement in sexual desire and function after 5 months of therapy. His control cavernosography showed no venous leakage in the profound veins, but only slight leakage in superficial veins. A sixth patient showed restored erectile function and no venous leakage after 11 months of treatment. In all patients sexual desire domain increased from 4 to 8 and erectile function domain from 10 to 24. The remaining six patients with persistent venous leakage (testosterone therapy for 3–7 months) are still under follow-up.

**Conclusion:** These results suggest that testosterone has a positive impact on haemodynamic processes and the veno-occlusive properties in the penile trabecular tissues. The disappearance of venous leakage in these six of twelve cases is a remarkable finding and encourages treatment with testosterone in hypogonadal ED patients and subjects with metabolic syndrome. The impact of a hormonal factor on veno-occlusive properties of the corpora cavernosa indicates that restoration of testosterone to normal may repair mechanical damage of the corpora cavernosa. This has also been found to be the case in laboratory animals.

F6

**'SEX CRISIS' AND THE PROGRESSING OF AGE IN MEN**

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Psychogenic and interpersonal factors may influence the etiologic, development and maintenance of sexual problems besides the probable role of sex hormone production in men as well as in women. However, especially in middle-aged and aging men these factors have been obscured by the successful discovery of hormone replacement treatment (HRT) and the initial success of the novel phosphodiesterase-5 (PDE-5) for the treatment of sexual problems (erectile dysfunction). Currently, debates have arisen on treatment failures with phosphodiesterase-5 (PDE-5) inhibitors or HRT alone. Although combination treatment of PDE-5 and HRT could augment successful rates of treatment in about 30%, the importance of psychogenic and interpersonal influences during the course of treatment should not be neglected to regain the harmony of life between partners.

Psychogenic and interpersonal factors were often downplayed due to the above mentioned initial success rate of treatment. But sexual assault and other sexual orientation aspects as results of sexual crisis in the progression of age in men and marriages with sexual problems (ED) were often neglected. Twenty-six promiscuities, 5 bisexual and 2 homosexual orientations were found on the influence of psychogenic and interpersonal factors that may influence the etiology, development and maintenance of sexual problems during the course of ED treatment in 64 middle-aged and aging men. A holistic patient-centred approach by clinical interviews is therefore of paramount important.

F7

**TESTOSTERONE ADDS TO THE THERAPEUTIC EFFECTS OF EXERCISE AND DIET IN DIABETES TYPE 2**F. Saad<sup>1</sup>, L. Gooren<sup>2</sup>, A. Heufelder<sup>3</sup>

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**Objective:** to test the potential therapeutic effects of testosterone (T) administration in addition to exercise and diet in men with metabolic syndrome and newly diagnosed diabetes type 2 with lower-than-normal free T levels.

**Patients and methods:** 32 men between 35–70 years with metabolic syndrome + diabetes type 2 followed a moderate exercise programme and Mediterranean diet. Sixteen received in addition treatment with transdermal T (50 mg/day).

**Results:** Exercise + diet had beneficial effects: waist circumference declined from 107 to 102 cms, HbA1c from 7.6 to 6.8%, triglycerides from 271 to 168 mg/dl, HDL increased from 38 to 43 mg/dl. In the men who received T in addition, the effects were significantly larger: waist circumference declined from 106 to 96, HbA1c from 7.5 to 6.3%, triglycerides from 286 to 149 mg/dl, HDL increased from 38 to 46 mg/dl.

**Conclusion:** Normalising T levels in men with metabolic syndrome and diabetes type 2, has additional therapeutic effects to exercise + diet alone.

F8

**MANAGEMENT OF SEVERE UPPER URINARY TRACT INFECTION IN ELDERLY MEN**

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Urinary tract infections (UTI) is one of the leading causes of infection in elderly patients. Upper UTI (pyelonephritis) also is the commonest cause of bacteraemia and septic shock in elderly patients. Mortality rate can be reduced when the patients are treated rapidly and properly. UTI in elderly patients may be more difficult to treat because of associated structural or functional genitourinary tract abnormalities; multi-drug resistant bacteria, and/or inadequate host defences. Radiologic evaluation should be performed earlier and look for obstructive disorders such as stones that lead to continuing sepsis. Hydration and parenteral antibiotic with high tissue penetration must be given in severe cases. Because elderly patients are very sensitive, so the selection of antibiotic must be based on pharmacokinetic alterations associated with aging, underlying diseases, drug interactions and side effects. Relief of the obstruction needs to be performed in obstructive cases.

F9

**ISSAM RECOMMENDATION FOR THE MANAGEMENT OF LATE-ONSET HYPOGONADISM – UPDATE**

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The field of hormonal alterations in the aging male is attracting increasing interest in the medical community and the public at large. Simultaneously, industry has realised the growing importance and enormous potential of the impact of a rapidly increasing population of males over the age of 50 years which will be positioned for special health needs in the first quarter of this century and probably beyond. Among these needs hormone therapy (HT) rates high. It is fully recognised that the endocrinological changes associated with male aging are not limited to sex hormones. On the contrary, profound changes occur in other hormones such as growth hormone, melatonin and thyroxin. However, late-onset hypogonadism (LOH) or testosterone deficiency is a fast developing field. The understanding of LOH among large sections of the medical profession dealing with mature men (i.e., primary care, internists, urologists, etc.) has not kept pace with the developments in the field. A great deal of confusion and misunderstandings surrounding diagnosis, treatment and monitoring of late-onset hypogonadism exist. Therefore, the ISSAM – in fulfilling its mandate – considered that this was an opportune time to provide factual information on the various clinical aspects of testosterone deficiency in the form of a set of practical recommendations dealing exclusively with testosterone therapy (TT). Opinions on the need for and effects of hormone supplementation in aging change frequently, and long held views are now being vigorously challenged. The material in this recommendation which will be discussed in detail, represents recent information on LOH; however, it may require frequent updates as new and relevant data becomes available.

F10

**IMPACT OF FOOD SUPPLEMENTS FOR MEN'S HEALTH AND THE AGING MALE**

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Use of food supplements and complementary products as well as herbal medicine has expanded globally and has gained popularity. They have been used for health maintenance including nutritional support, health enhancement, reduction of risk of a disease/disorder as well as assisting in the management of symptoms/disease/disorder.

Products proposed for men's health with indication for maintenance or enhancement of stamina, normally contain aphrodisiac substances that may have hormonal as well as non hormonal effects, for example *Panax ginseng*, *Eurycoma longifolia* Jack, *Lunasia amara* Blanco, *Talinum paniculatum* Gaertn, *Talinum racemosum* R.Bach, *Pimpinella alpina umbelliferae*, *Pausinystalia yohimbe*, etc.

Six hundred and seventy products have been approved for maintenance or enhancement of stamina.

Although many products have been approved for men's health, they may not have been approved for sexual dysfunction, and the data that might support these indications have not been established. The challenge now is to ensure that the products are used properly, and consumer awareness has become important because many of these products are distributed by direct selling (Multi Level Marketing).

With the tremendous expansion in the use of food supplements and complementary products as well as herbal medicine worldwide, safety and quality control have become an important concern for both the public and governments alike. For this purpose the Indonesian National Agency of Drug and Food Control (Badan Pengawas Obat dan Makanan) conducts a control system through 'pre-marketing evaluation' (evaluation of safety, efficacy and quality as well as labelling and advertisement) and 'post-marketing vigilance' that implements the inspection of facilities, product sampling and laboratory testing, and the monitoring of adverse reaction. Several follow-up actions are conducted routinely such as public warning, consumer empowerment, sanction and law enforcement.

## F11

### **EURYCOMA LONGIFOLIA JACK: A POTENT ADAPTOGEN IN THE FORM OF WATER-SOLUBLE EXTRACT (LJ100) IN MAINTAINING MEN'S HEALTH**

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Long Jack, Tongkat Ali or *Eurycoma longifolia* Jack is a common herbal shrub found along the slopes of hilly terrains of the Malaysian rainforests. Its medicinal value relates to the ground where it is found. The aphrodisiac phyto-compound found in the Malaysian Peninsular Tongkat Ali is in greater concentration when compared to the Tongkat Ali found elsewhere. Typically a herb it contains all sorts of alkaloids of the quassinoid variety which have the properties of healing malarial fever, in managing allergies and common fevers and tumours. The water-soluble extract contains phenolic compounds, tannins, high molecular weight polysaccharides, glycoproteins and mucopolysaccharides. The glycoprotein components exert anti-cancer, pro-fertility, aphrodisiac and anti-aging properties. Water-soluble extract is non-toxic even at higher dosage. However, studies showed that methanol extract of Tongkat Ali is toxic for human consumption.

*Animal studies:* Early studies on Tongkat Ali on the mouse animal model with organic extract and water-soluble extract done by Hooi Hoon and co-workers (Penang Science University) and Saad and co-workers (University of Malaya) reported increased levels of testosterone and increased fertility based on sperm motion and activation profiles using a computer assisted motion analyser. Azimahtol (Faculty of Science & Technology from the National University of Malaysia) evaluated the effect of LJ100 comparing with sildenafil citrate (Viagra) in triggering penile erection. LJ100 increases and enhances the levels of cGMP and cAMP, which ultimately leads to penile erection.

*In vitro studies:* Harniza and Johari (University of Malaya) isolated the bioactive eurypeptide and tested its effect on the biosynthesis of various androgens. Eurypeptide significantly increased CYP17 enzyme, suggesting that more of the CYP17 enzyme is being produced to metabolise pregnenolone to yield more testosterone (180×) and progesterone (190×).

*Early human trials on tongkat ali:* Early human trials prove the herb anabolic as it boosts production of testosterone in men through direct stimulation of steroidogenesis in the testis and the adrenals as well as its influence in the reduction of sex hormone binding globulin or SHBG that allows free testosterone in the blood. In a double blind, placebo controlled study conducted by Sareena (Department of Sport Science, University of Malaya) provided 14 healthy adult males with either 100 mg/day of LJ100 or placebo for 8 weeks. Both groups performed an intensive strength-training programme

for 8 weeks. The group on LJ100 showed improved body mass index as well as muscle strength.

*Toxicology and extended clinical trials:* A double-blind placebo controlled human clinical trial where 20 male volunteers of various health conditions from the ages of 38 to 58 were randomly given 200, 400, or 600 mg of LJ100 or placebo for 2 months. The SHIM scores were elevated to upper normal level showing improvement in sexual desire and performance for a majority of the volunteers. The AMS lowered showing improvement in sexual, physical, psychology, and vasomotor domains for a majority of the volunteers. Testosterone and DHEAS levels showed high normal levels when compared to baseline. Full blood examinations showed normal limits even at 600 mg dosage. Liver function and renal function tests were normal. AFP; PSA and rest of tumour markers were within normal levels. Lipid studies showed increment of high-density lipoprotein. Diabetic volunteers showed an improved level of blood glucose. Cortisol levels were higher than normal for the LJ100 group, suggesting it modulates the release of cortisol. The majority of volunteers on LJ100 have higher than normal levels of thyroxine compared to the placebo group, meaning a higher metabolism rate which can be translated to weight management. Volunteers taking LJ100 had higher than normal levels of IGF-1 at the end of the trials. Some with a low IGF-1 level increased to a normal level after 1 week.

*Conclusion:* Standardised water-soluble Tongkat Ali or LJ100 is non-toxic to vital body functions even at a high dose of 600 mg. Overall effects on the various hormones are also positive. It enhanced total testosterone and DHEA (Dehydroepiandrosterone) which also modulates testosterone level, ensuring enough free testosterone for the body's need. Its other adaptogenic effects include positive effect on body cortisol levels as well as on growth hormone as it modulates the released of IGF-1. With all these findings, LJ100 is not only a potential natural sex stimulant and energiser it is a potent adaptogen in maintaining men's health.

## F12

### **SEX HERBS AND TONICS OF ASIA**

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In the East, many herbal tonics and preparations are used to assist the aging male improve his ability to have sexual drive or perform penetrative sex by increasing sexual stimulation, erectile, ejaculatory, orgasmic and other responses for sexual function and satisfaction. Currently available herbals, tonics and therapies range from Tongkat Ali, *Ginseng*, *Tribulus*, etc. Those that act as testosterone releasers have some value especially if the male has andropause, and those containing some 'pick-me-ups' and energisers like ginseng help the tired and fatigued male and possibly those with asthenia. Deer horn contains growth factors, and taking these may help improve nocturnal erections in the male with somatopause. Popular in historic Singapore were remedies such as 'penis soup' and snake meat, whilst Surabaya was known for cobra meat and cobra blood which had claims of improving erectogenic prowess. These myths including that of taking dog, wild boar, bull and ostrich testicles are mainly village doctor remedies still being practised widely in the developing regions of Asia. In China the horny goat weed is currently still popular and may have some scientific merit for enhancing sexual drive. The myths and realities concerning many other herbs and potions for oral intake or local application used by traditional 'medical' practitioners and village doctors will be also discussed.

## F13

### **COSMETIC REJUVENATION IN THE AGING MALE**

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Health and appearance is very important for everybody, not only for females but also for males. As we age, our skin differs

from young people's skin. Skin becomes thin, translucent, loose, less elastic, wrinkling, and in some areas body fats increase.

The etiologies of skin aging are: intrinsic (chronologic) and extrinsic (external factors, such as UV light from sun). About 85% of skin aging is caused by external factors. Common skin diseases in the elderly are: sebaceous glands hypertrophy, pigmentary changes, wrinkles, seborrheic keratosis, malignancies, etc. Most of the diseases could be treated with creams, electro-surgery, chemical peeling, laser or cryosurgery. For more significant cosmetic improvement, we use botox, phototherapy (Laser/IPL), radiofrequency (thermage), or cosmetic surgery (blepharoplasty, facelift, and liposuction). Surgery in the aging male should consider the general health of the patients and any supplementation he takes. If patients take blood-thinning medication, he should stop 2 weeks before and 1 week after surgery. All surgeries were done on outpatient basis without the need for general anaesthesia, so this is not a complicated or risky procedure, but yet the results are significant. We will show the results from various skin conditions with every treatment modality to achieve a better and younger appearance. We could combine the treatment with intrinsic treatment such as oral supplementation, life-style (foods, reducing stress, sports) and hormone re-balancing to achieve a maximum result.

#### F14

### INTRAVESICAL PROSTATIC PROTRUSION (IPP) IN THE MANAGEMENT OF BENIGN PROSTATIC ENLARGEMENT (BPE)

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**Introduction:** IPP is the protrusion of the prostate seen on non-invasive transabdominal ultrasound in the sagittal plane, in a comfortably full bladder of about 200 ml. It can be measured easily from the tip of the protruding prostate to the base at the circumference of the bladder. It can be graded accordingly to 1) 5 mm or less, 2) more than 5 to 10 mm and 3) more than 10 mm. Our studies have shown good correlation between IPP and urodynamic evidence of obstruction. For IPP grade 1 only 21% are obstructed, while for grade 3, 94% are obstructed. It has good sensitivity, specificity and predictive values in diagnosing obstruction. IPP is related to prostate volume (PV) as well as the presence of the median lobe.

**Diagnosis of BPE:** BPE commonly presents with lower urinary tract symptoms (LUTS) and acute retention of urine. BPE can also present as raised Prostate-specific antigen (PSA), haematuria and Urinary tract infection (UTI) in males. Using transabdominal ultrasound, IPP is useful in diagnosing non BPE from BPE. **Predicting the natural history of BPE:** IPP is a strong predictor of the success of trial off catheter in patients with acute retention of urine (AUR). In our study in trial off catheter in patients with AUR 36% failed if IPP is grade 1, 67% if IPP is grade 3, and this has been validated in other studies. Also on long-term follow up of patients (mean 2 years) 8% deteriorated if IPP is grade 1, while 67% deteriorated if IPP is grade 3.

**Treatment of BPE:** IPP is important in the decision on the modalities of treatment of BPE when combined with other parameters such as persistent post void residual urine (PVR) and bothersome symptom score (QOL). Low grade IPP with no significant PVR (<100 ml) and no bothersome symptoms (QOL < 3) can be watched and reassured, while high grade IPP more than 10 mm with persistent residual urine (>100 ml) would need more aggressive treatment such as surgical removal of prostate as an option. Low grade IPP with bothersome symptoms can be treated with alpha blockers while high grade IPP would benefit from 5 alpha reductase inhibitors or combined therapy.

**Conclusion:** IPP is simple to measure with non-invasive transabdominal ultrasound, and can be used to diagnose BPE and predict the severity of obstruction and the progression of the disease. Combined with PVR and the bothersomeness of symptoms it is a useful guide in the cost effective management of patients with BPE.

#### F15

### COMPARISON OF TREATMENT OUTCOMES BETWEEN PHOTOSELECTIVE VAPORISATION AND TRANSURETHRAL RESECTION OF THE PROSTATE DEPENDING ON EXPERIENCES OF SURGERY

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**Purpose:** Since the advent of photoselective vaporisation of the prostate (PVP), it has been questionable if effectiveness of PVP is equivalent to that of the standard transurethral resection of the prostate (TURP). Taking into consideration the learning curve of PVP, we prospectively compared treatment outcomes of PVP with those of TURP.

**Materials and methods:** A prospective clinical trial was performed from October 2004 through June 2006, with 131 patients treated by PVP and 41 patients treated by TURP. PVP was performed by one operator who started the operation and TURP was performed by another operator who had previously experienced over 800 surgeries. Efficacy parameters were International Prostate Symptom score, Quality of Life score, peak urinary flow rate, postvoid residual volume, and prostatic volume reduction estimated by transrectal ultrasonography. In addition, perioperative parameters and complications were compared at 1, 3, 6 and 12 months following surgery, taking into consideration the operative period of PVP (the first half and second half).

**Results:** Baseline characteristics of both groups were similar. Operating time, catheter indwelling time, and hospital stays were significantly shorter in the PVP group. All efficacy parameters of the PVP group significantly improved compared to preoperative parameters irrespective of operative period; the degree of improvement of efficacy parameters was similar in both groups within 12 months. Prostatic volume reduction in the second half of PVP was larger than that of the first half, however, was less than that of TURP. Prostatic volumes at pre- and post-operative 6 months were  $41.7 \pm 15.6$  and  $33.1 \pm 12.4$  ml during the first half,  $42.7 \pm 13.0$  and  $30.9 \pm 10.7$  ml during the second half,  $47.4 \pm 17.1$  and  $25.4 \pm 9.5$  ml for TURP, respectively. In the PVP group, mean operating times for the first half and second half were  $49.9 \pm 22.0$  and  $52.9 \pm 16.9$  min ( $p > 0.05$ ); applied energies were  $95.0 \pm 44.5$  and  $143.2 \pm 40.7$  kJ, respectively ( $p < 0.001$ ). There were no differences in overall complications between PVP and TURP groups although more transfusions were required and capsule perforations occurred in the TURP group. In the PVP group, urethral stricture was more common in the first half and urinary retention requiring re-catheterisation was more common in the second half. Incidence of complications such as gross haematuria, frequency, urgency, and retrograde ejaculation was not different according to PVP operative period.

**Conclusions:** PVP provides excellent intraoperative safety and helps give immediate relief from obstructive voiding symptoms, similar to TURP, although operators do not have enough experience. The degree of prostatic volume reduction of PVP increases with the operator's experience but is less than that of TURP. Long-term follow-up is necessary to assess the durability of PVP.

#### F16

### THE INTIMATE NEXUS BETWEEN ERECTILE DYSFUNCTION AND CARDIOVASCULAR DISEASE

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The physiology of the smooth muscle and the endothelial cells of the cavernosal vasculature are central to the peripheral mechanism of erectile function. Penile erections are the result of smooth muscle relaxation in the cavernosal vasculature initiated by nitric oxide synthesised and released at the endings of non-adrenergic non-cholinergic parasympathic nerves and

maintained by nitric oxide from the endothelial cells of the cavernosal arterioles and sinuses.

Men with erectile dysfunction (ED) have impaired endothelium-dependent and endothelium-independent arterial vasodilatation. It is logical that deficient synthesis and release of nitric oxide from altered endothelial function, the hallmark of endothelial dysfunction, would lead to vasculogenic ED.

ED is frequently associated with cardiovascular (CV) risk factors and disease such as aging, smoking, hypertension, dyslipidaemia and diabetes. Men with CV risk factors are at significantly higher risk for ED, and the greater the number of such risk factors the higher the risk. ED is not only prevalent among patients with coronary artery disease but is also closely correlated with the number of stenotic and calcified coronary arteries. It is an independent predictor of asymptomatic CV disease and of prospective CV events.

Consistent with other published studies, the Western Australia Men's Health Study, a population-based cross-sectional observational study conducted in Perth, Western Australia, showed too that ED is significantly correlated with CV disease.

Lifestyle changes such as healthy balanced diet, regular physical activity, and cessation of cigarette smoking improve endothelial dysfunction, and are also beneficial for ED and CV disease. Primarily marketed for the treatment of ED, phosphodiesterase-5 (PDE-5) inhibitors, through enhancing the bio-effectiveness of nitric oxide, have been shown to benefit patients with ischaemic heart disease, chronic cardiac failure and pulmonary hypertension. Although statins have been implicated in the iatrogenesis of ED in spite of their known beneficial effects on endothelial function, combination of statin with PDE-5 inhibition has been shown to improve erectile function.

The implications of the intimate nexus between ED and CV disease are immense. Just as it is important to proactively inquire about possible ED in a patient with CV disease or risk factors, the unique opportunity must be seized to investigate for and identify incipient CV risk factors and disease in a patient presenting with ED. Understanding the ED-CV disease nexus helps enhance current management strategies for ED and CV disease and generate new strategies. It also provides opportunities for CV risk prevention and minimisation.

#### F17

##### EFFECT OF LATE-ONSET HYPOGONADISM ON NON-SEX STEROID HORMONES

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Aging in males is accompanied by a gradual decline of all endocrinological functions involving hypothalamus, pituitary, pineal, thyroid, adrenal, pancreas as well as gonad. These endocrine alterations induce growth hormone deficiency, hypothyroidism or hypogonadism, which reveal subclinical to severe clinical symptoms and signs in the aging process in male. At present moment it is evident that altered gonadal function plays a most important role in the aspect of the medical target for anti-aging, which affects directly and indirectly the secretion of non-sex steroid hormones. Therefore, we should pay careful attention to non-sex steroid hormones because aging-associated endocrinopathy or diseases are multifactorial in origin. The scientific evidences on the changes of non-sex steroid hormones in aging male are as follows: 1) growth hormone and insulin-like growth factor 1 levels obviously decrease, accompanied by sarcopenia, osteopenia, skin changes, sleep disturbance and decreased well-being; 2) melatonin deficiency is prominent and related to age-related insomnia; 3) adrenocorticoid secretion is essentially characterised by a decrease in adrenal androgen level, which DHEAS is a most prominent biochemical marker of aging, but no decline evidence for mineralocorticoid; 4) the endocrine change of pancreas related with insulin resistance is not yet clear; 5) the thyroid function is generally less affected although thyroid dysfunction is relatively frequent; 6) estrogen to testosterone ratio increases from the aromatisation of testosterone in the increased peripheral adipose as well as decreased androgen secretion.

As the above evidences, there is the objective role of non-sex steroid hormones as the primary or secondary causes of aging phenomenon, which support a rationale to investigate these hormones in elderly. Furthermore, we could expect that hormone replacement therapy with one or more preparation including non-sex steroid hormone may delay the aging process, cure age-associated diseases, enhance well-being or increase life-span in aging male.

#### F18

##### TESTOSTERONE AND METABOLIC SYNDROME

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Testosterone is the main sex steroid hormone in men. The decline of testosterone in advanced age may not only cause various signs and symptoms of deficiency, but also act as a contributing factor on the pathogenesis of various systemic diseases, such as metabolic syndrome. Several studies have found a meaningful relationship between serum testosterone level and the risk factors of metabolic syndrome. The observed scientific evidences are as follows: 1) total testosterone level is reduced in patients with risk factors of metabolic syndrome including insulin resistance and type 2 diabetes mellitus, central visceral obesity as well as atherosclerosis and cardiovascular disease; 2) the effect of testosterone is secondary to a decrease in obesity; 3) aromatisation of testosterone to estrogen plays a role in the testosterone effect. Estrogen to testosterone ratio is associated with an increased risk for metabolic syndrome but not when adjusted for BMI and waist circumference; 4) lower testosterone is associated with lower levels of HDL-C and triglycerides but with higher levels of the thrombotic factors, tissue PAI, fibrinogen, and factor VIII; 5) testosterone decreases regulators of metabolic syndrome produced by adipose tissue including fibrinogen, leptin, resistin, TNF, cytokine and free fatty acids, which leads to improved insulin sensitivity; 6) testosterone replacement at physiological dose has a role attenuating insulin resistance and enhancing insulin sensitivity.

Therefore, low testosterone is the major risk factor for developing metabolic syndrome. Furthermore, prospective study to determine whether long-term testosterone replacement therapy can prevent developing metabolic syndrome is mandatory.

#### F19

##### AN AGING WORLD – CHALLENGES AHEAD

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In the year 1500 the global population was around 400 million people. Population showed rapid growth in the 17th and 18th centuries and stood at 1 billion at the start of the 19th century. The estimates and projections of the United Nations indicate that between 1900 and 2100, world population will increase seven-fold, from 1.65 billion to 11.5 billion: an increase of almost 10 billion people. Better hygiene and public sanitation in the 19th century and the use of pesticides, modern medicine, and antibiotics led to extended life expectancy in the 20th century and quicker growth, primarily in developed countries. Demographic transition in the 19th and 20th centuries was the result of shifts from high to low mortality and fertility. The birth rate in about a third of the world's nations has slipped below the two-child replacement level, and by 2050, for the first time in human history, there will be more people over the age of 65 than under the age of 15. The population of those above 65 will increase from 400 million to 1.5 billion during the same time period. The proportion of oldest-old (those aged 80 years and older) will increase from 1.9% to 4.2%. The population of centenarians in 2050 will be 16 times larger than in 1998 (2.2 million compared to 135,000). Increasing longevity, declining birth rate and migration patterns are creating major demographic changes in developed and developing countries alike. These changes

present profound challenges to the world's social and economic systems and call into question some basic assumptions about continued prosperity and economic growth. Since the last years of life are accompanied by an increase of disability and sickness, the demands on the social and health services will increase immensely. The high cost in relation to these services will strain to the limit the potential ability of health, social and even political infrastructures not only of developing but also of the most developed and industrialised nations. Less developed countries—which have much lower levels of economic development and access to adequate health care than more developed countries—will be hard-pressed to meet the challenges of more elderly people, especially as traditional family support systems for the elderly are breaking down. Policymakers in the developing world need to invest soon in formal systems of old-age support to be able to meet these challenges in the coming decades. To the prudent health care administrators, the establishment of preventive measures, rather than concentration on intervention care, is an important strategic thrust in overall management of the aging population. Since frailty, disability and dependency will increase immensely, the demand for social and health services, the ability to permit men to age gracefully, maintain independent living, free of disability, for as long as possible is a crucial factor in aging with dignity and would furthermore reduce health service costs significantly. To achieve this objective, a holistic approach to the management of aging has to be adopted.

The promotion of healthy aging and the prevention or drastic reduction of morbidity and disability of the elderly must assume a central role in the formulation of health and social policies. It must emphasise an all-encompassing life-long approach to the aging process, beginning with pre-conceptual events and focusing on appropriate interventions at all stages of life.

Life-history studies of childhood and adolescence demonstrate clearly that social factors probably operate in a cumulative fashion. There are significant social class differences in attainment of height growth and other aspects of physical development, as well as in incidence of infectious and other diseases and risk of injury. Cross-sectional studies show differences in mortality and morbidity as a function of socio-economic status, across various disease categories throughout the life span. Poverty has a significant impact on both life and health expectancy. It should not only be measured in terms of property, employment, wages and income, but also in terms of basic education, healthcare, nutrition, water and sanitation. Educational attainment and marital status have also been shown in several longitudinal studies to be powerful predictors of morbidity, health expectancy and mortality. The economic consequences of retirement place many older citizens in positions of financial vulnerability. As populations age, in both the developing and the developed worlds, the issue becomes how to keep older persons economically viable within their respective societies. No community is exempt from the financial hardships experienced by ageing populations. The remarkable demographic transformations in this century have not only led to increased medical needs of older people, who often have multiple chronic conditions, decrements in functional ability and age-related disease, but also to the increase of social expenditures, such as pension funds and health insurance to support them. The life course perspective leads to important policy and strategy decisions. A complementary approach to improving the health of older men should focus on appropriate interventions at all stages of their lives. The determinants of 'aging' and of 'life expectancy' extend from genetic and molecular determinants to the increasingly powerful forces of environmental, economical, technological and cultural globalisation. Specific measures for the promotion of healthy aging should therefore include: 1) the promotion of a safe environment; 2) healthy lifestyle including proper nutrition; 3) appropriate exercise; 4) avoidance of smoking; 5) avoidance of drug and alcohol abuses; 6) social interactions to maintain good mental health; 7) Preventive medical strategies to delay, decrease or prevent frailty and disabilities, and 8) medical health care including the control of chronic illnesses.

If done effectively, the above measures should result in an increase in the quality of life with a delay, decrease or prevention of disabilities. This would increase the length of productive life of aging populations, decrease dependency, and as a result decrease health costs related to expensive curative

and palliative services. The medical profession, pharmaceutical and health industries will need to be prepared to face up to these challenges.

## F20

### **MEN'S HEALTH RESEARCH IN ASIA – THE DEPTHS AND THE DIMENSION**

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Being male is recognised and proven to be the single largest demographic factor for early death, and this appears to afflict mankind only the last 70 years or so. This daunting fact continues to haunt all of us and puzzle our medical scientists and researchers.

To unravel this medical or human mystery, extensive in-depth researches will be needed. This includes researches on epidemiology to identify the extent of the problems of men's health in the respective communities, clinical researches on key medical problems afflicting men and basic or molecular researches to identify the underlying genetic or molecular differences in the sexes. As understanding of the psycho-behaviour of men is crucial to identifying numerous men's health issues, research in psychological aspects and in social marketing will be vital to bring about effective and powerful forces for behavioural changes. Studies on women's role in motivating and influencing healthy habits and lifestyle changes in men are also increasingly being recognised and verified.

In men's health research, qualitative research is important to understand the social behaviour, the emotions, perception and the action of men which make them more vulnerable to early onset and higher intensity of major diseases. Researchers have long felt that threats on billboards, warnings on products or lectures from doctor are less effective than development of new habits within social groups. Peer opinion leaders and group support are believed to be most critical aids to change lifestyle habits, namely, lose weight, quit smoking and exercise. The 'stick and carrot' approach may be used by insurance companies to bring about healthy habits and vice versa. To bridge the gap between public knowledge and personal health, we may need to evoke strong emotional responses with issues that affect men's thoughts and feelings. To understand all these complex habits, behaviours and attitudes of men, and to bring about a change in health seeking behaviour, broad in-depth research including that used in commercial marketing will be needed to promote health 'products'.

The objective for men's health research is to obtain evidence-based knowledge which is important and could be used in health promotion to reach the target audience – men. This aim is to achieve optimal prevention, early detection of risk factors, increase the opportunity for healthy aging and improve the quality and quantity of life.

Broad-based research in Asian countries should be collaborated spirit to develop an in-depth understanding of men's health issues. Concerted programmes and strategies can then be developed to tackle the problems of men's health and its imminent economic consequences to the Asian countries as a whole.

## F21

### **HUMAN GROWTH HORMONE REPLACEMENT THERAPY AND ANTI-AGING: AN UPDATE**

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Over the past few years, the development of the world's population has continued to switch its path from a state of high birth and death rates to one characterised by low birth and death rates. The current demographic revolution implicates the growth in the number and proportion of older persons, and the older population itself is aging. A major issue at the individual and population levels is how to live these years at a high functional level crucially influencing the quality of life.

Healthy aging in elderly individuals is characterised by a progressive reduction of the daily spontaneous growth hormone (GH) secretion associated with declining levels of the insulin-like growth factor I (IGF-I) leading to a state of functional GH insufficiency. Additionally in women oestrogen deficiency and in men symptoms of testosterone insufficiency occur.

In otherwise healthy elderly individuals age-related changes such as accumulation of abdominal visceral fat mass, demineralisation of the skeleton, reduced lean body mass, increased incidence of cardiovascular morbidity and mortality in consequence of accumulating cardiovascular risk factors, increased fatigue, decreased physical performance, diminished libido and potency and impaired psychological well-being have been observed, similarly in GH-deficient patients.

Case reports as well as results of many short-term and long-term studies about growth hormone replacement therapy in adults demonstrate beneficial effects such as a normalisation of body composition, increase of bone mineral density resulting in a reduction in fracture rate, a significant reduction of cardiovascular risk factors leading to a decrease of cardiovascular morbidity and mortality, and improvement of psychological well-being. Other studies show that GH replacement therapy in combination with testosterone administration in men and exercise performance increases muscle mass, muscle strength and enhances physical vigour and sexual function.

Side-effects following GH replacement such as weight gain arising from fluid retention, arthralgias and muscle pains frequently occurring within days or weeks result from excess replacement alone. These symptoms resolve rapidly with dose reduction or occasionally disappear without any action. Hence, the dose selection should be at a low dose and then titrated according to clinical response and circulating IGF-I levels aiming for IGF-I levels in the upper part of the normal age-related reference range. To date, there is no evidence that GH replacement therapy increases *de novo* malignancies or tumour regrowth in patients. Even with additional administration of testosterone GH replacement does not cause any increase in prostate abnormalities or prostate cancer development.

In summary, there is no doubt that GH continues to play an important role throughout normal adult life. Abundant data of reported beneficial effects of GH replacement therapy in GH-deficient patients cannot be disputed. Long-term follow-up data demonstrate that GH replacement therapy is safe. The pursuit of physical and mental health in increasing aging is more than human, it is humanistic.

## F22

### THE ETERNAL TRIANGLE OF ANDROGEN, SEX AND THE PROSTATE IN THE AGING MALE

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Age-related gender-specific changes affecting the blood androgen profile, sexual function and the prostate status of the ageing male are physiological.

Serum levels of total testosterone (the principal androgen in men) have been shown to decrease by 1–1½% *per annum* after the age of 35 years. The age-related decrease is even more evident when serum free testosterone levels are measured.

Age-related changes in male sexual function include a decline in libido and sexual arousal, delayed and decreased erectile response, retarded ejaculation, quicker detumescence and an increase in refractory period. The size and functional activity of the prostate increase with age after the fourth decade, associated with a gradual rise in the serum levels of prostate specific antigen.

An intimate physiological inter-relationship is inherent between androgen, various aspects of male sexual function and the prostate.

Testosterone exerts its physiological and pharmacological effects via its bioavailable fraction and through its metabolites dihydrotestosterone and oestradiol from 5 $\alpha$ -reductase and aromatase activities. Its main effect on sexual function is centrally mediated through libido. Testosterone modulates the activity of cavernosal nitric oxide synthase, hence enhancing in hypogonadal men the treatment outcome of erectile dysfunction with phosphodiesterase-5 inhibitors. However, testosterone deficiency *per se* is an uncommon cause of erectile dysfunction.

Prostate diseases and their treatment (particularly the treatment of prostate cancer) may be associated with erectile or ejaculatory dysfunction. A history of prostate cancer is an absolute contraindication to testosterone supplementation. When properly indicated for appropriately confirmed androgen deficiency, testosterone supplementation must be accompanied by a vigilant surveillance programme for possible side effects, particularly those on the prostate.

A sound knowledge and understanding of the eternal triangle of androgen, sex and the prostate is essential and central to the management of androgen deficiency, sexual dysfunction and prostate diseases.

## F23

### NATIONAL SURVEY ON MEN'S HEALTH

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A National Survey on Aspects of Men's Health in Singapore was done from 2001–2003. The aims of this national male study were: to conduct a population-based study of males aged 45 to 70 and to determine the prevalence of 'andropausal' symptoms with attention to age-specific prevalence, race-specific prevalence and median age of onset. Risk factors for 'andropausal' symptoms were evaluated by looking at: demographic and ethnic factors, co-morbidities and treatment, lifestyle practices, International Index of Erectile Function (IIEF), knowledge, attitudes and practices for 'andropause', major life events and work related stress, social support and network.

The study involved men aged 45–69 years amongst 490,000 Singapore nationals residing in Singapore. The total sample population came from 1500 computer-generated statistically selected men. The response rate was from 1073 men (71.5%). 167 refused the interview (11.1%). The non-contact rate was from 260 men (17.3%). The survey was conducted via a direct personal face-to-face interview using a 19-page questionnaire.

Classification of andropausal status utilised a ADAM/PADAM Self Rating Scale as follows to make a clinical diagnosis of 'andropause': Physical/vasomotor score  $\geq 5$ , Psychological score  $\geq 4$ , Sexual score  $\geq 8$ . The overall prevalence of 'andropause' in Singaporean males 45 to 70 was: positive physiological scores 16.5%; positive psychological scores 18.3%; positive sexual scores 8.8%. Using the IIEF the prevalence of various grades of ED was: IIEF mild 29.6%; IIEF moderate 16.4%; IIEF severe 13.3%. Correlation of andropausal symptoms with free and total testosterone levels varied between  $-0.68$  to  $+0.68$ . We noted that low hormones do not always lead to problems, not all males with andropause have low hormones, relationship between low hormones and andropause score was not always demonstrated.

We concluded from the study that andropause may be a multifactorial condition. While advancing age is a significant factor in most symptoms, so were other preventable/treatable conditions like diabetes, heart disease and lifestyle factors such as exercise, financial and work related stress, smoking, alcohol intake, regular social activities. Of note were the differences in risk factors for mild and severe ED. We plan future longitudinal studies for correlation with testosterone/free testosterone and bio-available testosterone levels.

## F24

### EVIDENCE-BASED PHYTOPHARMACEUTICALS FOR SEXUAL DYSFUNCTION

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Until recent history in medicine, herbal remedies have been the mainstay for man's ailments. Significant advancement in



plant-derived medicines in the last two centuries in such areas as central nervous system, anti-tumour and anti-inflammatory activities has led to the development and identification of active chemicals and understanding of their modes of action.

While plants and their crude extracts have been in use throughout the history of man as aphrodisiacs, very few of them went through proper scientific methodology in the identification of the constituents and delineation of effectiveness and modes of action. The term 'aphrodisiac' has a collective meaning, which describes improvement of arousal, libido and/or sexual energy and activity. It may either be acting at central/peripheral levels or as an enhancer of endogenous hormones.

One such compound that is extensively studied in our laboratory is *Tribulus terrestris* (TT) (with about 50% of protodioscin extract as active ingredient). TT increased the proerectile relaxant effect and nitrenergic neurotransmission in the rabbit corpus cavernosum and improved sexual behaviour in rats. It also showed an increase in androgenic activity in primates and is used extensively as an energy booster by man. Hence, it appears that TT would also be useful in the treatment of desire or arousal disorders in women. Other such compounds used as aphrodisiacs include *Pausinystalia yohimbe* (yohimbine), *Ptychopetalum olacoides* (Muiru puama), *Eurycoma longifolia* (Tongkat Ali), root of ginseng plant, *Ginkgo biloba* and green oats extract. All these phytochemicals have mild to moderate effects and may be useful as aphrodisiacs in patients with hormonal problems and in psychogenic and mild organic cases of erectile dysfunction. Their efficacy in more severe cases of ED and female sexual dysfunctions needs to be evaluated further.

## F25

### MANY ELDERLY HYPOGONADAL MEN WITH ERECTILE DYSFUNCTION RESPOND FAVOURABLY TO TREATMENT WITH TESTOSTERONE ONLY

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**Introduction:** With the introduction of the phosphodiesterase-5 inhibitors, the role of testosterone in the treatment of erectile dysfunction (ED) went largely into oblivion. This study assessed the efficacy of administration of long-acting testosterone as sole treatment to restore erectile function in men with testosterone deficiency.

**Patients and methods:** A group of 771 patients consulting for ED were analysed. The average period of time they had suffered from ED was 3.6 years. Blood tests included total testosterone, DHT, lipid profile, blood glucose and HbA<sub>1c</sub>, as well as prostate specific antigen. A total of 141 turned out to be hypogonadal men (18.2%), (mean age: 56 yr). Their baseline testosterone levels were  $1.9 \pm 0.5$  ng/ml ( $6.7 \pm 1.7$  nmol/L). Of these 141 men, 122 received IM injections of long-acting testosterone undecanoate at day 1, again after six weeks and thereafter three-monthly, and were prospectively evaluated for a mean of five months (3–11 months). Digital and sonographic examination for prostate was performed every three months. Sexual function was assessed using the International Index of Erectile Function (IIEF) with several domains, at baseline and after 12 weeks of testosterone administration.

**Results:** No patient dropped out of the study in this period of time. No patient reported irritation or pains in the gluteal injection areas or any other adverse events. Following treatment for 12 weeks, of the total of 141 patients, 71 patients reported significant improvement in the sexual desire domain (main value 4.5 to 8.0) and the erectile function domain (from 12 to 25). The remaining 51 patients who had suffered from ED longer than 7 years reported an improvement of sexual desire but no significant improvement in erectile function domain, despite the fact that their testosterone values were normalised ( $4.6 \pm 0.5$  ng/ml or

$15.9 \pm 1.7$  nmol/L). All subjects are still under follow-up. No alterations in prostate parameters were noticed so far.

**Conclusion:** These results show that testosterone-only therapy restored erectile function in the majority of the hypogonadal patients of this group, particularly in patients whose complaints of ED had not been longstanding. These results suggest that testosterone should be considered more often as first line therapy. In case the treatment is not successful, PDE-5 inhibitors or the combination of PDE-5 inhibitors with testosterone might be helpful. In the short-term there are no side-effects of testosterone administration.

## F26

### CONCOMITANT ERECTILE DYSFUNCTION AND PREMATURE EJACULATION: HOW TO MANAGE?

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Erectile dysfunction and premature ejaculation are men's major sexual concerns. Approximately 30% of men with premature ejaculation have co-occurring erectile dysfunction. Men with erectile dysfunction can develop secondary premature ejaculation. Functional neuroanatomy of ejaculation showed that erection and ejaculation share, at least partially, higher neurological control. The first line therapy of erectile dysfunction is phosphodiesterase type-5 inhibitors (PDE-5 Is) such as sildenafil, vardenafil, tadalafil and udenafil. Recently, PDE-5 Is have been reported to have encouraging results in alleviating premature ejaculation. One of the possible mechanisms of PDE-5 Is in the treatment of premature ejaculation is through the NO-cGMP pathway. According to the AUA guideline on the pharmacologic management of premature ejaculation, erectile dysfunction should be treated first in men with concomitant erectile dysfunction and premature ejaculation. The guideline emphasised that premature ejaculation is not a life-threatening condition, therefore, the primary target for premature ejaculation is patient and partner satisfaction.

## F27

### THE AGING MALE – SYMPTOMS' SCALES AND THEIR CORRELATES

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Since time immemorial, self confidence and self esteem have been eroded by signs and symptom of decreased libido, erectile dysfunction, loss of physical strength, changes in body composition and depression. The constellation of symptoms of hormonal deficiency is similar to those related to the aging process. Many clinical features of aging in men are similar to clinical changes seen in younger hypogonadal men.

Testosterone deficiency syndrome (TDS) or symptomatic late-onset hypogonadism (SLOH) were first reported in the literature about 60 years ago. However, extensive clinical research has only been carried out in the last 15 years or so. Numerous studies of late continue to validate the extent and significance of TDS or SLOH in the general male population.

Overall, one third of all men suffer from symptoms suggestive of TDS. Besides sexual dysfunction, TDS affects other important bodily systems and functions, and these include haematopoiesis, bone mineralisation, CNS (behaviour & mood), carbohydrate & lipid metabolism, calcium haemostasis and prostate growth. Common disabilities associated with adult TDS include frailty (contributed by anaemia, musculoskeletal changes, and osteoporosis), CVS diseases (related to lipid and carbohydrate abnormalities), CNS changes (behaviour and mood) and sexual dysfunction (ED, libido and ejaculatory problems).

Adult TDS or SLOH can therefore significantly affect men's overall health and well being, and severely compromise the quality of life of aging men. Many well validated symptoms scales are now being used to assist in detecting aging men with

bothersomeness or disabilities which significantly affect their daily lives.

These commonly used symptoms scales, namely, St Louis ADAM scale, Heinemann's Aging Male Symptoms Scale, The International Index of Erectile Function and The International Prostate Symptoms Scale have been increasingly shown to be correlated with numerous health parameters and medical conditions. Even after allowing for age, many of these correlates were found to be significantly associated with these symptoms scales which are commonly used in the aging male population. More studies need to be done to validate the numerous associations between these clinical instruments and correlate them with important health and disease risk factors of the aging male population. These symptoms scales may prove to be very useful in detecting and treating aging males with hormonal deficiency which may improve their overall health and quality of life.

Studies using clinical symptoms scales which are validated and adapted to local cultures will further enhance the robustness of these internationally used instruments. With the higher expectations of health and quality of life of the aging baby boomers throughout the world, evidence-based clinical instruments may prove to be very useful in the management and promotion of men's health in the aging male population.

## F28

### ENDOCRINOLOGICAL ASPECT OF MALE OSTEOPOROSIS

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Before, osteoporosis was thought of as a disease of postmenopausal women. It is believed that older men have lower risk of fracture than women. But many studies have been developed and are still ongoing, which found that osteoporosis and fractures represent a substantial health burden in older men. In the US, about one fifth of the annual economic cost of osteoporosis fractures is spent on the care of men. A white man of fifty years old of age has about 6% risk of hip fracture and 16%–25% risk of any osteoporosis fracture in the rest of his life.

The National Institute of Health of the United States in their consensus define osteoporosis as progressive bone skeletal disease marked by low bone mass density and bone tissue micro-architectural damage that increases bone fragility and bone fracture. While according to WHO, the term osteoporosis in men refers to >2.5 standard deviation below the bone mass of healthy young men. In this case approximately 1–2 million men in the US are affected, and 8–13 million men have osteopenia. In Indonesia there is no recent epidemiological study to find out the incidence of osteoporosis in older men. Increasing life expectancy in men will surely increase health problems because of osteoporosis in the world.

Osteoporosis fractures usually occur in vertebral bone (compression fracture), distal radius and proximal femur (hip fracture). It also could happen in proximal humerus, distal femur and in the rib bones. Fracture of proximal femur correlates with increasing mortality rate 15–20% in older people.

Due to the definition of osteoporosis there are two factors that contribute to bone strength, they are: bone mass density and bone quality. Bone quality refers to bone macro-architecture, bone turnover and bone micro-architecture damage.

Bone mass density is affected by bone peak mass. Bone mass is formed during childhood and puberty. Bone mass formation during puberty depends on sex hormone level and epiphyseal plate closure. Peak bone mass is usually achieved within 20–30 years of age and will decline after age 35. In older people this decline happens because of bone remodelling. Unbalanced process between bone resorption and bone formation caused by imbalance works of osteoclast and osteoblast is affected by two factors: 1) external factors including genetic and environmental factors, such as: physical activities, life style (smokers, alcoholic, drug abuse), nutrition

(low calcium intake, maintaining certain blood calcium level involving hormones such as parathyroid, glucocorticoid, insulin, growth hormone, oestrogen, progesterone, calcitriol); 2) internal factors: a) osteoblast. Osteoblast are cells that form bone matrix. They produce intracollagen fibres. Oestrogen is one of the hormones that sensitises osteoblast activity to produce collagen, while calcitriol sensitises osteoblast to form bone mineralisation. Both collagen and bone mineralisation will form perfect bone; B) osteoclast. Osteoclast are cells derived from macrophage that absorb bone. They are formed in the bone medulla. Oestrogen inhibits osteoclast activity at certain levels.

So it is fully understood why in postmenopausal women osteoporosis happens, because oestrogen level decline till diminished so that the coupling process between osteoblast and osteoclast becomes disrupted. There is more bone resorption due to the remodelling process that isn't followed by enough bone formation. At the end it will result in decrease in bone mass density.

What happens in male osteoporosis? Even though oestrogen and bio-available estradiol in some studies show better predictor of bone density, it cannot be abandoned that there are androgen receptors found in osteoblast and mesenchymal cells. The effect of testosterone on bone is both a direct effect as well as through aromatisation to estradiol. Short term studies found that androgens reduce bone resorption rather than effecting new bone formation. In a study by Kenny et al. in 76 men age 65–87 years old, randomly receiving transdermal testosterone and placebo, all men who received supplemental calcium and vitamin D for 1 year found an increase in bone density especially at femoral neck and an increase in muscle strength. Somehow the effect of testosterone on bone is still controversial as not all investigators found improvement with testosterone. Some people concluded that male osteoporosis usually secondary osteoporosis because of certain diseases and drugs.

A recent study found that several men who lack the alpha oestrogen receptor or lacking the aromatase enzyme required to convert testosterone to oestrogen have low bone mass, high rates of bone turnover and unfused epiphyses. This prompted many studies on how oestrogen and estradiol affect male osteoporosis. A study by Gennari et al. reported men with low estradiol had higher levels of bone turnover and high rates of bone loss at the hip. A study by Khosla et al. found that oestrogen levels in multivariate models were more strongly related to bone loss and bone resorption markers than were testosterone levels.

Although there are many controversies about factors affecting male osteoporosis, newer studies help us to find another alternative therapy in treating osteoporosis in male. Today bisphosphonates and TSH using testosterone still become preferable therapy in male osteoporosis. But we still need long-term studies to find out whether this therapy may actually decrease fracture rates in men.

## F29

### LOSS OF LIBIDO IN MEN: EVALUATION AND TREATMENT

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**Introduction:** The overall prevalence of reduced or absent libido in men is 31%, only slightly lower than in women (43%). This increases with aging. The andropause, though important, is not the only cause. Physicians must therefore guard against specialty-skewed biases about etiology and treatment. It thus behoves all physicians to be well informed and open-minded about this. If necessary, a multi-disciplinary or team approach must be used in the better interest of the patient.

**Causes:** Broadly, these may be classified as: i) relationship-related causes; ii) lifestyle-related causes; iii) circumstantial causes; iv) endocrinological causes; v) other organic disease; vi) substance and drug use/abuse, and; vii) miscellaneous.

**Evaluation:** A detailed history is important. It is recommended that both man and partner be interviewed. Multiple causes

may co-exist in the same patient. Each must be treated separately. A high index of clinical suspicion is important. Laboratory tests, especially endocrine, must be performed as indicated.

*Treatment and results:* Treatment will depend on underlying cause/s and must be monitored/reviewed periodically. Many men will respond well if the cause is corrected. Some, however, will remain refractory to treatment. Good counseling, peer support, and discussion groups are helpful. This author offers an online discussion group. This confers anonymity on discussants.

*Conclusion and discussion:* The WHO, in 1994, has recognised that sexual health is a fundamental human health right. Today, we know that this applies to aging and aged males as well. Sexually conservative societies should wake to this reality and enrich their lives.

### F30

#### PEYRONIE'S DISEASE IS A DISEASE OF AGING MALES

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*Introduction:* Peyronie's disease (PD) has been known for more than 400 years. Still, however, not too much is understood about its etiopathogenesis or therapeutic alternatives. PD is primarily a disease of elderly males above 50, and is characterised by the development of one or more plaques or nodules in the tunica albuginea layer of the penis. This is usually accompanied by pain, varying degrees of deformity, and sometimes, erectile dysfunction (ED, impotence). Though etiopathogenetic theories abound, the pathology is basically one of idiopathic inflammation and fibrosis and has a natural progression course of 12 to 18 months, at which point the inflammatory and fibrotic processes come to an end.

Pain relief, arrest of progression of deformity, rectification of fixed end stage deformity, and treatment of concomitant erectile dysfunction are the main therapeutic considerations. Multiple modalities for each have been described over the years. This paper will present an overview of all these with a special focus on the penile dermal flap operation, first described by this author in 1992.

*Materials, methods and results:* 102 cases with end stage PD, who have undergone surgery using the penile dermal flap

between 1989 and the present, and who have been followed up at least for 24 months after surgery, have been included in this study. Cumulative complication and failure rates have been less than 8%.

*Conclusion and discussion:* The penile dermal flap operation is simple, safe and highly effective in PD. It is recommended in both circumcised and uncircumcised populations.

### F31

#### THE IMPORTANCE OF YOGA, MEDITATION AND LIFESTYLE MODIFICATION IN THE MANAGEMENT OF THE AGING MALE

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*Introduction:* With the worldwide increase in human life expectancy, aging medicine (gerontology, geriatrics) has become an important specialty. Many health conditions and diseases are associated with the aging process. It is important to be able to prevent/treat these in order to preserve/improve the quality of life (QoL) in old age. Longevity has no meaning if good health cannot be enjoyed until the very end of life.

*Materials and methods:* A study of some of the oldest living people on earth, and extrapolations from centuries old lifestyle practices like yoga and meditation, have led to a renewed interest in what is referred to condescendingly as 'alternative' or 'complementary' medicine. Lately, many scientific publications extolling the beneficial effects of these have begun to appear in the 'mainstream' scientific literature.

*Results:* Benefits with yoga, meditation and lifestyle modification have been reported in many aging-related disease states, e.g., cardiovascular and pulmonary disease, osteoarthritis and backaches, diabetes, metabolic disorders, post-stroke hemiparesis, memory, neuro-cognitive function, musculoskeletal suppleness and strength, body weight, sexual function, prostatic and other urologic disease, anxiety, depression, stress, backaches, cancer, and indeed, on QoL and life expectancy itself in general.

*Conclusion and discussion:* Many diseases of aging are related to faulty lifestyle practices and stressful living conditions in earlier years. A high index of awareness of this is important, and, since prevention is always better than cure, pre-emptive steps should be begun in middle age itself. Yoga and meditation can and do make a big difference, and are cost-effective moreover.

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