

Translational andrology and urology research: Where is it heading? --Report of the 5th Greatwall Translational Andro-Urology Forum (GTAUF2012)

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The 5th Greatwall Translational Andro-Urology Forum (GTAUF2012) in conjunction with the launch of the new journal *Translational Andrology and Urology* (TAU) was successfully held in Hainan International Conference and Exhibition Center, Haikou, China on March 8-12, 2012 (Figure 1). The forum was co-chaired by Prof. Ying-Lu Guo and Prof. Tom F. Lue, both lifetime presidents of GTAUF and Editor-in-Chief of TAU and professor Zhi-Ming Bai, the president of local organizing committee of GTAUF2012 (Figure 2).

Embracing the concept of the translational medicine, over 800 attendees from domestic and abroad gathered together to discuss how the scientific results of andrology and urology research can be translated into the clinical practice for better care of human health (Figure 2). More than 230 research papers were presented this forum and more than 100 lectures were delivered by 40 experts from America, Europe, Asia and 50 experts from China, lectures delivered by some of the editorial board members of TAU (Figure 3, 4, 5), such as Dr Arthur Burnett from The Johns Hopkins, Dr Run Wang from University of Texas Medical School, Dr Gerald Brock from University of Western Ontario (Table 1). In addition to Plenary Sessions, China-Japan-Korea (G3) Andrology-Urologist Symposium and the 3rd Cross-Strait Andro-Urologist Symposium were specially organized to strengthen regional scientific exchanges and cooperation. Live surgery & Video presentation at Haikou City Hospital on March 11th was informative, vivid and dynamic and were warmly welcomed by attendees. This report summarized the key

content discussed in this forum.

Calculus

Nephrolithiasis is a common disease in urology. Professor Stoller from UCSF gave us some reports about the relationship between nephrolithiasis and systemic diseases. Nephrolithiasis is a risk factor for systemic diseases including hypertension, diabetes, obesity and vice versa. Some proposed mechanisms within this relationship were also presented. New research shows accumulating epidemiologic and anatomic evidence for vascular etiology of urinary stones. All these may have an impact on therapy of nephrolithiasis in the future.

CP (chronic prostatitis) & BPH (benign prostate hyperplasia)

For this topic, Professor Jong Kwan PARK gave the speech about Nocturia and sex hormones in men with symptomatic BPH. Their survey conducted on 924 male patients indicated the conclusion that the severity of LUTS (lower urinary tract symptoms) was associated with age and serum levels of TT (total testosterone), but only age correlated with the measures of BPH, especially prostate volume. Their findings also support that testosterone deficiency may be a pathophysiological mechanism connecting with LUTS.

Treatment of BPH & CP is one of the hot topics in this field. Professor Yong Yan introduced current management of BPH including the latest development in the diagnostic



Figure 1 Opening ceremony of the forum.



Figure 2 A: Ying-Lu Guo, MD. Institute of Urology, Peking University, Beijing, China; B: Tom F. Lue, MD, ScD (Hon), FACS. Department of Urology, University of California, San Francisco, San Francisco, USA; C: Zhi-Ming Bai, MD. Department of Urology, Haikou Municipal Hospital, Haikou, China; D: Attendees from more than 30 countries.



Figure 3 A: Arthur Burnett, MD. Johns Hopkins Medical Institutions, Baltimore, Maryland, USA; B: Run Wang, MD, FACS. University of Texas Medical School at Houston and MD Anderson Cancer Center, Houston, TX, USA; C: Gerald Brock, MD, FRCS. Professor of Surgery Division of Urology University of Western Ontario, Canada; D: David Ralph, MD, BSc, MS, FRCS. Institute of Urology, University College, London, UK.



Figure 4 A: Leland W. K. Chung, MD. Uro-Oncology Research, Samuel Oschin Comprehensive Cancer Institute, Cedars-Sinai Medical Center, Los Angeles, CA, USA; B: Li Qun Zhou, MD. Department of Urology, Peking University First Hospital, Institute of Urology, Peking University, Beijing, China; C: Michael Coburn, MD. Scott Department of Urology, Baylor College of Medicine, Houston, Texas, USA; D: Nianzeng Xing, MD. Department of Urology, Affiliated Beijing Chaoyang Hospital of Capital Medical University, Beijing, China.



Figure 5 A: Shu Jie Xia, MD. Department of Urology, Shanghai First People's Hospital, Shanghai Jiao Tong University, Shanghai, China; B: Zhi Jie Chang, PhD. Department of Biological Sciences and Biotechnology, School of Medicine, Tsinghua University, China; C: Zhong-Cheng Xin, MD. Andrology Center and the Department of Urology, Peking University First Hospital, Beijing, China.

Table 1 Lectures at GTAUF2012 by some of the editorial board members of TAU

Speaker	Lecture	Reference
Arthur Burnett (USA)	Testosterone therapy in Hypogonadal man with sickle cell disease	(1)
Arthur Burnett (USA)	Testosterone replacement after prostate cancer treatment	(2)
Ching Shwun Lin (USA)	Stem cell for urinary incontinence	(3)
Ching-Shwun Lin (USA)	PDE5, the key enzyme for erectile function	(4)
David Ralph (USA)	Phalloplasty for the genetic male	(5)
Gerald Brock (Canada)	Post prostatectomy erectile optimization	(6)
Gerald Brock (USA)	PDE5i's are they too important a drug class to be used only for erectile dysfunction?	(7)
Hong Li (Chengdu)	Male sexual function before and after urethral stricture surgery	(8)
Jae-Seung Paick (Korea)	Ejaculatory disorder in Medical and surgical Therapy of BPH	(9)
Jun Kyu Suh (Korea)	Cavernous angiogenesis as a novel therapeutic strategy for erectile dysfunction	(10)
Leland Wei-Kuo Chung (USA)	Osteomimicry in Prostate Stromal-Epithelial Interaction: From Biology to Therapy	(11)
Li Qun Zhou (Beijing)	Laparoscopic surgery on Urology in China; Present and future	(12)
Li Qun Zhou (Beijing)	Retroperitoneal laparoendoscopic single-site radical nephrectomy using self-made single-port device: Initial experience	(13)
Michael Coburn (USA)	Male Genital Trauma and Reconstructive Surgery - "The Houston Experience".	(14)
Nam Cheol Park (Korea)	Current Management of Hemospermia	(15)
Nian Zeng Xing (Beijing)	Laparoscopic Nephron-Sparing Surgery with Selective Clamping of Renal Arterial Branches Using Laparoscopic Ultrasonography	(16)
Run Wang (USA)	Androgen Deprivation therapy for prostate cancer and the impact on male sexual function	(17)
Sae Woong Kim (Korea)	Phytotherapy : Emerging Therapeutic Option in Urologic Disease	(18)
Sang Wen Han (Korea)	Vesicoureteral reflux and bladder dysfunction	(19)
Shu Jie Xia (Shanghai)	The Exploitation and application of the new laser technology in minimally invasive urologic surgery	(20)
Tom F Lue (USA)	New concept and algorithm for priapism	(21)
Tom F Lue (USA)	The challenges of Peyronie's disease	(22)
Xin Gao (Guangzhou)	Nerve-sparing laparoscopic radical prostatectomy (100 cases report)	(23)
Yong Yang (Beijing)	Painful bladder syndrome/interstitial cystitis	(24)
Zhi Jie Chang (Beijing)	A Novel Gene Regulates Tumorigenesis at the Transcriptional Level	(25)
Zhong Cheng Xin (Beijing)	AI-Ghorab Shunt plus Intracavernous Tunneling for Prolonged Ischemic Priapism	(26)
Zhong Cheng Xin (Beijing)	Combined oral therapy with sildenafil and doxazosin GITS for treating Chinese patients of ED with LUTS/BPH	(27)

evaluation, treatment alternatives, and follow up plan of BPH. As for the treatment of BPH, we have so many new choices, including TUNA (transurethral needle ablation), TUMT (transurethral microwave thermotherapy), HoLRP (HoLEP, transurethral laser enucleation with Holmium), transurethral ablation etc. Professor Hongjun Li talked about the new insight into CP. His opinions include: take CP as a symptoms, rather than a disease entity; gold standard for the diagnosis does not exist; target for the treatment is to release symptoms and improve quality of life; combined treatment can expect to good results; antibiotics is not important; cure or radical treatment is not a question; time is very important in the restoration process. Professor Haisong Li gave a speech about "The study on the safety and efficacy of GR-QLX sonostat in treating CP". Their results suggested that GR-QLX sonostat therapy is safe and effective for treating CP, yet further study is recommended.

Prostate cancer

The basic research in prostate cancer is always the focus in andrology field. Professor Long Cheng LI introduced KLF4 gene - a metastasis suppressor gene for prostate cancer. Their study suggests that KLF4 is a strong predictor of prostate cancer metastasis and may play an important role in governing key cell growth, motility and invasion events. Professor Leland Wei-Kuo Chung's topic is "Osteomimicry in prostate stromal-epithelial interaction". They found that prostate cancer cells with bone metastasis potential often expressed bone-like proteins (osteomimicry), including osteocalcin, osteopontin, RANK (receptor activator of NF- κ B) and RANKL (RANK ligand) etc. new approaches targeting osteomimicry and the converging signaling between RANKL/RANK and HGF/SF/c-MET would be novel therapies for the control of bone metastasis and the lethal progression of prostate cancer in patients.

The kinds of treatment for prostate cancer are abundant, including surgery, radiotherapy, and chemotherapy etc. Professor Xin Gao introduced NSLRP (nerve-sparing laparoscopic radical prostatectomy). They performed NSLRP on 100 patients, and after surgery continually low dose of PDE5 inhibitor was used. The results showed that about 67% of the patients preserved sexual function 1 year after the surgery. Most (73%) patients' IIEF5 scores varied from 8 to 21. Urinary control rate at 1 year after the surgery was 99%. These

data suggest that the NSLRP could effectively preserve the most of the patients' sexual function, enhance the early recovery of erectile function and urinary continence. After the surgery, using low dose of PDE5i at early stage could benefit the early recovery of erectile function. Professor Zhiping Wang talked about IHT (intermittent hormone therapy). For the treatment of prostate cancer, he considers IHT as a promising alternative comparing to continuous HT (hormone therapy). IHT has many benefits including reduction of treatment-related side effects, potential delay of progression to CRPC (castration-resistant prostate cancer), and reduced health care costs. However, questions remain as to whether the current scientific evidence supports the use of IHT and how IHT should be applied in daily clinical practice. Professor Yi Huang's topic was "The combination of IHT with 125I BT (brachytherapy) for the treatment of locally advanced prostate cancer". They applied this joint treatment to 46 cases of prostate cancer with T3 clinical staging, after the operation, they received the follow-up treatment (varying from 1 to 4 cycles). Eventually, 5 patients developed bone metastasis, 1 patient was diagnosed as bone metastasis and died 52 months after operation, 21 patients did not suffer the PSA relapse during the follow up. So the combination of these two treatments may be an effective and safe alternative for locally advanced prostate cancer, but their result need to be approved by more multicenter prospective randomized trial.

Laparoscopic Surgery

Professor Liqun Zhou from Peking University first hospital introduced the laparoscopic surgery on urology in China. He focused on LESS, a technique which has lesser complications compared with traditional endourology operations and has brighter future in China. But LESS requires more complicated skills and its advantages need to be supported by more EBM trials.

Professor Weixing Zhang shared their clinical experience in the application of extravascular stenting for the treatment of Nutcracker Syndrome. Comparing to conventional treatments, extravascular stenting through laparoscope is a feasible, safe option for the treatment of this disease. Its advantages include avoiding sewing of the vessels, without the risk of thrombosis, lesser operation time etc. But the impact of the ligation of left reproductive vein needs more advanced discussion.

Surgery related sexual dysfunction

Many experts talked about the surgery related sexual dysfunction in this forum. Professor Gerald Brock introduced the mechanisms underlying the impact of surgery in the pelvis on erectile function. He highlighted the strategies aimed at preserving the function of nerve, vessel, and cavernous muscle including use of PDE5i, penile traction devices, intracavernous injections, sexual counseling and other supportive measures. Professor Jae Seung PAICK's topic was "EjD (Ejaculatory disorder) in medical and surgical therapy of BPH". He introduced the results of survey for EjD and LUTS/BPH done at his institution. They found about 49.7% of the patients were sexual active (had sexual relationship during the last 4 weeks), while the remaining 50.3% of the patients were sexual inactive. In sexually active men, ejaculatory function could be significantly worsened after medical or surgical treatment on LUTS/BPH. They think that the evaluation of ejaculatory function is mandatory and that questionnaire assessing ejaculatory volume and satisfaction is appropriate tool for evaluating before the initiation of the treatment. Professor Run Wang talked about ADT (androgen deprivation therapy) for prostate cancer and the impact on male sexual function. ADT as a powerful treatment option for advanced prostate cancer has many side effects including sexual dysfunction. Currently intermittent androgen deprivation, penile rehabilitation, and prosthesis implantation may be the promising alternatives to minimize these side effects. Professor Hong Li focused on the male sexual function before and after urethral stricture surgery. They investigated the sexual function in men with urethral stricture before and after the surgical treatments. The data suggested that the declined erectile function was more possibly occurred in patients with recurrence of urethral stricture and surgical complication. The postoperative urination function status was directly related to the erectile function.

Priapism

Priapism is one of the tough conditions in andrology field. In this forum, Professor Xinhua Zhang introduced a newly established model. It is an easily initiated, long duration BLEB (blebbistatin) - induced rat priapism model. The subsequent trials showed that corpus cavernosum contractile molecules were up regulated and relaxation molecules were down regulated with ICP (intracavernous

pressure) reversible in the early compensated stage while these pathways were oppositely affected in the later decompensated stage with eventual fibrosis and necrosis.

Professor Zhongcheng Xin shared their experiences in CC-CSS+ICT (corpus cavernosum-corpora spongiosum shunt/AI-Ghorab shunt +intracavernous tunneling) for the treatment of PIP (prolonged ischemic priapism). Their recent study to investigate the efficacy and safety of CC-CSS+ICT showed that this combined therapy could quickly reduce penile rigidity and pain so as to improving the symptoms of PIP. CC-CSS+ICT may be a promising therapeutic method for this troublesome condition.

PDE5 & PDE5i

The invention of PDE5i was a milestone in the treatment of male sexual dysfunction. With the widely usage of PDE5i, research about PDE5 also gets more and more attention. In this forum, professor Ching Shwun LIN gave a speech titled "PDE5: a research odyssey". He proposed some natural or man-made issues which may help us perform effective studies and avoid making erroneous interpretations.

Professor Jad, Amr Momtaz A talked about the effectiveness of PDE5i in Saudi men with ED in clinical practice. Their findings suggest that both sildenafil and tadalafil may assist an individual in extending/enhancing the excitement phase or prolonging the sexual interaction, but there is a major point of difference between the short-acting agent sildenafil and the longer acting tadalafil. While Professor Gerald Brock's focus was "Are PDE5is too important drugs to be used only for ED". PDE5i are currently approved in many parts of the world for a diverse group of targets, including BPH/LUTS, primary pulmonary hypertension and of course ED. Over the next few years other therapeutic targets such as hypertension, Raynaud's and endothelial dysfunction may also achieve approval. Here, professor Gerald Brock showed a review of the pathophysiology and mechanism of action of PDE5i for these areas of medicine.

Testosterone

Testosterone supplementation is a common and controversial issue. We here summarize the content about this issue in this forum.

Professor Kwang Sung PARK talked about the role of testosterone as a biomarker in aging male. He showed that

decreased testosterone levels in aging male were associated with negative health outcomes. Lifestyle interventions such as weight control or healthy diet might have a role in prevention of age related decline in testosterone level. Randomized, controlled clinical trials have found a favorable effect of testosterone supplementation in men with low-to-normal testosterone levels.

Professor Xiaowei Zhang introduced the relationship between androgen replacement therapy and psychological distress/quality of life in LOH (late onset hypogonadism) patients in Chinese population. They conducted their experiments mainly by androgen administration and psychiatric questionnaires. The results showed that androgen replacement not only improve androgen deficiency associated symptoms, but also induce comprehensive improvement in psychological issues.

Professor Arthur Burnett gave us two excellent speeches about testosterone supplementation in this forum. The first is about testosterone replacement after prostate cancer treatment. His opinions include there is no evidence that normal levels of testosterone promote carcinogenesis; there is no evidence that therapy initiates or promotes de novo or pre-existing prostate cancer; establish a clear benefit of treatment before assessing long-term risks; larger randomized trials with extended follow-up are needed. His second speech is about testosterone therapy in hypogonadal men with sickle cell disease. Their research indicated that hypogonadism occurs commonly in patients with SCD, and primary testicular failure is likely the main cause for this hormonal abnormality; testosterone deficiency may be involved in the etiopathogenesis of SCD-associated priapism; preservation of a eugonadal environment may serve to maintain normal penile homeostasis in SCD, and judicious testosterone replacement in this population offers a possible treatment for recurrent priapism.

ED

The discussion about ED was abundant including the basic research, etiology, diagnosis, and treatment etc.

Professor FX .Arif Adimoelja gave a speech titled “What do obesity and ED mean to men’s health”. He pointed out that obesity is related to decreased level of blood serum testosterone, ED, prostate health, CVD (cardio-vascular disease), diabetes etc. Healthy life style and habits are very important to men’s wellbeing. While, Professor Yutian Dai introduced the relationship between aging and ED. Their team have done some basic research about the function

of SIRT1 (Sirtuin1) gene in aging-related ED. STR1 is a member of Sir (silent information regulator) gene family, which has important function in the regulation of life span. Their results indicated that SIRT1 gene may be a new target for the treatment of aging-related ED.

Jintetsu Soh did some research on normal erectile function. They used real-time motion analysis of penile erection with Turbo-FLASH MR imaging system to analyze the dynamic morphological changes in the penis during a normal erection. The results showed that from initiation to completion of erection, the required time ranged from 110 to 120 (median 115) seconds, changes in volume of corpus cavernosum ranged from 28 to 35 (median 32) mL, maximum volume increase rate ranged from 0.5 to 0.8 (median 0.66) mL/s. Because the number of the involved volunteers was only 5, further study may be needed to prove these novel parameters. Professor O Apolikhin introduced multispiral computed pharmacocavernosography. Their study showed that dynamic cavernosography computer is a high-sensitive method of “second-line diagnostics” in determining the type of venoocclusive ED and identifying structural organic changes of the corpora cavernosa.

Diabetes and ED have close relationship in etiology. Professor Hunter Wessells talked about the mechanisms of diabetes associated ED. By using pilot genome wide association research, professor Wessells’s team identified two SNPs (single nucleotide polymorphism) located on chromosome 3 in one genomic loci that were associated with ED. Their data also justified a combination of intensive glucose and blood pressure that has the potential to reduce the risk of ED in men with type I diabetes. Professor Chunhua Deng focused on the impact of GSP (glycosylated serum protein) on endothelial dysfunction and vascular ED. They conducted their experiments on male SD rats and ED patients (with control). They found that GSP could impair endothelium-dependent dilation of rat aorta in vitro. Potential endothelial dysfunction and glycometablism disorder might present in young ED patients without obvious causes. GSP significantly correlated with endothelial dysfunction and ED and it might be an early predictor of ED.

LUTS/BPH also has close relationship. Francois Giuliano talked about the link between ED and LUTS. His opinions include there is an association between BPH/LUTS and ED which is independent of age and co-morbidities; Further studies are required to more fully understand of the Pathophysiological mechanisms for

BPH/LUTS-associated ED; PDE5i taken daily improve LUTS associated with BPH. Professor Zhongcheng Xin introduced combined oral therapy with sildenafil and doxazosin GITS for treating Chinese patients of ED with LUTS/BPH. They conducted their trial on 250 patients corresponding to the criteria in 5 big cities in China (Beijing, Shanghai, Changsha, Wuhan, and Guangzhou). The result indicated that this combined therapy for the treatment of ED with LUTS secondary to BPH is safe and effective comparing to Sildenafil monotherapy. Akira Tsujimura introduced combined testosterone and PDE5i for ED and LUTS. Because the effect of testosterone on LUTS is still controversial and PDE5i has recently been proven to not only improve ED symptoms but also improve LUTS, professor Tsujimura introduced several data of the treatment for patients with ED and LUTS by combining TRT (testosterone replacement therapy) with PDE5i administration.

For the treatment of ED, we have so many choices. Professor JiuHong Yuan introduced VT (vacuum therapy), including VCD (vacuum constriction device) and VED (vacuum erectile device). Recently, the rat VED had been created and applied on the bilateral cavernous nerve crush rat model. Their team had been in the investigation of the underlying molecular mechanisms and optimal protocols. With more related research undergoing, we believe VT will play a more and more important role in the treatment of ED. Professor Zhichao Zhang proposed a new concept for treating ED -- Planning therapy. This therapy mainly involves PDE5i administration, but it has courses of treatment and criterion of decreasing dosage or stopping medicine. They believe that ED should be treated as chronic disease like hypertension or diabetes. The goal of planning therapy is to achieve the maximum effect with minimal dosage or cure ED. They conducted a prospective, randomized, controlled trial. The results showed that comparing with control group and sildenafil-on-demand group, the sildenafil-low-dose-everyday group could restore better sexual function, which indicated that planning therapy might have the possibility to cure ED. But more patients and information are needed to form a consummate therapy model. Feng Zhou introduced the effects of icariin on improving erectile function in STZ (streptozotocin)-induced diabetic rats. Their results showed that icariin treatment preserved penile hemodynamics, smooth muscle and endothelial integrity, and nNOS expression in the penis of diabetic rats. Down regulation of TGF β 1/

Smad2 signaling pathway might mediate these effects. At the same time, Alan Shindel also gave a speech on Icariin for the management of sexual health concerns in men. He discussed the existing evidence supporting the use of icariin as a treatment for ED in men and discussed future directions of this traditional remedy. Professor Jun Kyu SUH introduced a novel therapeutic strategy for ED -- cavernous angiogenesis. They conducted their experiment on ED model by local delivery of both COMP-ang1 or angiopoietin-1 and VEGF gene in order to enhance angiopoietin-1/Tie2 signal pathway which had been proven to be down regulated in ED with hypercholesterolemia. The studies showed that enhancement of angiopoietin-1/Tie2 signal pathway promoted endothelial cell regeneration and strengthen the endothelial cell integrity. This local therapy may have great impact on the treatment of vascular disease-induced ED. Xuefeng Qiu talked about neurotrophic effect of BM-MSC (bone marrow mesenchymal stem cells) for ED in diabetic rats. Their results showed that intracavernous injection of BM-MSC is effective on improving nerve regeneration in diabetic rats and paracrine effects of BM-MSCs may be involved in this improvement.

For the surgery for the treatment of ED, Professor Zhongcheng Xin shared his experience of AMS penile prosthesis implantation for treating Chinese patients with severe ED. Professor David Ralph introduced several kinds of complication in penile implant surgery and some tips were also recommended including having all of the devices available with the appropriate instruments, taking care about device contamination, correcting intraoperative complications in time, paying attention to detail about post operative care etc.

Hemospermia

Nam Cheol PARK introduced variable etiologies, diagnostic tools, and therapeutic options for hemospermia. Weidong Song shared his experience for treating hemospermia by transutricular seminal vesiculoscopy. Their experiments involving 89 patients demonstrated that transutricular seminal vesiculoscopy was safe and effective in the diagnosis and treatment of recurrent hematospermia with minimal complication.

PE (premature ejaculation)

Professor Chin Pao CHANG introduced the latest

development on research of PE, including its epidemiology, etiology, diagnostic criteria, and treatment. Based on the surveys, he highlighted that PE is very common in men with an occurrence of 20-40%, but only 9% of men with self-reported PE sought help from a physician. Of the men who had sought treatment for their PE, 92% reported little or no improvement in their condition. So, all these emphasize the need for effective, well-tolerated, and acceptable treatments for PE.

Leydig cell

Bin Yao gave us a speech on “Annexin 5 stimulates testosterone release from the primary cultured rat Leydig cells”. In their experiments, isolated rat Leydig cells were treated with annexin 5 and related siRNA in sequence, then testosterone production and expression of related enzymes (StAR, 3 β -HSD etc) were detected. The results showed that annexin 5 significantly stimulated testosterone secretion from rat Leydig cells in dose and time dependent manners, the mechanisms might be related to ERK1/2 signaling that mediated the expression of related enzymes. Weiren Li talked about the relationship between autophagic deficiency and steroidogenic decline in Leydig cells of aged rat. They found that reduced testosterone production in Leydig cells of aged rats was associated with decreased autophagic activity and increased intracellular ROS (reactive oxygen species) might be involved in this process.

Stem cell

The usage of stem cells in the field of andro-urology is a hot point in this conference.

Professor Ching-Shwun Lin talked about stem cell therapy for SUI (stress urinary incontinence). He pointed out the defection of existing treatments and the advantages of the stem cell therapy might have. ADSC (adipose tissue derived stem cell) is a kind of stem cells located in the inner and outer membrane of the capillaries in adipose tissue. They have promising prospect, because they are easily to get and with little ethical issues. After injection, these cells can migrate to the injured positions and promote the angiogenesis and muscle growing by secreting many kinds of cell factors. These are to the beneficial of the treatment of SUI.

Professor Yuanyuan Zhang introduced USCs (urine-derived stem cells) which have many stem cell markers, could

renew themselves, and have multi-potent differentiate ability. USCs can generate into smooth muscle, endothelia, and urothelial cells etc. The number of cells from one 200 mL urine sample can provide enough cells to cell therapy in andrology. Therefore, USCs might be a viable source for the treatment of ED, SUI, vesicoureteral reflux and engineering urethral or bladder tissues.

Doctor Guangyong Li also gave us a lecture about his research of periurethral injection of ADSC for the treatment of SUI in a rat model. The rats were induced to develop SUI by postpartum vaginal balloon dilation and bilateral ovariectomy and the ADSCs were isolated from the periovary fat and labeled with EdU (thymidine analog). Cystometric analysis showed that ADSCs treatment resulted in significant recovery of urinary voiding function, as compared with SUI group. Histological analysis showed that ADSCs were capable of restoring the fibrous-muscular system and vessel system in the urethra. The expression of VEGF and P-ERK1/2 protein were higher in ADSCs treated group and this might play an important role in restoring pathologic changes of SUI.

Varicocele

Professor Koichi Nagao shared their experience of microsurgical varicocelectomy at Toho University. He described the procedures they performed on spermatic veins and post operation follow ups in detail. They mainly handled the internal and external spermatic veins with a diameter of 2 mm or more, the artery were preserved with particular care. The patients recovered smoothly after the operation without serious complication. The semen analysis showed a enhanced quality comparing to preoperative analysis. Yiming Yuan shared Chinese experience of microsurgical subinguinal varicocelectomy for infertile men. Their results provided the evidence that this kind of surgery is effective for infertile men with palpable varicoceles and impaired semen quality. After the operation, increased spontaneous pregnancy rate and improvements in semen characteristics, testosterone, and inhibin were observed. Jinxin Lv gave us speech on “Efficacy and safety of RPLV (retroperitoneal laparoscopic varicocelectomy): a comparative study with TPLV (transperitoneal laparoscopic varicocelectomy)”. Their data suggested that, comparing to TPLV group, the operative time of RPLV group was shorter. At the same time, there were less complications in RPLV group.

EDO (ejaculatory duct obstruction)

Professor Yin hao Sun shared their initial experience on TRU-SVS (Transurethral seminal vesiculoscopy) using for EDO. They performed a retrospective study on TRU-SVS using a 6F vesiculoscopy and its impact on the diagnosis and treatment of EDO. The data indicated that this method provided direct access to the seminal vesicle and offered the advantages of fewer complications and optimal sperm recovery.

Idiopathic azoospermia

For the etiology of idiopathic azoospermia, Professor Yaoting Gui did the screening and identification of the genes related to idiopathic azoospermia. They detected the mutations in the genes related to spermatogenesis in patients with idiopathic azoospermia or fertility by massively parallel sequencing. They focused mostly on the rare non-silent variants and identified a total of 84 genes showing substantial enrichment of novel mutations. The data showed that the patients with idiopathic azoospermia harbored more rare non-silent mutations in multiple genes, which may confer risk to idiopathic azoospermia. William J. Huang did the genetic testing of infertile males with NOA (non obstructive azoospermia) or severe oligozoospermia in Taiwan. They analyzed the karyotyping patterns of infertile males with azoospermia or severe oligozoospermia in Taiwan and high incidence of chromosomal anomalies was found. This suggests the need for routine genetic testing and counseling in these patients, especially when certain hormonal characteristics were reported. Specific cytogenetic abnormalities or chromosome loci might be worth of further investigation to discover their possible relationship with infertility. With their limited data, gr/gr deletion seemed to be a poor prognostic factor for successful sperm retrieval, but we can't confirm it now.

For the Y-CMD (Y chromosome microdeletions), Eitetsu Koh introduced a novel Y-CMD With the Loss of an Endogenous Retrovirus Related, Testis Specific Transcript in AZFb Region. Their opinions included a possibility of the deletion mechanisms of AZFb region is that 5' and 3' LTR (long terminal repeat) of full length HERV (human endogenous retroviruses) structure enable the occurrence of homologous recombination; The evolutionary dynamics of the Y chromosome are generally much faster than those of the autosomes and the X chromosome due to deletions and mutations; ERVs

may lead to genomic instability by inducing new insertions and causing deletions via homologous recombination of intrinsic ERV sequences, particularly LTRs; These deletion events may be associated with some cases of male infertility that are due to genomic instability. Sung Won LEE talked about the Clinical implication of Y-CMD. His opinions included Y-CMD screening had become part of the routine diagnostic work-up of severe male infertility; The identification of Y deletions had a diagnostic, prognostic, and preventive value.

Long Tian talked about the current management for non-obstructive azoospermia. He introduced the methods and note points of sperm retrieval and ICSI (intracytoplasmic sperm injection) for patients with NOA.

Trauma, repairmen, and plasticity

Professor Tom F Lue gave us a speech on "The challenges of Peyronie's disease". He raised the problems faced by us in the diagnosis and treatment of Peyronie's disease. He also recommended the task we need to do, including stop the inflammatory process, preserve and restore the elastic fibers, and prevent deposition of new scars etc.

Dae Yul Yang talked about the Tolerability and efficacy of newly developed penile injection of cross-linked dextran and PMMA (polymethylmethacrylate) mixture on penile enhancement. Their experiments showed that this kind of injection led to a significant increase in penile size with good durability and well tolerated. No serious adverse events were observed during the process.

For trauma, Michael Coburn shared their experience on male genital trauma and reconstructive surgery. Professor Coburn introduced some kind of common male genital traumas and their treatments. Some of his principles and tips were also recommended. Professor David Ralph detailed the management of 68 men who had requested a total reconstruction with the forearm flap phalloplasty. Despite the multiple stages and high complication rates, the satisfaction rate was 90%. Huang Yang introduced Partial inferior pubectomy combined with the abdominal perineal approach in the management of post traumatic complex posterior urethral distraction defects. Their data showed that this combined therapy was effective and safe with the following advantages: better visualization of the surgical field, reduced length of the reconstructed urethra, without immediate or remote effects on the stability of pelvis or bladder.

Other issues about urological- reproductive medicine

Professor Jihong Liu talked about KS (Kallmann syndrome) in China. He introduced their experiences in diagnosing and treating KS. Because most patients with KS have unknown genetic defects, they investigated a genome-wide profile of structural variation and linkage analysis in a consanguineous Chinese family. Although no significant linkages were found in polymorphic markers, the results revealed that the three affected individuals had common in CNV (copy number variants) on chromosomes 1p21.1, 2q32.2, 8q21.13, 14q21.2, and Xp22.31. moreover, the CNVs on Xp22.31 were located in the intron of KAL1 gene, which may causes X-linked KS.

Liang Qiao talked about some issues about over expressed AR (Androgen receptor) in boys with severe hypospadias and the regulation of ZEB 1 on AR expression in human foreskin cells. They examined the interaction between ZEB1 and AR in vitro and the expression of AR in boys with hypospadias. The data showed that ZEB1 could physically interacts with AR in human foreskin cells. AR is over expressed in boys with severe hypospadias. Environmental estrogenic compounds may increase the risk of hypospadias by facilitating the interaction between ZEB1 and AR.

Myung Chan GYE introduced his research on ER (estrogen receptor) α in mouse testes. Their results showed that whole body ER α KO (knock out) resulted in spermatogenic defects largely due to pituitary dysfunction. ER α expressed in Leydig cells may negatively affects steroidogenesis in aging male.

Kuang-Kuo CHEN talked about the role of bilateral MPG (major pelvic ganglia) in the neural pathway of electrical stimulation of LSN (lesser splanchnic nerve)-induced SVP (seminal vesical pressure) increase in the rat. The results suggested that electrical stimulation of the MPG and LSN might induce a simultaneous significant, comparable amount of SVP increase on the left and right side seminal vesicle. The electrical stimulation of LSN-induced bilateral SVP increase was eliminated after resection of bilateral MPG which implied that the neural pathway was through at least one side MPG in the rat.

Han Sun CHANG's research was about the genetic expression in the infertile men with congenital absence of vas deferens. They concluded that CBAVD (congenital bilateral absence of the vas deferens) patients in Taiwan, who express a very low incidence of CF (cystic fibrosis),

were less affected by CFTR mutations, with the exception of IVS8-5T, which does exhibit a high prevalence among CBAVD patients tested.

Lifeng Zhang's research was about the differential expression of the Wnt/ β -catenin pathway in the GT (genital tubercle) of fetal male rat following maternal exposure to DBP (di-n-butyl phthalate). Their findings indicated that DBP might affect the development of GT in fetal male rats by down regulating the Wnt/ β -catenin pathway.

Bianjaing Liu did the combined assessment of human sperm acrosome integrity and ionophore A23187 induced acrosome reaction by using anti-VDAC (voltage dependent anion channel) 2 antibody. They focused on the presence of VDAC2 in human spermatozoa and its possible role using specific anti-VDAC2 monoclonal antibody. Their results exhibited that native VDAC2 existed in the membrane components of human spermatozoa. The co-incubation of spermatozoa with anti-VDAC2 antibody did not affect the acrosomal integrity and acrosome reaction, but inhibited ionophore A23187-induced intracellular Ca^{2+} increase, which might play putative roles in sperm function.

Professor Longcheng Li talked about saRNA (small activating RNA) as a therapeutic option for the treatment of urological cancer. saRNA can serve as activators of gene expression by targeting non-coding regulatory sequences. In his rat model, a saRNA designed to target the p21 gene can activate endogenous p21 protein in prostate and bladder cancer cells, and significantly impede in vivo tumor growth.

Professor Sae Woong Kim talked about phytotherapy. Need and interest of phytotherapy have been growing in the world. Based on the information available now, the effect of natural product on urological disease like ED, BPH, and male infertility seems to be promising. However, standard method is lacking now, and well designed evidence based study is necessary.

The three-day meeting was completed in the warm applause of scientists and clinical doctors. For more information, please visit <http://www.giaf2012.org/>. Proceeding is available at <http://www.amepc.org/tau/issue/view/12>.

We look forward to a more exciting and successful forum, the 6th Greatwall Translational Andro-Urology Forum (GTAUF2014) and Asia Pacific Society for the Study of Aging Male (APSSAM2014), which will be held in autumn of 2014 in Beijing.

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Footnote

Conflicts of Interest: The authors have no conflicts of interest to declare.

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