SSMR NEWS

Fall *Society for the Study of Male Reproduction* 2008

President's Message

Stanton C. Honig, MD

Dear SSMR Members:

Welcome to the fall newsletter of the SSMR. This is the FIRST time it will be sent as an e-blast, in addition to being posted online.

We have an exciting year planned for the SSMR membership!

The 2008 Annual SSMR Meeting on Current Controversies in Vasectomy in Orlando was organized by Dr**.** Ajay Nangia. He did an outstanding job coordinating a program of nationally and internationally recognized speakers. Slides of the 2008 meeting are available online in the Members Only section. Visit www.ssmr.org to review them or to see the interesting slide presentations that were given, if you missed the meeting.

The 2008 – 2009 year brings new and exciting things associated with the SSMR.

With the SSMR guidance, a committee has been developed with Dr. Ira Sharlip as chairperson, to review data on vasectomy and set **"Clinical Guidelines for Vasectomy"**. This project is expected to take approximately one to two years and we will be asking many of our members for their expertise in reviewing preliminary documents. Your input is VITAL to the success of this project.

The newsletter has been expanded to include a section on **"State-of-the-Art Review"**. In this issue of the newsletter, Dr. Darius Paduch will discuss the treatment of azoospermia in Klinefelter's patients, specifically adolescent Klinefelter's patients. If you have a topic that you would like to submit for the newsletter, please email me at stan.honig@gmail.com.

The Society for the Study of Male Reproduction was initiated in 1993. This year, we will award the **1st Annual Distinguished Service Award** to one of our senior members. Our society has matured to the point where we need to acknowledge the hard work and efforts that members have provided to the society and their national and international promotion of male reproduction. You will be hearing from me in the next few months regarding nomination requests.

The SSMR will be developing a slide set for members to use for presentations. This has been a successful endeavor by the Sexual Medicine Society of North America. Dr. David Shin has accepted the position of coordinating this endeavor. It will allow members to utilize a standardized **"SSMR-approved" slide set**, for presentations on male reproduction that can be utilized for presentations to medical students, residents, reproductive endocrinologists, urology grand rounds, etc. We would appreciate the input from members by submitting slides that could be utilized for this project. In addition, we would appreciate the help of any members, especially new members who are interested in getting involved with projects like this for our society.

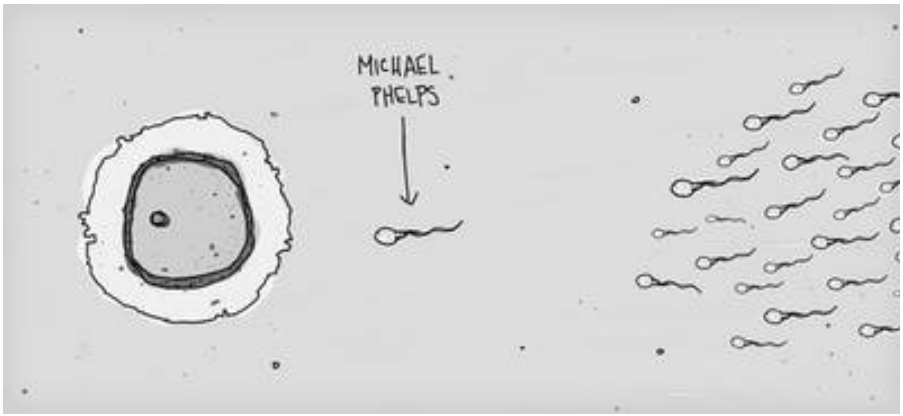
Following in the footsteps of Dr. Sharlip's work with the ISSM (International Society of Sexual Medicine), we will be starting a **"Humor in Reproductive Medicine"** contest. Many of us love to share funny cartoons or jokes with our colleagues and use them in presentations. Slides and videos which are clever, subtle, witty, funny and easily understood by an international audience will be favored for presentation, without any hardcore, nasty, offensive or crude pornography. Material must be inoffensive to the diverse cultures, religions and genders of SSMR members and the general public. Formal guidelines for the contest will be forthcoming. The winning videos, cartoons, etc. will be presented in a three-minute session after the break at the 2009 SSMR meeting and will be available to SSMR members on our website to download for their own presentations.

President's Message continued on page 2

CONTENTS

President's Message continued

Here is my early entry!



The topic for the 2009 SSMR meeting will be **"Endocrinology of Male Reproduction"**. Dr. Peter Kolettis will be the program chairman. Topics that will be discussed include: Effects of Anabolic Steroids on Male Reproductive Function, Update on Male Hormonal Contraception, Manipulation of the HPT Axis Prior to Cancer Treatment to Preserve Fertility, and Endocrine Treatment of Low Testosterone in the Infertile Male. Dr. Kolettis is in the process of selecting nationally recognized endocrinological experts as well as SSMR members to speak at the meeting. It will be on April 28, 2009, a Tuesday afternoon again.

Thanks to our outgoing president, Dr. Jay Sandlow! Dr. Sandlow continues to be an integral asset to the Board of Directors of the SSMR. His professionalism, national relationships and expert advice have been extremely valuable on topics relating to development, program committee and new projects.

I would like to welcome our newly elected officers: Dr. Natan Bar-Chama (treasurer) and Dr. Paul Shin (member at large). Our returning board members are Dr. Bob Brannigan (vice president), Dr. Ajay Nangia (secretary), and Dr. Victor "Trey" Brugh (member at large).

We have an exciting year planned for the SSMR! I look forward to seeing many of you at the ASRM meeting in San Francisco! ⌘

Sincerely,
Stanton Honig MD
President, SSMR

2008 ASRM Events of Interest

American Society for Reproductive Medicine
64th Annual Meeting
November 8 – 12, 2008
Moscone Convention Center
San Francisco, CA

SUNDAY, NOVEMBER 9, 2008

Postgraduate Program
One-Day Course
"Unraveling the Mysteries of Spermatogenesis: Contemporary Therapies, Stem Cells and Beyond"
Faculty: Robert E. Brannigan, MD, Chair
Dolores J. Lamb, PhD
Paul J. Turek, MD

6:30 p.m. **Opening Ceremony with Opening Reception to Follow**

MONDAY, NOVEMBER 10, 2008

12:15 p.m. – 1:15 p.m. **Society for Male Reproduction and Urology / Environment and Reproduction Special Interest Group Interactive Session**
"Male Reproductive Toxicology"
Chairs: Robert E. Brannigan, MD;
Linda C. Giudice, MD, PhD
Presenters: Susan H. Benoff, PhD;
Mark Sigman, MD

12:15 p.m. – 1:15 p.m. **Roundtable Luncheons**

Male Reproduction and Urology
RTM19 **"Genetic Anomalies and Male Infertility: A State-of-the-Art Overview"**
Robert D. Oates, MD

RTM20 **"Effect of Sperm Source on IVF Outcomes"**
Christopher Schrepferman, MD

RTM21 **"Microsurgical Pearls for Vasectomy Reversal and Varicocelectomy"**
Marc Goldstein, MD

RTM22 **"FSH Effect on Sperm Ultrastructure and its Outcome on Pregnancy"**
Michel Abou Abdallah, MD

Sexuality
RTM43 **"Erectile Dysfunction as a Marker of Cardiovascular Disease"**
Natan Bar-Chama, MD

1:45 p.m. – 2:30 p.m. **Plenary Session 2**
Society for Male Reproduction and Urology and the Bruce Stewart Memorial Lecture
"Androgens in Men and Women: A State-of-the-Art Overview"
Rebecca Z. Sokol, MD, MPH
Professor of Medicine and Obstetrics and Gynecology
University of Southern California,
Los Angeles, CA

3:15 p.m. – 5:15 p.m. **Abstract Sessions**
Society for Male Reproduction and Urology / Mini-Symposium

4:45 p.m. – 5:15 p.m. **Society for Male Reproduction and Urology Mini-Symposium**
"Klinefelter Syndrome: Novel Scientific and Clinical Insights"
Darius A. Paduch, MD

5:15 p.m. – 5:45 p.m. **Members' Meetings**
Society for Male Reproduction and Urology

5:45 p.m. – 7:00 p.m. **Poster Presentations and Reception**

TUESDAY, NOVEMBER 11, 2008

12:15 p.m. – 1:15 p.m. **Roundtable Luncheons**

Fertility Preservation
RTT11 **Fertility Preservation in Men**
Ashok Agarwal, PhD

RTT12 **Testicular Stem Cell Transplantation**
Herman Tournaye, MD, PhD

Male Reproduction and Urology
RTT18 **Environmental Factors that Impair Male Reproduction**
Susan H. Benoff, PhD

2008 ASRM Events of Interest continued on next page

	RTT19	**Preservation of Male Fertility in Cancer Patients** Daniel H. Williams, MD
	RTT20	**Medications that Impair Male Reproduction** Ajay K. Nangia, MD
	RTT21	**Diagnostic and Therapeutic Approach to Ejaculatory Duct Obstruction** Mohit Khera, MD
		Surgery
	RTT46	**Vasectomy Reversal — When to and Not to Offer Therapy** Peter N. Schlegel, MD
3:15 p.m. – 5:15 p.m.		**Abstract Sessions** Male Reproduction and Urology / Mini-Symposium
4:45 p.m. – 5:15 p.m.		**Society for Male Reproduction and Urology Mini-Symposium** **"The Reproductive Aspects of the Prostate: Growth, Development, Function, and Impairment"** Gail S. Prins, PhD
5:45 p.m. – 7:00 p.m.		**Poster Presentations and Reception**

WEDNESDAY, NOVEMBER 12, 2008

8:45 a.m. – 9:00 a.m.		**ASRM Awards Ceremony**
10:15 a.m. – 12:00 p.m.		**Special Research Presentations**
12:15 p.m. – 1:15 p.m.		**Roundtable Luncheons**
		Male Reproduction and Urology
	RTW17	**Optimization of the Reproductive Health of Men with Spinal Cord Injuries** Nancy L. Brackett, PhD
	RTW18	**Reproductive Options in the Neurologically Impaired Patient** Dana A. Ohl, MD
	RTW19	**ART or Vasectomy Reversal: Helping Patients Navigate the Decision-Making Process** Aaron Spitz, MD
	RTW20	**Varicoceles and ART** Edmund S. Sabanegh, Jr., MD
2:45 p.m. – 4:45 p.m.		**Abstract Sessions** Male Reproduction and Urology Traveling Scholars / Mini-symposium
4:15 p.m. – 4:45 p.m.		**Society for Male Reproduction and Urology Mini-Symposium** **"Sperm Biochemical Markers and Their Relationship to Sperm Morphology"** Gabor B. Huszar, MD

State-of-the-Art Review

Toward Comprehensive and Lifelong Management of Men and Children with Klinefelter Syndrome (47,XXY)

Darius A. Paduch, MD, PhD
Department of Urology and Reproductive Medicine
Weill Cornell Medical College.
New York, NY

Over the last 10 years, with advancements in artificial reproductive techniques and the successful delivery of healthy children from men with Klinefelter Syndrome (KS), the involvement of urologists in the care of patients with KS is increasingly important. (Schiff, et al., 2005, Tournaye, et al., 1996)

Epidemiology

KS (47, XXY) is the most common numerical chromosomal aberration among men, with an estimated frequency of 1:500 – 1:1000 of live deliveries. (Lanfranco, et al., 2004) Men with KS represent a broad spectrum of phenotypes, professions, incomes and socioeconomic status. Severe intellectual deficits are rare. Most commonly, men with KS will present to their urologist with infertility: azoospermia or severe oligospermia, low testosterone and complications of low testosterone such as erectile dysfunction, and poor libido. Spermatogenic and steroidogenic dysfunction are cardinal and the most prevalent signs of KS.

Pathophysiology, Epidemiology and Mechanisms of Spermatogenic Failure

The 47, XXY karyotype of KS arises spontaneously when paired X chromosomes fail to separate. Advanced maternal and paternal age is associated with increased risk of KS. (Lowe, et al., 2001)

The X chromosome carries genes that regulate testis function, brain development and growth. The fact that sperm can be found in the testes of men with KS has challenged the previous assumption that men with KS are always sterile. This raised the hypothesis that children with KS are born with spermatogonia and later in life, most likely during early puberty; spermatogonia undergo massive apoptosis that results in depletion of spermatogonial population and subsequent azoospermia. (Aksglaede, et al., 2006)

This hypothesis is based primarily on three observations: testicular sperm can be identified and recovered from at least half of adult men with KS; in rare cases, sperm can be found in ejaculates of adult men with KS; and results of testicular biopsy in adolescents in different development stages indicate that boys with KS have spermatogonia at birth, but that damage to the germinal epithelium occurs early during puberty. (Wikstrom, et al., 2004) Molecular mechanisms of spermatogonial loss are not known at this point. Sperm found in testes of men with KS have only a slightly increased frequency of sex chromosome polysomies, indicating that during early stem-cell proliferation or meiotic division, the checkpoint mechanisms are able to overcome X chromosome polysomy resulting in sperm with a single X (or Y) chromosome. (Yamamoto, et al., 2002)

Laboratory and Auxiliary Evaluation

All men with KS should have a full hormonal evaluation including FSH, LH, testosterone, estradiol, prolactin and IGF-1, and cortisol; adrenal steroidogenic deficiency may be seen in 47% of men with KS. Men with KS have increased risk of osteopenia and osteoporosis, hence DEXA scan is recommended. KS increases the risk of deep vein thrombosis, and hematocrit should be kept in normal range to avoid increased blood viscosity. (Campbell and Price, 1981)

The Physiological Approach to the Management of Men with Klinefelter Syndrome

In adolescents, treatment of hypogonadism, follow-up of pubertal progression, and fertility preservation are the goals of therapy. Fertility preservation in adolescents is not yet a standard of care, and each team needs to solve complex ethical, legal and logistics issues that arise when a child with a genetic defect is subjected to collection and storage of semen, and a potential surgical procedure. We currently prefer to check semen in adolescents who already masturbate and are in Tanner stage group II/III. We found sperm in ejaculate of 2/10 adolescents younger than 14. Both boys were masturbating for over a year, had just 1 – 2 armpit hairs, and FSH below 20. Semen was cryopreserved with density of 1 and 3 mil/ml, respectively. There are promising benefits of early sperm retrieval programs, but it will take 15 years to accrue enough patients to compare reproductive outcomes using sperm from adolescents with KS versus fresh sperm obtained through testicular biopsy later in life. The prospect of storing the sperm during adolescence facilitates discussing the impact of KS on fertility in adolescents, who in our practice seem to have an easier time accepting the KS diagnosis knowing they are not sterile. Having sperm available simplifies the future IVF procedure itself, avoids general anesthesia and reduces the cost associated with procurement of sperm in adult men (typically done by TESE).

In adults the best success rate of IVF in KS seems to be obtained by using fresh sperm through testicular biopsy performed the same day as egg retrieval. Optimal timing of sperm retrieval as well as optimal hormonal treatment prior to sperm retrieval has not yet been established. Injectable testosterone may lower sperm recovery rate. In our practice, we cease injectable testosterone in men with KS prior to any treatment for infertility. Men who are used to normal levels of circulating testosterone are placed on topical testosterone, most commonly AndroGel (Solvay, Marietta, Georgia, USA), which achieves physiological levels of testosterone and does not suppress FSH and LH as much as injectable testosterone. An aromatase inhibitor like Arimidex (AstraZeneca, Wilmington, Detroit, USA) is used in all patients for a minimum of six months to decrease intratesticular estradiol levels and increase testosterone production. Aromatase inhibitors have been shown to increase testosterone and improve sperm recovery rates. (Raman and Schlegel, 2002)

In patients who are not interested in fertility treatment, the focus is on testosterone replacement therapy, health maintenance, adequate bone health and decreasing the risk of deep vein thrombosis. We follow our patients with KS long-term and manage endocrinological and urological issues related to KS.

Conclusion

Many questions remain before recommendations about optimal treatment and long-term management of KS can be determined by outcomes of clinical trials. Better understanding of molecular mechanisms governing X chromosome inactivation, regulation of meiosis and timing, as well as the pathophysiology of loss of spermatogonia, should allow for the development of new treatment options in the future. Although these are daunting challenges, we cannot forget that just a decade earlier most of us considered our patients with KS sterile and without hope for paternity.

References

Aksglaede L, Wikstrom AM, Rajpert-De Meyts E, Dunkel L, Skakkebaek NE, Juul A. Natural history of seminiferous tubule degeneration in Klinefelter Syndrome. Hum Reprod Update.2006;12:39-48.

Campbell WA, Price WH. Venous thromboembolic disease in Klinefelter's Syndrome. Clin Genet.1981;19:275-80.

Friedler S, Raziel A, Strassburger D, Schachter M, Bern O, Ron-El R. Outcome of ICSI using fresh and cryopreserved-thawed testicular spermatozoa in patients with non-mosaic Klinefelter's Syndrome. Hum Reprod.2001;16:2616-20.

Krausz C, Forti G. Sperm cryopreservation in male infertility due to genetic disorders. Cell Tissue Bank.2006;7:105-12.

Lanfranco F, Kamischke A, Zitzmann M, Nieschlag E. Klinefelter's Syndrome. Lancet.2004;364:273-83.

Lowe X, Eskenazi B, Nelson DO, Kidd S, Alme A, Wyrobek AJ. Frequency of XY sperm increases with age in fathers of boys with Klinefelter Syndrome. Am J Hum Genet.2001;69:1046-54.

Morel F, Bernicot I, Herry A, Le Bris MJ, Amice V, De Braekeleer M. An increased incidence of autosomal aneuploidies in spermatozoa from a patient with Klinefelter's Syndrome. Fertil Steril.2003;79 Suppl 3:1644-6.

Raman JD, Schlegel PN. Aromatase inhibitors for male infertility. J Urol.2002;167:624-9.

Schiff JD, Palermo GD, Veeck LL, Goldstein M, Rosenwaks Z, Schlegel PN. Success of testicular sperm extraction [corrected] and intracytoplasmic sperm injection in men with Klinefelter Syndrome. J Clin Endocrinol Metab.2005;90:6263-7.

Tournaye H, Staessen C, Liebaers I, Van Assche E, Devroey P, Bonduelle M, Van Steirteghem A. Testicular sperm recovery in nine 47,XXY Klinefelter patients. Hum Reprod.1996;11:1644-9.

Wikstrom AM, Raivio T, Hadziselimovic F, Wikstrom S, Tuuri T, Dunkel L. Klinefelter Syndrome in adolescence: onset of puberty is associated with accelerated germ cell depletion. J Clin Endocrinol Metab.2004;89:2263-70.

Yamamoto Y, Sofikitis N, Mio Y, Loutradis D, Kaponis A, Miyagawa I. Morphometric and cytogenetic characteristics of testicular germ cells and Sertoli cell secretory function in men with non-mosaic Klinefelter's Syndrome. Hum Reprod.2002;17:886-96. ⌘

2008 SSMR Meeting at the AUA Course Summaries

Infertility: Evaluation and Therapy (I)
Moderated Poster Session 59
Wednesday, May 21, 2008
Moderators: Stewart J. McCallum, MD and Paul J. Turek, MD
Summarized by Heidi Stephany, MD

Abstract 1738: Analysis of 2,967 Semen Retrieval Trials in 481 Men with Spinal Cord Injury (SCI)
Emad Ibrahim, Nancy L. Brackett, Teodoro C. Abalia, Charles M. Lynne; Miami, FL

"Best Poster" Recipient. The authors reviewed semen analyses from patients with spinal cord injuries to assess semen quality as well ejaculation success rates. Most men had either penile vibratory stimulation (PVS) or electroejaculation (EEJ) procedures and a total of 3,694 semen analyses were reviewed. They found that 85% of subjects with a T10 or higher injury responded to PVS verses 15% of men whose injury was T11 or lower. Sperm was present in the ejaculate in 91% of trials and most had reasonable yields of motile sperm. The authors recommend evaluating ejaculate before performing surgical sperm retrieval.

Abstract 1727: Six Years of Experience with Microsurgical Longitudinal Intussusception Vasoepididymostomy (LIVE): A Prospective Analysis
Peter T. Chan, Richard Lee, Philip S. Li, Jamie Libman, Marc Goldstein; Montreal, QC, Canada, and New York, NY

The authors report their six-year experience performing longitudinal intussusception vasoepididymostomy (LIVE) and report their outcomes of 72 men who underwent LIVE for epididymal obstruction. The mean follow-up period was 16.3 months and they found an overall patency rate of 92% (66/72). The natural pregnancy rate for patients with over one year of follow-up was 31% (11/36) and 39% achieved pregnancy through assisted reproductive techniques using fresh ejaculated sperm. The clinical experience of the authors supports LIVE as an effective treatment modality for epididymal obstruction with high patency and natural pregnancy rates similar to those with primary IVF/ICSI.

Post-Vasectomy SA: Risk Factors for Noncompliance
Alek Mishail, Jacqueline Lee, David Schulsinger, Yefim R. Sheynkin; Stony Brook, NY

Objective risk factors including demographics for noncompliance with post-vasectomy semen analyses (PVSA) were assessed through a retrospective review of 214 patients undergoing vasectomy. Patients failing to provide two post-vasectomy semen analyses were defined as noncompliant. Ninety-nine patients (46.2%) provided no PVSA. Patients younger than 35 years of age, as well as smokers, and men with lower educational levels were identified as risk factors for noncompliance. If men had four or more children, they too were found to be at higher risk for noncompliance, however marital status did not have any impact on noncompliance. Patient education and reminders may aid in decreasing the high rate of noncompliance in post-vasectomy patients.

The Assessment of Serum Hormone Levels in Patients with Non-Obstructive Azoospermia after Microdissection Testicular Sperm Extraction
Yutaka Kondo, Tomomoto Ishikawa, Kohel Yamaguchi, Atsushi Takenaka, Masato Fujisawa; Kobe, Japan

Few studies have compared postoperative serum hormone levels between 46 XY males with non-obstructive azoospermia (NOA) and 47 XXY (Klinefelter's Syndrome) undergoing microdissection testicular sperm extraction (MD-TESE). In a retrospective review of 80 azoospermic males, serum levels of FSH at 6 and 12 months and LH at 6 months post-op were significantly increased in 46 XY males, whereas LH at 12 months and testosterone at 6 and 12 months were not significantly different compared to baseline. In 47 XXY patients, testosterone significantly decreased and 6 and 12 months but FSH and LH levels were not significantly changed. Long-term evaluation of serum hormone levels is warranted in males status post MD-TESE to identify and treat hypogonadism, especially in 46 XXY patients.

Infertility: Physiology, Pathophysiology and Basic Research (I)
Podium Session 41
Wednesday, May 21, 2008
Moderators: Lawrence S. Ross, MD and Dolores J. Lamb, PhD
Summarized by Kristopher Whitehead, MD

Abstract 1798
The Cornell group identified specific gene deletions in men with Y chromosome microdeletions (YCM) and mapped out their function based upon phenotype-genotype correlative analysis. Demonstrated 5 candidate genes in the AZFa region associated with germ cell migration (loss of which leads to Sertoli cell-only), 3 candidate genes in the AZFb region for progression from spermatocyes to spermatids (loss of which leads to maturation arrest), and 12 candidate genes in the AZFb for spermatozoa development (loss of which may result in late maturation arrest).

Abstract 1799
The Cornell group also identified a way to sort sperm based on the amount of chromatin damage in order to utilize sperm with intact DNA. Currently, commonly used techniques require fixation of sperm, leaving them unsuitable for clinical use. This new technology allows for the identification and utilization of live sperm without DNA damage. The group states that the next step is to apply this to severely oligospermic samples.

Abstract 1803
The group from the University of Iowa utilized immunofluorescence (IF) to identify spermatogenesis in mice using IF antibodies to human sperm acrosomes. After injecting into the testicular vascular pedicle, they examined the testes using IF. They compared fertile and genetically sterile mice and found that 22/26 fertile mice had positive results, whereas none of the 16 sterile mice were positive. The group is hoping to further refine this in order to apply it to humans.

Abstract 1806
The group from Sao Paulo, Brazil studied the effect of male partner age on the outcome of in vitro fertilization with intracytoplasmic sperm injection (IVF/ICSI) cycles. In men with oligospermia (<20 million/mL), male age was a negative influence on implantation rate, whereas male age had no effect when the sperm concentration was >20 million/mL. Female partner age does continue to play a major role in IVF/ICSI outcome.

Abstract 1807
The group from Haifa, Israel studied the effect of allopurinol on ischemic-reperfusion injury in a rat model for testicular torsion. They demonstrated that allopurinol decreases the ischemic injury in both the ischemic and contralateral testis, as measured by apoptosis and Johnsen score. The group suggests that giving allopurinol and anti-oxidants prior to detorsion may prevent reperfusion injury in testicular torsion.

Course Summaries continued on next page

Course Summaries continued

AUA 2008 Session Highlights
Infertility: Evaluation and Therapy (II)
Podium Session 43
Wednesday, May 21, 2008
Infertility: Physiology
Moderators: Larry I. Lipshultz, MD and Arnold M. Belker, PhD
Summarized by Peter Stahl, MD

The 43rd podium session at the annual meeting of the American Urological Association (Infertility: Evaluation and Therapy II) featured diverse reports of the exciting clinical and basic scientific research in male fertility that is ongoing in America and throughout the world. One prominent and exciting theme in the discussion was the association of male factor subfertility with overall health and somatic malignancy. This association emphasizes that male infertility specialists are uniquely positioned to have a great impact on men's health extending well-beyond the diagnosis and treatment of subfertility

Thomas Walsh from the University of California at San Francisco presented epidemiological research into the association of male infertility with somatic cancer. Walsh et al.'s abstract, entitled "Infertile Men Have Increased Risk for Non-Germ Cell Cancers: Data from 51,138 Infertile Couples," was recognized by the AUA as the best male infertility abstract presented at the 2008 annual meeting. When compared with age-matched controls from the general population, men with male factor infertility were 1.2 times more likely to be diagnosed with colon cancer, 1.7 times more likely to be diagnosed with melanoma, and 2.9 times more likely to be diagnosed with prostate cancer. Furthermore, the relative risk of developing high-grade prostate cancer was 2.1 times higher in men with male factor infertility than in age-matched controls. The critical importance of this work is that it provides the first substantial evidence that male factor infertility may be associated with non-germ cell somatic cancers. While it remains to be elucidated whether these results reflect a screening bias or a true biological phenomenon, this work strongly demonstrates the need for subsequent epidemiological and scientific exploration.

Dr. Andrea Salonia from Milan presented preliminary data from his institution suggesting that men with male factor infertility are less healthy than fertile men ("Are infertile men less healthy than fertile men?: Preliminary results of a survey at a major tertiary academic centre"). Dr. Salonia used the Charlson Comorbidity Index to compare the overall health status of 344 consecutive men treated for male factor infertility to the health status of 208 fertile volunteers. Infertile men had higher BMIs and rates of comorbidities than fertile men. Even after controlling for age, BMI, and educational status, infertile men had still had significantly higher Charlson scores indicative of poorer overall health. Dr. Salonia's research echoes the work from the UCSF group and lends great support to the notion that male factor infertility may be associated with other male health problems.

In addition to the presented data linking male subfertility to somatic health problems, many other important studies were presented during this podium session. Drs. Ramasamy, Lin, and Schlegel from New York presented their data showing high serum FSH values do not preclude successful microsurgical sperm retrieval in azoospermic men. Dr. Alukal and the Baylor research group reported elegant data suggesting that men with oligoasthenoteratozoospermia have highly abnormal levels of sperm DNA damage, which may explain poor ART outcomes in affected men. Drs. Nelson and Williams from Wisconsin presented data from their survey of fertility websites, suggesting that information on male factor infertility is under-represented on the Internet. Dr. Sonksen from Denmark reported his updated experience in the treatment of spinal cord injured men with vibratory ejaculation and home insemination, and in so doing strongly demonstrated the efficacy of this approach. Dr. Mills et al. reported on the time-course of recovery of spermatogenesis after cessation of exogenous testosterone treatment, which was approximately 3 months in men taking injectable testosterone and 8 months in men who were supplemented transdermally.

SSMR Annual Program:
Post-Op Vasectomy Check Summaries
Summarized by Aimee Wiltz, MD

Post-Op Vasectomy Check-Up — What is the Best Practice?

Following vasectomy, the time to spermatozoa clearance can vary widely and there is no standard protocol. One suggested protocol by the WHO is to examine seminal fluid under high power microscope after 15 minutes of centrifugation at 3000 rpm, using two separate specimens showing the complete absence of sperm to define azoospermia. However, some have proposed that rare, non-motile sperm is adequate, and that perhaps centrifugation is unnecessary. These are two issues requiring further definition.

Of Importance: Time and Patient Compliance

To evaluate the impact of postvasectomy protocols, semen analysis was requested at 2 and 3 months post-vasectomy in 436 patients. Compliance was low in both groups of men who were given a specific date of follow-up versus those who just received instructions. Of note, only 75% presented for follow-up overall, 58% submitted a single sample, and only 21% complied with instructions to provide semen analysis two times within two months. Thus, the recommendation for confirming semen sterilization should be a semen analysis at 3 months. Patients can be advised that they are likely sterile if they are azoospermic or have RNMS.

Number of Ejaculations

Literature review regarding post-vasectomy monitoring has revealed no consensus on minimum number of ejaculations prior to semen testing, ranging from no testing to a median of 25-30 in a Mexican study. In that study, median time to azoospermia was 5 weeks faster for men who ejaculated 3 or more times a week. Immotile sperm at low concentrations can be used to determine sterility, and achieved in 10-15 ejaculations. Age and anatomy of the vas deferens may influence the number of ejaculations required. If the number of ejaculations can be determined, this may be more useful than semen analysis testing as follow-up compliance is so poor after vasectomy.

AUA 2008 Session Highlights
Infertility: Physiology, Pathophysiology, and Basic Research (II)
Moderated Poster Session 63
Wednesday, May 21, 2008
Moderators: Harris M. Nagler, MD and Marc Goldstein, PhD
Summarized by A. Nisbet, MD

The effects of cellular injury, inflammation and oxidative stress in the role of male fertility played a significant part in this poster session. Dr. Kondo's group from Japan contributed a number of articles detailing the effects of ischemia-reperfusion injury to testicular function, reducing testicular damage in cryptorchidism with administration of tetrahydropbiopterin, and measuring oxidative stress in seminal plasma of patients with varicocele with levels of nitric oxide and other factors. Their studies showed that levels of vascular endothelial growth factor increased in a time-dependent manner from the onset of torsion in male rats and that nitric oxide production could be attenuated with dietary administration of tetrahydrobiopterin. In addition, by studying levels of nitric oxide, IL-6, IL-8 and TNF-alpha in seminal plasma, they found significant reductions in levels of these substances following varicocelectomy. Similarly, Dr. Mammen's group found that ischemia-reperfusion damage induced by testicular torsion revealed that eNOS regulated selectin expression in vivo, which regulates neutrophil recruitment leading to germ cell apoptosis. They concluded that further studies of the germ cell apoptosis pathway could lead to therapies to target and moderate testicular stresses as in the setting of torsion. Dr. Smith's group investigated the relationship between prostate biopsy and ejaculate volume and sperm count. They observed decreases in ejaculate volume, sperm concentration, and total motile sperm counts, postulating that direct injury to the ejaculatory ducts or peri-ejaculatory duct fibrosis could be responsible for these changes.

Dr. Steger's group from Germany compared ratios of two types of protamine in infertile patients in two different studies and found that infertile men exhibit aberrant protamine ratios in their sperm. Their group showed that in testicular biopsies and ejaculate samples of infertile men there were significant differences in protamine ratios and Bcl2 mRNA content compared to controls. They postulated that protamine is a reliable biomarker for the presence of spermatozoa in comparison to histological evaluation of testicular biopsies.

Two studies looked at the relationship between increasing age and decreasing fecundity in the male. Dr. Cocuzza's group determined that levels of reactive oxygen species in seminal plasma were significantly higher in older men than younger men. In addition, levels of these same factors were negatively correlated with sperm concentration and motility. They concluded that these species contribute to lower rates of pregnancy in older men, and that treatment with antioxidants may be indicated in men older than 40 years attempting to father a child. Along similar lines, Dr. Olmedo's group from Argentina found a significant decrease in seminal volume, total sperm count, normal morphology and normal values of fructose in patients 45 years of age or older. Dr. Herwig's group also studied oxidative stress and sperm motility. They analyzed the use of carbonyl protein analysis in semen and found it to be a reliable marker for both midpiece sperm deformities and increased reactive oxidative stress.

Two studies examined the effects of toxin exposure on infertility. Dr. Akbal's group studied three groups of rats, two of which were exposed to cisplatin in varying concentrations and found a dose-dependent decrease in levels of testis-specific protein, Y-linked mRNA, a factor important in spermatogenesis. This appears to be another mechanism for male infertility following exposure to cisplatin as part of standard chemotherapeutic regimens for testis cancer. Additionally, Dr. Ercolani's group found that chronic cadmium exposure caused a time- and dose-dependent decline in testicular spermatogenesis and the number of sperm in the epididymis of male rats, suggesting that this environmental toxin could be a source for human infertility.

In conclusion, today's poster session was a fascinating look at the role of cellular injury, oxidative stress, and inflammation in male infertility. Future studies will be needed to further elucidate biochemical pathways and develop novel therapies to help men attempting to father children.

State-of-the-Art Lecture:
"An Evidence-Based Approach to History Gathering from the Infertile Male"
Wednesday, May 21, 2008
Summarized by Brian T. Helfand, MD, PhD

Calls for evidence-based approaches to patient care are increasingly common in medicine, and the field of urology is no exception. In this plenary session, an overview of the available literature regarding evidence-based history gathering from the infertile male was presented. While approximately 50% of infertility is related to male factors, the literature is rife with conflicting recommendations on the appropriate work-up of men in couples experiencing infertility. Dr. Robert Brannigan presented a plenary lecture that reviewed the available evidence-based literature for consideration by clinicians pursuing the workup of men from infertile couples.

The work-up of the infertile man can be difficult for primary care physicians, gynecologists and urologists alike. Dr. Brannigan emphasized the current tendency of some physicians to limit the evaluation of the male partner in an infertile couple to a simple, single semen analysis. By focusing only on this single semen analysis, clinicians may overlook many important factors that can result not only in decreased reproductive health, but impaired overall health as well.

Dr. Brannigan explained that the comprehensive evaluation of the infertile couple should include a thorough history and physical examination of the male. Included in this are the following:

The history should include an investigation of the patient's prior ability to achieve pregnancies, sexual health/behavior, medication history, developmental history and exposure to gonadotoxins. The developmental history should be directed at identifying other surgeries possibly impacting his ability to conceive. For example, men with a history of undescended testicles often have diminished sperm production even

Course Summaries continued on next page

Course Summaries continued

after surgical correction. Additionally, a prior hernia repair as a child may have led to iatrogenic obstruction of the vas deferens. Dr. Brannigan noted that erectile and ejaculatory dysfunction are more prevalent in the infertile male than in controls. These medical problems should also be addressed, as they can impair reproductive potential and may not be indicated via semen analysis results. Also, the patient should be warned about the use of lubricants, as many can inhibit sperm motility and viability. Only lubricants with pH values similar to vaginal fluid pH at the time of ovulation should be employed.

The history of the infertile male should also determine current/past medication use and attempt to identify other environmental gonadotoxins. For example, many medications such as the SSRI class of antidepressant medications can impair both libido and erectile function. It has also been shown that Beta-blockers and thiazide diuretics can impair erectile function. Similarly, a patient should not be on testosterone therapy as this may partially or completely inhibit spermatogenesis. Finally, a social history including occupational exposures and drugs such as marijuana, cocaine and other elicits should be taken, as this information may identify potentially reversible causes of male infertility.

Dr. Brannigan emphasized that while semen analyses are an important aspect of the work-up of the infertile male, this testing alone often does not tell the entire story. Indeed, this approach runs the risk of overlooking many important health conditions and sexual practices that can adversely affect male reproductive potential. There is ample evidence from the aggregate of available clinical and basic science literature suggesting that prior surgeries, sexual practices, medications, and environmental exposures can all impair male fertility and should be considered when assessing a man's reproductive health. This important information is often not forthcoming via a cursory look at a patient's semen parameters. Identification of these factors is important and may result in optimized male reproductive potential; identification and treatment of male factor issues may also alleviate the diagnostic and therapeutic burden often reflexively placed on the female partner in an effort to optimize the couples' reproductive potential.

SSMR Annual Program Summary:
European Guidelines on Vasectomy
Gert Dohle, MD, PhD
Erasmus MC Rotterdam, The Netherlands
Summarized by Neil Haraway, MD

Vasectomy is a simple and reliable method of definitive contraception and is performed in 21% of Dutch men. Although infrequent, problems and complications may occur including insufficient patient counseling, bleeding and infection, chronic scrotal pain and recanalization. High quality guidelines should give the physician evidenced-based recommendations for optimal patient care. Recommendations should be based on strong (level one) evidence.

In the European guidelines, there are several recommendations. For the safest surgical approach, a no scalpel technique is recommended. There is insufficient evidence regarding effectiveness, safety and acceptability of vas occlusion techniques since only low-quality and underpowered studies are available. Fascial interposition and cauterization have improved success rates in terms of low numbers of recanalization. Semen analysis should be performed 3 months after the vasectomy and clearance can be given in cases of azospermia. If occasional immotile spermatozoa are found, "cautious assurance of success" (special clearance) can be given.

Medical Malpractice and Urology
Francis E. Pierce, III

The basic concepts of a medical malpractice case include: duty of care, breach of duty or deviations from standard of care, causation, and damages. Informed consent is extremely important; lack of informed consent is considered negligence and absence of informed consent is considered battery. Elements of proper informed consent include: a diagnosis, nature of the procedure, risks involved, prospects of success and reasonable alternatives. Disclose the risks that are known or should be known. There is no duty to disclose remote or inconsequential risk. If a case is taken to court, the consent is usually shown as evidence for all to see.

Vasectomy litigations have included wrongful birth and life cases, complications such as hematoma, pain, infection, and family law issues. A national computer search showed 900 total cases of vasectomies that were taken to court. A report from one professional liability representative showed 10 urology cases, of which 7 were vasectomy cases. Risk management tools include documentation of the consent, video presentation, technology aided consents with computers, and thorough history and physicals of pre-existing conditions.

"Male Infertility: How to Treat, Prevent, and Collaborate with IVF Doctors"
Course Faculty:
Marc Goldstein, MD, Course Director
Peter Chan, MD
Marc Sigman, MD
Summarized by Eric Laborde, MD

This course began with a compehensive review of male reproductive anatomy and physiology. Next, the appropriate evaluation of the infertile male was discussed, with mention of the significant medical conditions that can lead to impaired male reproductive health. Genetic issues were discussed next. Specifically, it was noted that major birth defects have a 4.2% incidence in offspring conceived via natural conception, 8.6% incidence in offspring conceived via IVF, and 9% incidence in children conceived via ICSI.

Surgical therapy for male infertility was discussed, including testis biopsy, vasography, reconstructive techniques (Vasovasosotomy, Vasoepididymostomy, TUR ejaculatory ducts, and varicocele repair). Options for sperm extraction for men with unreconstructable excurrent duct defects were also addressed (MESA, PESA, TESE, TESA). Finally, assisted reproductive techniques were addressed, in particular IUI, IVF, and ICSI. The faculty stressed that MESA and PESA are not options for sperm extraction in men with nonobstructive azoospermia. ⌘

8th Annual SSMR / SMSNA Traveling Fellowship Program

The 8th annual traveling fellowship program took place in conjunction with the AUA in Orlando, Florida and was a great success. This year was the third combined fellowship with the Sexual Medicine Society of North America (SMSNA).The SSMR would like to express our gratitude to the SMSNA for their academic and financial support of the fellowship. These awards are designed to expose young urology residents to the field of sexual medicine, including male infertility and erectile dysfunction, and allow them to participate in many of the events at the AUA.⌘

2008 Men's Health Fellowship Recipients

Allen Haraway	University of Mississippi
Brian Helfand	Northwestern University
Aaron Johnson	Georgetown University
Eric Laborde	Louisiana State University
Stephen Lukascwycz	University of Minnesota
Andrew Nisbet	University of Connecticut
Peter Stahl	Weill Cornell Medical College/ New York Presbyterian Hospital
Heidi Stephany	University of Kansas
Kristopher Whitehead	Mayo Clinic, Jacksonville
Aimee Wiltz	University of Chicago

2008 Allied Health Fellowship Recipients

Karen Chamuel	Jackson Memorial Hospital
Kevin Flinn	Men's Health Boston
Nikunj Gajarawala	Mayo Clinic – Jacksonville
Rachel Natale	Univ. of Pennsylvania Health Sys.
Monique Wilson	Cooper Urologic Institute

2009 SSMR Program

"Endocrinology of Male Reproduction"
Peter N. Kolettis, MD, Program Chair

Endocrine disorders are uncommon but treatable causes of male infertility. This year's program will review endocrine disorders and their relationship to male reproduction and sexual function. Among the controversies to be discussed include the definition, diagnosis and treatment of male hypogonadism.

Certainly, with availability of alternative routes of testosterone supplementation, marketing, and media attention, the diagnosis and treatment of hypogonadism has increased dramatically. Many questions remain; including "What is low testosterone?" What are symptoms of hypogonadism? Do asymptomatic men need to be treated? What are the consequences of treatment vs. no treatment? How strong is the evidence to support these recommendations? What about testosterone supplementation and prostate disease? What should we do with an infertile man with a low testosterone? The program will also address two other related issues, manipulation of the hypothalamic-pituitary-testicular axis prior to chemotherapy and anabolic steroid use and male infertility.

Finally, as a natural extension of a discussion of endocrine disorders and male reproduction, the program will address nonsurgical contraception. We are fortunate to have Dr. John Amory, one of the leaders in this field, review this topic and discuss key issues, including efficacy, compliance, and reversibility.

We hope the program is educational for the audience and will give them new information that they can apply to the care of their patients. We invite all members of the Society for the Study of Male Reproduction and all attendees of the American Urological Association meeting to attend and look forward to a program which is sure to generate discussion and debate.

ASRM Annual Meeting
November 8 – 12, 2008
San Francisco, CA

ASA 33rd Annual Conference
April 4 – 7, 2009
Hyatt Regency Philadelphia
Philadelphia, PA

ASA Testis Workshop
April 1 – 4, 2009

Andrology Lab Workshop
April 4, 2009

AUA 2008 Annual Meeting
April 25 – 30, 2009
Chicago, IL

SSMR Annual Meeting at the AUA Annual Meeting
Tuesday, April 28, 2009
Chicago, IL

Mark Your Calendars!

Online Voting for SSMR Leadership
From February 15 – April 15, 2009, you will be able to vote for the 2009 – 2010 open SSMR leadership positions on line at www.ssmr.org.

Exercise your RIGHT TO VOTE!

SSMR Board of Directors

PRESIDENT
Stanton C. Honig, MD

VICE PRESIDENT
Robert E. Brannigan, MD

SECRETARY
Ajay K. Nangia, MBBS

TREASURER
Natan C. Bar-Chama, MD

MEMBERS AT LARGE
Victor M. Brugh, III, MD
Paul R. Shin, MD

PAST PRESIDENTS
Jay I. Sandlow, MD
Jon L. Pryor, MD

DIRECTOR OF DEVELOPMENT
Harris M. Nagler, MD

DIRECTOR OF TRAVELING FELLOWSHIP
Raymond A. Costabile, MD

EXECUTIVE DIRECTOR
Wendy J. Weiser

ASSOCIATE DIRECTOR
Debbie Roller

Men's Health Traveling Fellowship Program 2009

Dear Urology Residency Directors and SSMR Members:

The Society for the Study of Male Reproduction (SSMR) and the Society for Sexual Medicine of North America (SMSNA) are proud to announce the Ninth Annual Traveling Fellowship Program with the SSMR and the fourth combined award for the two societies. This will take place in conjunction with the 2009 AUA meeting in Chicago, Illinois.

The SSMR and SMSNA, AUA-affiliated subspecialty societies, have a mission to promote the advancement of the science and treatment of male reproduction and sexual disorders through education of practitioners, public education, and informational exchange of research and new advances through meetings. The SSMR and SMSNA are committed to cultivating interest in infertility and sexual medicine treatment careers in trainees.

Our goal is to present residents in training with the opportunity, while attending the AUA meeting, to have a more intensive exposure to male infertility and sexual medicine issues. The fellowship program will include mandatory attendance at the SSMR and SMSNA educational programs and complimentary SSMR banquet participation and SMSNA lunch. Fellows will also attend AUA post-graduate courses in male infertility, erectile dysfunction and the infertility podium and poster sessions, as well as a symposium with fellowship directors and faculty members on how to prepare for a future successful career as an andrology specialist. The program will allow significant contact between fellows and leaders in the field.

Preference will be given to those in earlier years of training. This does not mean, however, that senior residents and fellows cannot apply. Their applications will be considered along with the others. Participants accepted into the program are expected to take part in all components. This means that attendance at the meeting from Sunday through Tuesday will be required.

Meeting expenses covered by the program may include airfare, hotel accommodations, SSMR and SMSNA meeting and banquet, tuition for the post-graduate course, and all special lectures. The maximum stipend will be $1,000 per fellow. Overages are the responsibility of the fellow or the home institution.

An application is attached, which needs to be completed by the applicant and signed by the director of the training program, assuring commitment from the chief to allow full attendance of the fellowship program, should the applicant be accepted. The applicant should solicit a letter of recommendation from a mentor of his/her choice. **Applications are due by January 15, 2009.** The awards will be announced by February 15, 2009.

We hope you will consider supporting this program through the application of trainees in your program. We look forward to another successful Men's Health Traveling Fellowship!

Sincerely,

Raymond A. Costabile, MD
Director of Traveling Fellowship

Craig F. Donatucci, MD
SMS, President

Stanton Honig, MD
SSMR, President

Application for the 2009 Men's Health Traveling Fellowship Program

Sunday, April 26 – Tuesday, April 28, 2009 | Chicago, Illinois

Please print or type.

Name:_____Degree(s):_____

Work Address:_____

City:_____State:_____Zip:_____

Home Address:_____

City:_____State:_____Zip:_____

Work Phone:_____Home Phone:_____

ogo.jpg Fax:_____E-mail:_____

Current Position (Resident / PGY Year, Post-Doc):_____

Institution / Department:_____

Please attach the following:

1. Curriculum vitae
2. Personal statement (1 page or less)
3. Letter of recommendation from chairman or selected mentor

Signature of Applicant:_____

Chairman Signature: By signing below, I am supporting the application of the above-named member of our department as a traveling fellow of the SSMR and SMSNA. I understand that attendance at the AUA meeting will be subsidized by the award to a maximum of $1,000, and that attendance of the fellow at all traveling fellowship functions is expected. Sunday through Tuesday evening at a minimum.

Signature of Department Chairman:_____

Send completed applications to:
SSMR/SMS Traveling Fellowship
Two Woodfield Lake
1100 E. Woodfield Road, Suite 520
Schaumburg, IL 60173

Deadline: January 15, 2009

Many Thanks To Our 2008 Industry Partners

Bedford Scientific
Coast Reproductive
GSK/Schering Plough
Gyrus/ACM
Sexual Medicine Society of North America
Vasowear
Vasectomy.Com

Society for the Study of Male Reproduction
Two Woodfield Lake
1100 E. Woodfield Road, Suite 520
Schaumburg, IL 60173-5116
Phone: 847-517-7225 • Fax: 847-517-7229
E-mail: info@ssmr.org
Website: www.ssmr.org

The Society for the Study of Male Reproduction (SSMR) encourages organizations and individuals to link to www.ssmr.org.

SSMR

Two Woodfield Lake
1100 E. Woodfield Road, Suite 520
Schaumburg, IL 60173-5116