NEWS

SSMR

SOCIETY FOR THE STUDY OF MALE REPRODUCTION

SSMR NEWSLETTER FALL 2003

PRESIDENT'S MESSAGE

ROBERT OATES, M.D.

Welcome, everyone, to the SSMR 2003 fall newsletter. I hope all of you are having a wonderful summer. It is not too late to e-mail me with suggestions for the 2004 SSMR scientific program. I have received a number of excellent suggestions, which will simply allow us to generate a program that meets your needs, the membership, as best possible. Dr. Mark Sigman is program director for the 2004 SSMR scientific session and I know that he will put together an exciting and stimulating program. Look for details in your e-mails as well as in the spring newsletter. Please feel free to e-mail me at Robert.Oates@bmc.org and pass along any thoughts that you might have.

Within this newsletter you'll find that Dr. Craig Niederberger, our Vice President, has provided us an outline and summary of the upcoming sessions at the 2003 ASRM meeting to be held in San Antonio, Texas, beginning Sat., October 11, and ending Wed., October 15. The weekend Postgraduate Course, chaired by Dr. Paul Turek, looks to be a timely update on the basic biology and testing of male reproductive failure. Along with Dr. Turek, Dr. Keith Jarvi, Dr. Renee Reijo and Dr. Renee Martin comprise this most accomplished faculty. On Monday there is a fantastic plenary session, the AUA Bruce Stewart Memorial lecture, given by Dolores Lamb, Ph.D., on the new Genetics of Male Infertility in the Era of ICSI. As you look through the remainder of the schedule, you can see that on Monday, Tuesday and Wednesday there are numerous workshops, plenary sessions, scientific podiums and poster sessions, as well as a host of luncheon roundtables, which should be of interest to the SSMR membership.

As we always do in our fall newsletter, a comprehensive review of the presentations of interest to members of SSMR from the past AUA meeting is included. Jon Pryor, as Chair of the 2003 SSMR Program Committee, reviews the SSMR scientific session, which was held on Saturday afternoon, April 26. It was quite an interesting forum dealing with very practical issues surrounding the practice of male reproductive medicine and surgery, and was quite well received and enjoyed by all. Every other session at the AUA of direct importance to our membership was attended by at least one of our intrepid Board of Directors members and also reviewed for us. This includes all of the

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relevant podium, poster and plenary sessions. Dr. Dale McClure provides us a synopsis of the Endocrine forum, while Dr. Larry Lipshultz summarized this all this with his perspective on the "take-home messages" session, which he presented to the membership on Thursday morning. In reading through myself, I was reminded of many of the facts and concepts I had learned during the AUA and I hope you find our efforts in providing this review helpful to you as well.

The annual SSMR traveling fellowship program also took place at the AUA this past year and was a great success. Dr. Jay Sandlow, who has headed up this program since its inception, provides a brief synopsis of the who's, where's, and how's of this great program. The 2004 SSMR traveling fellowship information is included in this newsletter. We would love to have every resident of every program attend our 2004 SSMR scientific session (some as Traveling Fellows) and ask that you encourage your resident staff and program directors in this direction. Our goal this year is to increase our membership and awareness by reaching out to as many potentially interested parties as we can – your help in this endeavor would be appreciated.

In other news, we are grateful to Larry Levine for arranging the SSMR banquet for us this past spring. It was a significant amount of effort that was rewarded by a delightful evening. We are trying to line up a unique dinner for next year – details to come, but it looks to be a lot of fun. Dr. Jon Pryor was elected Secretary and Dr. Peter Kolettis was elected as Member-at-large by your votes during the business meeting. Congratulations. Once again, I would like to personally thank Dr. Peter Schlegel for his leadership of SSMR this past year. He provided me with a great example of how it's done. He left us in an even stronger position than when he started. The Board of Directors agreed unanimously to extend the contract of W.J. Weiser and Associates, as they have been the backbone of the day-to-day management of our organization. We are delighted that they have agreed – it is a mutual partnership that is thriving.

Have a good remainder of the summer and, hopefully, when I see all of you at the 2003 ASRM, my Red Sox will be headed to their first World Series Championship since 1918 (we can all dream). ◆

3rd SSMR Traveling Fellowship Program

The 3rd SSMR Traveling Fellowship Program took place at the AUA in Chicago this year and was a great success. These awards are designed to expose young urology residents to the field of male infertility, and allow them to participate in many of the events at the AUA. Ten fellows from various institutions were selected. The fellows attended the SSMR Postgraduate Course and banquet, went to all of the infertility podium and poster presentations, and participated in a roundtable discussion with some of the up-and-coming leaders in the field of male infertility, including Cathy Naughton and Peter Kolettis. The experience ended with an informal cocktail party, where the fellows were able to meet with many of the SSMR members. The program was sponsored by a generous grant from Bayer, and allowed these young urologists-in-training to attend the AUA meeting, as well as gain exposure to the field of male infertility. The fellows who participated this year were:

Stephen Boorjian
Weill Medical College of Cornell University

Weber Chuang
Baylor College of Medicine

Margaret Hollingsworth
Medical College of Wisconsin

Carin Hopps
Weill Medical College of Cornell University

Edward Karpman
University of California-Davis

Kirk Lo
Baylor College of Medicine

Sejal Soni Quayle
Washington University

Jonathan Schiff
Weill Medical College of Cornell University

Richard Sowery
Queens University-Ontario

Edward Yun
University of California-San Francisco

The feedback has been tremendous and we will continue to offer this great experience to all urology residents. Questions may be directed to Jay Sandlow, M.D., at jaysandlow@uiowa.edu. ◆

2003 ASRM Events of Interest

ASRM Annual Meeting
October 11-15, 2003
San Antonio, Texas

Saturday, October 11 – Sunday, October 12
Full Weekend Course:
Gamete Development, Genetics, and Testing in Male Reproductive Failure
Faculty:
Paul Turek, M.D., Chair
Keith Jarvi, M.D.
Renee Martin, Ph.D.
Renee Reijo-Pera, Ph.D.
This course has been developed in cooperation with the Society for Male Reproduction and Urology.

Sunday, October 12
One-Day Course: *Immunology of Infertility: From Laboratory to Clinic*
Faculty:
Rajesh K. Naz, Ph.D., Co-Chair
Dana A. Ohl, M.D., Co-Chair
Dan I. Lebovic, M.D., M.A.
This course has been developed in cooperation with the Reproductive Immunology Special Interest Group.

Monday, October 13
Plenary Session 1 of the Scientific Program:
AUA Bruce Stewart Memorial Lecture: The New Genetics of Male Infertility in the Era of ICSI
Dolores Lamb, Ph.D.

Monday, October 13; 10:45 a.m. – 12:00 p.m.
SMRU Traveling Scholar Abstracts

Monday, October 13; 12:00 p.m. – 2:00 p.m.
Male Reproduction and Urology Roundtables:

Treating Ejaculatory Dysfunction
Dana A. Ohl, M.D.

Sperm Retrieval in Non-Obstructive Azoospermia
Peter N. Schlegel, M.D.

Genetic Evaluation of the Infertile Male
Robert D. Oates, M.D.

Cancer and Male Infertility
Mark Sigman, M.D.

Clinical Significance of Seminal Oxidative Stress
Ashok Agarwal, Ph.D.

Vasovastomy, Vasoepidymostomy and Sperm Retrieval: How, Why and When
Marc Goldstein, M.D.

Monday, October 13;
2:00 p.m. – 5:15 p.m.
Concurrent Session: *Male Reproduction and Urology Abstracts and Lectures*

Tuesday, October 14;
10:45 a.m. – 12:00 p.m.
SMRU Workshop: *Genetic Evaluation of Male and Female Reproductive Failure*
Faculty:
Peter N. Schlegel, M.D., Chair
Lawrence C. Layman, M.D.
Paul G. McDonough, M.D.
Robert D. Oates, M.D.
This workshop is intermediate level, appropriate for practicing clinicians, embryologists, and basic science researchers. The contribution of genetics to the production of male and female infertility will be critically evaluated. Modern methods for detection of such genetic defects and the impact of these defects on the outcome of assisted reproduction will be reviewed and discussed.

Tuesday, October 14;
10:45 a.m. – 12:00 p.m.
Reproductive Biologists Professional Group Workshop: *Future of Spermatogonial Stem Cells and ART*
Faculty:
Gary D. Smith, Ph.D., Chair
Dolores J. Lamb, Ph.D.
Derek J. McLean, Ph.D.
This workshop will focus on recent advances in spermatogonial stem cell research, with an emphasis on potential future applications in human assisted reproductive technologies. Presentations will identify areas requiring future basic and translational research before this technology is efficient and applicable in a clinical setting.

Tuesday, October 14;
12:00 p.m. – 2:00 p.m.
Male Reproduction and Urology Roundtables:

Testicular Mapping and Sperm Retrieval
Paul J. Turek, M.D.

Varicocele Repair Prior to ART: Does it Make a Difference?
Jay I. Sandlow, M.D.

Spermatogonia: Renew, Differentiate or Die
Cathy Naughton, M.D.

Percutaneous Sperm Acquisition Techniques
Joel L. Marmar, M.D.

Preparation and Cryopreservation of Testicular and PESA Samples for ICSI
Nina N. Desai, Ph.D., H.C.L.D.

Predicting Successful Vasectomy Reversal
Harris M. Nagler, M.D.

Tuesday, October 14;
2:00 p.m. – 5:15 p.m.
Concurrent Session: *Society for Male Reproduction and Urology Abstracts and Lectures*

Tuesday, October 14; 5:15 p.m.
SMRU Business Meeting

Wednesday, October 15;
10:45 a.m. – 12:00 p.m.
SMRU Workshop: *New Methodologies for Propagation of Male and Female Germ Cells*
Faculty:
Susan A. Rothman, Ph.D., Chair
Roger G. Gosden, Ph.D., D.Sc.
Pasquale Patrizio, M.D.
This workshop will address the future of reproductive medicine and explore recent advances in germ propagation in vivo and in vitro. The implications of these procedures will also be reviewed.

Wednesday, October 15;
2:00 p.m. – 5:15 p.m.
Concurrent Session: *Male Reproduction and Urology Abstracts and Lectures* ◆

Highlights of the SSMR Annual Meeting

Saturday, April 26, 2003

Submitted by Jon L. Pryor, M.D.

On Saturday afternoon of April 26, 2003, the SSMR held its 2003 Annual Scientific Meeting. The Program Chair was Jon L. Pryor, M.D., from University of Minnesota and the theme was "Practical Practices in Infertility." The first talks were centered on the Andrology Laboratory. Bruce Gilbert, M.D., Ph.D., a urologist who is a certified High Complexity Laboratory Director in a private practice in New York, gave the opening talk entitled "Practical Aspects of Setting up the Lab: How to do it Right." Dr. Gilbert started with the pros and cons of setting up your own lab, with an upside that includes practice revenue, and a downside that it takes effort and additional training. If a semen analysis is being performed, by definition it's considered a high complexity test. For an M.D. (non-pathology trained) to become a laboratory director of a high complexity laboratory requires two years of experience, which basically means someone else must be the director for two years while the urologist gains experience. Certification requirements were discussed. He estimated start-up expenses, which include basic equipment like a centrifuge and refrigerator, were $6,000 to $15,000 the first year and then yearly fees of $1,000 to $3,000, not including staff time. In summary, he felt that urologists could start and direct their own andrology labs, and it could increase their revenue and quality of care, but if it's going to be done, do it right. This means do your homework, use consultants, and develop a procedure manual with an emphasis on QA and QC.

The next talk in this area was by Brooks A. Keel, Ph.D., an Associate Vice President for Research at Florida State University. Dr. Keel's talk was "The Andrology Laboratory: How to do it Wrong." The first part of Dr. Keel's talk was on the significant lack of standardization of labs performing a semen analysis, and when sent standard samples, the great variation in reported results, i.e. andrology laboratories are not doing a good job. He emphasized physicians should exercise caution in using and interpreting lab tests. The lab should be CLIA (Clinical Laboratory Improvement Amendments) approved, as they have certain standards they adhere to. The urologist can also tell a lot from looking at the andrology report. The report should contain things like: date and time of collection, time analysis performed, abstinence period, method of collection, units of measure and normal values for semen parameters, which includes the morphology criteria being used. For example, if you read a motility that is 90%, or 88% normal forms for morphology, beware. In summary, Dr. Keel felt there were a lot of bad labs out there and physicians need to exercise caution in interpreting lab reports.

The next group of lectures was on "Non-Surgical Therapy of Infertility." Dr. Mark Sigman, an Associate Professor of Urology at Brown University, talked about medical and empirical therapy for infertility. He began with a discussion about hormonal deficiency or secondary hypogonadism. The primary defect is GnRH deficiency; it's a rare (<3% incidence) but very treatable problem. Most cases of hypogonadotropic hypogonadism (HH) are congenital, with 38% being Kallmans syndrome (anosmia, cleft palate, deafness, renal anomalies, cryptorchidism, and micropenis) and 54% are normosomic, which is like Kallmans but without the anosmia. 8% of cases are acquired. These patients are primarily treated with hCG (Dr. Sigman recommends 2000 IU 2x/ week) for at least six months, and if there is no response in improved sperm concentration, add pure FSH or hMG. It may take a total of 18 months of therapy to see a response. He then spoke about hormone excess: androgen excess, estrogen excess, and hyperprolactinemia. Androgen excess, which can be from anabolic steroid abuse, congenital adrenal hyperplasia, or tumors of adrenal gland or testis, should be treated as HH above. He stated that estrogens inhibit gonadotropin secretion and can be from adrenal or testicular tumors, hepatic dysfunction, or obesity (aromatase in adipose tissue converts testosterone to estrogens).

Hyperprolactinemia can be from a pituitary macroadenoma or microadenoma; hypothyroidism; stress; liver disease; or medications such as phenothiazines, tricyclic antidepressants, and some antihypertensives; as well as idiopathic. He stated that hyperprolactinemia without HH is not likely to be a cause of infertility. Patients with hyperprolactinemia should undergo evaluation by a MRI and the underlying cause should be treated.

The second portion of Dr. Sigman's talk was on empirical therapy. Empirical therapy can be tried on patients with idiopathic infertility, which he defined as those with no identifiable etiology and an abnormal semen analysis. In general, he felt that most empirical therapies were largely ineffective or unproven. They can be tried for 1-2 spermatogenic cycles (i.e. 6 months) and if the semen analysis is improved, continued and if not, stopped. One empirical therapy, androgen therapy or androgen rebound therapy, is not only ineffective, but may decrease spermatogenesis and therefore should not be used. He did feel that patients with decreased T/E2 ratios (fertile men have ratios around 10-22, mean of 16; NOA patients 7, and Klinefelter patients 4), may benefit from aromatase inhibitors (i.e. testalactone or non-steroidal Anastrozole) prior to sperm retrieval, but that placebo-controlled, randomized studies are needed. Finally, Dr. Sigman reviewed the carnitine data and said that there has been only one report of a placebo-controlled study (Lenzi et al, 2003) that resulted in improved semen parameters, and more studies are needed.

The next talk on non-surgical therapy was on complementary/alternative medicine therapy. It was delivered by Mark W. McClure, M.D., who is the founder of Landmark Urology and Complementary Medicine in North Carolina and a speaker and author in the field of complementary medicine. He reviewed the literature in this field as it applied to the testicle, epididymis and prostate/seminal vesicles and then looked at specific applications to improve semen quality. The common recommendations to maintain health in all of these genitourinary structures and to improve sperm parameters is to avoid gonadotoxins (excessive alcohol intake, illicit drugs, smoking, certain OTC drugs, and anabolic steroids), and to take antioxidants (e.g. vitamin C, L-carnitine, zinc, vitamin E, and selenium).

The final part of the program was on best surgical techniques. Joel Marmar, M.D., Professor of Urology at the Robert Wood Johnson Medical School in Camden, N.J., spoke on best techniques of doing a varicocelectomy. After reviewing the goals of a varicocelectomy, he felt that the best technique was his as described in 1984. It can be done with sedation and local anesthesia. Under magnification, a 2 cm incision is made over the external ring and the spermatic cord is isolated. The internal spermatic fascia is opened to expose the varicose veins and papaverine is applied to the cord to amplify the arterial pulse. All veins that are 2 mm or greater are clipped with hemoclips. With penrose drains cinched proximally and distally to temporarily occlude a section of the cord, 0.5 to 1.0 ml of a sclerosing agent (Sotradecol 3%) is injected directly into one of the veins to sclerose the remaining collaterals. The advantage of this technique

is low hydrocele formation, low recurrence rate (0.8%), and the sclerosing method should occlude all collaterals. Dr. Stuart Howards, Professor of Urology at the University of Virginia critiqued Dr. Marmar's talk. Dr. Howards uses a micro-doppler probe to help find the artery and uses Marcaine or Lidocaine to dilate the artery, as it is less expensive and more available in the O.R. than Papaverine. Because he uses a microsope to identfy and occlude all the veins, and there is no randomized study to show that injecting a sclerosing is advantageous, they do not inject during the procedure. Both Drs. Marmar and Howards concluded that the best method depends on the surgeon's preferences as well as patient preferences and the particulars of the institutional facilities.

Dr. Richard Berger, Professor of Urology at the University of Washington, spoke on the best techniques for a vasectomy reversal. After reviewing numerous studies and discussing the pros and cons of the studies, he concluded that a microscopic is better than a macrosopic vasovasostomy and a two-layer approach is better than a stented approach. He reviewed various techniques for vasoepididymostomy and concluded that a microscopic technique is best. His triangulation (invagination) technique has been a wonderful modification with 92% patency when done bilaterally. Dr. Arnold Belker, Clinical Professor of the Division of Urology at the University of Louisville, concluded the session by critiquing Dr. Berger's talk. Dr. Belker felt that Dr. Berger's triangulation vasoepididymostomy appears to produce results that are at least as good as those obtained by the end-to-side microsurgical method first reported by Thomas. Dr. Belker stressed that when doing the triangulation technique, place all three sutures before pulling them through the wall of the tubule, to prevent the partial collapse of the tubule. He also stressed that the anastomosis must be performed at a level where whole sperm are present in the epididymal fluid, that the learning curve for a vasoepididymostomy is steep, and that surgeons should inform patients of their own results. He also does not recommend cryopreservation of sperm at time of vasectomy reversal, primarily because of higher costs compared to doing TESA at a later date, if necessary. ◆

Highlights from the State-of-the-Art Lecture

The Molecular Basis of Congenital Genitourinary Anomalies

Sunday, April 27, 2003; 10:40 a.m.

Reviewed by Robert Oates, M.D.

Lecture given by: Kenneth Glassberg, M.D.
Children's Hospital of New York Presbyterian, Division of Pediatric Urology,
Columbia University, College of Physicians and Surgeons

Dr. Glassberg gave a fascinating lecture on the basic science involved in the earliest events in formation of the kidney. This involves a host of genes that assist/cause ureteric bud outgrowth and metanephric differentiation. There is a tremendous amount of cross-talk between these two structures and a defect in any of the multiple gene products involved in the process will lead to deficiency in formation of the kidney or in regulation of growth of the kidney. For example, homozygous loss of Gdnf in the mouse will lead to a syndrome of absent ureteric bud formation and renal agenesis, while a similar loss of both Wnt-4 genes may only lead to small dysplastic kidneys. While the knowledge base is growing in the mouse model and the molecular mechanisms and interactions are being explained and understood, human syndromes are also being investigated. There are a number that already have a genetic basis established, such as the Renal-Coloboma Syndrome, due to a mutation in PAX2, or the BOR Syndrome, due to a mutation in EYA1. Many human conditions have yet to have their genetic etiology defined, but this is an area ripe for inquiry. Is there a link to any of these genes and bilateral vasal agenesis associated with unilateral renal agenesis? Perhaps. If so, what would be the transmission pattern and will the offspring of our patients with this condition be affected in some way? Dr. Glassberg's talk can be accessed at www.prous.com/aua2003. ◆

Highlights from the State-of-the-Art Lecture

Long-Term Consequences of Testicular Cancer

Monday, April 28, 2003; 8:00 a.m.

Reviewed by Phil Wise, M.D.

This state-of-the-art lecture covered areas of interest to the general urologist regarding several areas of concern, in addition to the well-known effects on the fertility aspects of testis tumors of all varieties. He grouped his talk according to physiologic systems after detailing some of the evidence with respect to secondary tumors in general

He started by producing evidence to show that there is an increase in secondary cancers, especially after radio therapy, and that there is a particular etoposide related leukemia.

Fertility effects:

Of those who were normo-spermic pretherapy, 20% were azoospermic, 16% were oligospermic and 64% were normospermic after chemotherapy. In this study, 30% were treated with carboplatin-based regimens. The effects were more pronounced in men with poorer quality semen prior to treatment.

For Low dose chemo (two courses of BEP) in high-risk disease patients the numbers aren't large enough to make a definitive statement; however, the trend is toward less impact on the semen analysis but there is some impact nonetheless.

The effects of XRT scatter are usually transient in seminoma patients.

Cardiovascular effects:

Cardiovascular events are higher in groups treated with chemo than those treated with orchiectomy alone. There are other cardiovascular related diseases such as elevate insulin to glucose ratios, hypertension and dyslipidemias.

Renal effects:

In a study of 85 patients, 2 had impaired renal function after RPLND and 23 had impaired function after chemo or XRT for testis tumors.

Neurologic effects:

Decrease cognitive function was found in the patients treated with platinum-based chemo. In another group, 38% had non symptomatic neuropathy, 28% symptomatic neuropathy and 6% disabling polyneuropathy.

Sexual/Psychological effects:

Decrease in spermatogenesis and decrease in Leydig cell function. Fatigue, depression, anxiety are increased compared to Hodgkin's lymphoma survivors.

Late relapse, defined as greater than two years, is usually of the yolk sac variety and is not very sensitive to standard chemotherapy regimens.

At the end, Dr. Foster made some recommendations regarding the discussion of the risks of surveillance, chemotherapy and radiotherapy in relation to that of RPLND.◆

Highlights from the AUA Update

Pharmacologic Management of Ejaculatory Disorders

Monday, April 28, 2003; 11:50 a.m.

Reviewed by Stephen Shaban, M.D.

This is a brief review of the AUA guidelines for such. A meta-analysis of more than 40 articles was undertaken. The more commonly used terminology "premature ejaculation" has been renamed "rapid ejaculation."

The preliminary guidelines for treatment include the route of using selective serotonin reuptake inhibitors and/or topical Lidocaine products. The dosing of the SSRIs was either on an as needed single dosing regimen a couple of hours before coitus vs. using q-day for several weeks to months at a time. ◆

Highlights from the Endocrine Forum

Monday, April 28, 2003; 1:00 p.m. – 3:00 p.m.

Reviewed by Dale McClure, M.D.

An excellent Endocrine Forum focused on the rapidly expanding areas of clinical and basic research in erectile dysfunction (ED) and on new therapeutic options. The session ended with a timely lecture on the topic of testosterone therapy and prostate cancer.

Dr. Gregory Broderick's lecture discussed whether lower urinary tract symptoms (LUTS) and ED were a coincidence or a causation. As both sexual dysfunction and BPH/LUTS increase with advances in age, it appears that the severity of LUTS is directly correlated with the prevalence of male sexual dysfunction. A multinational survey of 14,000 men ages 50-80 years old found that sexual function indices where statistically correlated with the international prostate symptom score (Rosen et al, IJIR: 2002; 14(3)). Urgency, nocturia, and intermittency were positively associated with self-ratings of ED and ejaculatory dysfunction. Possible mechanisms include sleep disturbance, psychological anxiety, and the pathophysiological effects of BPH or shared pathology, implicating the molecular modulators of smooth muscle tone. In conclusion, sexual function should be taken into account in the initial evaluation and treatment of BPH/LUTS patients.

Dr. Tom F. Lue discussed gene therapy and ED. Recently scientists have begun to explore the feasibility of targeting molecules in the pathway of penile erection for the prevention and treatment of ED. Angiogenin and neurotrophin therapy have possibilities, as vascular insufficiency is the most common cause of ED and neurogenic (neurogenic/vasculogenic) ED is common after radical surgery for prostate and bladder cancer and in diabetic patients. The following molecules have been studied in animals with promising results: iNOS, eNOS, and nNOS. Several growth factors have also been studied, including: calcitonin gene-related peptide (CGRP), vascular endothelial growth factor (VEGF), fibroblast growth factor (FGF) and brain-derived neurotrophic factor (BDNF). In the rat model, Rogers et al (Int J of Impot Res 2003; 1:26-37), showed that intracavernosal vascular endothelial growth factors (VEGF) injection and adeno-associated virus-mediated VEGF gene therapy prevented and reversed venogenic ED in rats. In recent laboratory studies, Dr. Lue and associates have demonstrated nerve regeneration and the possibility of enhancing nerve growth with VEGF and BDNF. As a result of these studies, a better understanding of angiogenesis and neuro regeneration might help prevent and cure venogenic and neurogenic ED due to various causes.

> ***"...individuals on hormone replacement therapy should have their prostates and their PSA values carefully monitored..."***

Dr. Ridwan Shabsigh discussed the importance of combined therapy (androgens and sildenafil) in sildenafil non-responders. In animal models, testosterone replacement after castration reversed the reduction in nitric oxide synthase-stained nerves in the erectile tissue and corrected the erectile dysfunction. Dr. Shabsigh discussed the safety and efficacy of testosterone-gel 1% 5 g daily plus sildenafil 100 mg in producing an erectile response in hypogonadal men who have failed previously with sildenafil alone (abstract # 954, AUA). The sildenafil non-responsive individuals had low to low-normal testosterone, i.e. <400ng/dL. An analysis of 67 patients at week 4 showed that testosterone gel 1% significantly improved response to sildenafil on the erectile function (EF) domain of the International Index of Erectile Function (IIEF), orgasmic function (OF) and overall satisfaction (OS) domains in the IIEF total score. In summary, androgen replacement should be considered for treatment of ED in men with low or low-normal testosterone who have failed prior treatment with sildenafil alone.

Dr. Abraham Morgentaler's important and timely lecture was entitled "Testosterone Therapy and the Prostate: Is this Really a Problem?" In the last several years, the diagnosis and treatment of hypogonadism has been an increasingly popular topic. A commonly asked a question is "if reducing serum testosterone make prostate cancer regress, then might not testosterone supplementation cause undiagnosed prostate cancer to grow?" The signs and symptoms of hypogonadism include low libido and sense of vitality, erectile dysfunction, diminished muscle strength and bone density, impaired cognition, and depressed mood. Testosterone replacement therapy can significantly improve many of these areas, thereby significantly improving the quality of life. Because older men are at greatest risk for both hypogonadism and prostate cancer, it is important to assess both the risks and benefits of testosterone replacement. In a review of 7 testosterone therapy trials, in which 461 men were followed for 6 to 36 months, prostate cancer was diagnosed in 5 new cases (1.1%). This incidence is no different than the cancer detection rates in the general population. Among 12 prospective studies investigating the relationship of endogenous androgen levels and the development of prostate cancer, only one showed any connection. This one study, The Physicians Health Study (J Nat Canc Inst 1996;88:1118), showed no difference in testosterone levels between men who subsequently developed prostate cancer and those who did not. It was only with simultaneous adjustment for four other hormone levels that a relationship between higher testosterone and prostate cancer could be identified. The clinical significance of this type of analysis is uncertain at best.

Only with completion of large-scale, long-term studies can a definitive statement regarding the risks of testosterone therapy be of value. At the present time there is no compelling evidence that hormone replacement therapy increases the risk of prostate cancer; however, individuals on hormone replacement therapy should have their prostates and their PSA values carefully monitored and ultrasound and prostate needle biopsy carried out when indicated. ◆

Highlights from the State-of-the-Art Lecture

Androgen Deficiency in the Aging Male and Female

Tuesday, April 29, 2003; 11:30 a.m.

Reviewed by Stephen Shaban, M.D.

Dr. John Morley, Professor of Gerontology at St. Louis University, did a fine job of reviewing androgen deficiency in the aging male and female. He discussed the fact that we, in general, are all living longer. That the use of testosterone replacement therapy in men is for improvement of quality of life. He reviewed the various interpretations of the definition of hypogonadism. He wanted to stress andropause has not been developed by the pharmaceutical industry. He went into a very nice and amusing history of how mankind used testosterone as replacement therapy for centuries.

He went on to discuss the difference between bio available Free and Total testosterone levels. In essence, 60% is sex hormone bound, globulin bound. 38% is tissue available or bio available and albumin bound and 2% is free. He reiterated that measuring total testosterone is not really a good idea in older men. He went on to reiterate that testosterone therapy can improve the quality of Viagra in promoted erections and that an AUA abstract at this current meeting substantiated this. In general, remember that TRT improves libido, increasing lean body mass, improves bone mineral density and general well-being.

The remarkable major side effects of TRT include: 1) polycythemia and 2) worrying about promoting prostatic disorders. (He impressed again that this is not proven yet.)

He went on to talk about the utility of using the ADAM questionnaire to help screen patients as well as checking bio available T levels and then consider TRT replacement.

As far as his review of androgen deficiency in the aging female, he felt that studies were essentially terrible and scant but that it is known to increase libido and has similar effects in women as it does in men. Certainly we are in need of more trials in the female population. ◆

Highlights from the Podium Session

Infertility Therapy

Tuesday, April 29, 2003; 3:30 p.m. – 5:30 p.m.

Reviewed by Robert Oates, M.D.

Dohle et al from the Netherlands performed a well-conducted prospective randomized trial on varicocele treatment in oligospermic men, comparing treatment to watchful waiting. All men had oligospermia (no patient was azoospermic) according to WHO guidelines and all female partners were without evident problem and were < 36 years of age. 72 couples were randomized to varicocele correction or no treatment. Those in the control arm that did not achieve pregnancy after the first year were offered varicocele correction or ART. While both count and motility increased in the varicocele group after surgery, most importantly, 36% of the treated couples achieved pregnancy in that first post-operative year, while only 9% of the controls did so. For those of us who believe in varicocele correction in appropriate couples, this study is welcomed evidence for our side of the "debate."

Kolettis et al from Birmingham compared the naturally conceived pregnancy rates following vasectomy reversal in their patients to those resulting from ICSI (using 1999 age-range SART data) in a subgroup of their couples in whom the female partner was > age 35 years. In this retrospective review, almost all 46 patients had vasovasostomies. Unfortunately, only 27 returned for follow-up semen analysis. Of those, the patency rate was 81% and the pregnancy rate for 38 evaluable couples was 34%. The authors concluded that vasectomy reversal is at least as successful as a single cycle of ICSI in this cohort of patients. If the goal of the couple is to achieve pregnancy, how can it be a negative to have sperm in the ejaculate each and every month? (personal statement, RD Oates)

Marmar and colleagues from Philadelphia, New York and San Francisco pooled their data and reported on 8 couples that had opted for PESA/ICSI instead of vasectomy reversal and then come back for reconstruction. The intent of their abstract was to investigate how much trauma to the epididymis resulted from PESA and whether this affected the outcome of reconstruction. VV was appropriate in 5 men, VV/VE in 2 men and bilateral VE in 1 man. All patients were patent and 3 achieved pregnancy. They concluded that PESA produced limited trauma to the epididymis and that VV and/or VE could be performed successfully after PESA.

Boorjian et al from New York studied "the impact of the time interval from vasectomy to reversal and the presence of sperm granuloma on the outcome of vasectomy reversal." Patency was no different across obstructive intervals, ranging from 88 - 92%. Pregnancy rates were fantastic for all obstructive intervals (81% for the cohort <15 years) but for those >15 years from the vasectomy it dropped to 44%.

There was no difference in pregnancy rates in those with a palpable sperm granuloma preoperatively to those who did not even though there was a better patency rate in the former. The authors also concluded that the pregnancy rates for men with obstructive intervals >10 years (even 15 years) were higher than those for PESA/ICSI and, therefore, recommend reconstruction.

Crain et al from San Diego polled practicing Urologists in the Western Section in regard to their techniques of vasectomy reversal with a 20-question survey. Of the many interesting pieces of data they accumulated, 7% of fellowship trained, 35% of academic, and 44% of community Urologists do not use the operating microscope. Of those groups, vasal fluid is not examined at the time of the procedure by 17%, 25%, and 33%, respectively. Approximately 50% of respondents do not recommend evaluation of the female partner. Surgical technique varied as would be expected.

Tash et al from New York related to us their guidelines for post-mortem sperm procurement. Of the 22 requests, 18 were immediately denied for not meeting one or more of the 4 principle criteria. One of the 4 procedures went on to ICSI, which was not successful. To paraphrase, the 4 criteria are: "implied consent by the deceased; only the wife can give consent; death was sudden and suitable cryopreservation facilities must exist; the wife must consent to a 1-year period of quarantine... so that additional counseling may be provided." Instituting these guidelines may minimize the number of retrievals that are unlikely to be used at a later date.

Erol et al from Turkey detailed 16 men whom they felt had isolated FSH deficiency. 8 were azoospermic and 8 were oligospermic. The androgenic axis was normal in all patients as was pituitary MRI. Gonadotropin treatment improved the semen analysis in 11 men (6 of the azoospermics). Although the etiology was undefined, isolated FSH deficiency should be looked for as it is a potentially treatable condition.

Kendirci et al from Turkey reported on 57 men who underwent TURED. 33 (58%) of the men showed improvement in their semen parameters following surgery. The success rate was markedly better for those with a cyst (either midline or eccentric) within the prostate as imaged by TRUS. Patients with partial EDO fared better than those with complete EDO.

SEE INFERTILITY THERAPY, page 8

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Apaydin et al from Turkey related their technique of TRUS guided seminal vesiculography just prior to TURED using methylene blue. The main advantage is that there is immediate confirmation that the ejaculatory ducts have been entered and theta the seminal vesicles are draining through them when the methylene blue is seen effluxing from the incision/resection site.

Okada et al from Japan presented their experience with 20 men who had immotile spermatozoa and in whom those sperm were used for ICSI. 5 men had classic Kartagener syndrome. Those with a 9+0 axoneme (lack of the central doublet) had ADPKD. Pregnancy was achieved only when motile spermatozoa could be found and used. The immotile sperm were not successfully employed. ◆

Highlights from the State-of-the-Art Lecture

Sperm Banking: When, Where and How?
Wednesday, April 30, 2003; 8:35 a.m.
Reviewed by Peter Schlegel, M.D.

The Plenary session reviewing male infertility subjects was started off by Dr. Leslie Schover, who overviewed sperm banking for cancer patients. First, the presentation provided details of appropriate specimen collection and transport for freezing. For patients with cancer, it was noted that 90% of patients are expected to have live sperm in samples after freeze-thaw, despite initially poor semen quality seen for men with advanced cancers. The cost of cryopreservation of 3 samples for 5 years was estimated at $1,000 - $2,500. The experimental procedure of testicular biopsy retrieval and freezing of testicular biopsy specimens from boys was also discussed.

Surveys of oncologists and male cancer patients performed by Dr. Schover, a psychologist, indicated that 66% of men would want to have children, even if they died prematurely. If unable to conceive, only 35% of men indicated an interest in donor sperm use, whereas 66% would consider adoption. Only 37% of childless men banked sperm before potentially sterilizing chemotherapy, and they were more likely to bank sperm if the option was provided by an oncologist. Unfortunately, 48% of oncologists rarely offer sperm banking to their patients, and only 10% of oncologists offer it all the time. Infertility is only discussed as a complication of potentially sterilizing chemotherapy by 60% of oncologists, whereas nearly half of oncologists consider banking too expensive, that no cryopreservation facility is available, or that they don't have enough time to present this option.

Although only 10% of survivors used banked sperm specimens historically, this number may be changing with improved assisted reproductive techniques. Recent data from Cleveland Clinic suggest that 17% of men now use banked specimens provided by men prior to chemotherapy or sterilizing radiation.

Taken together, these observations indicate that educational tools are needed for patients who are candidates for potentially sterilizing chemotherapy, but a significant need for oncologists to increase advocacy for sperm banking is necessary. Urologists seeing men with testicular cancer should certainly be active in recommending sperm banking as well, especially if more advanced therapy is planned after orchiectomy. ◆

Highlights from the State-of-the-Art Lecture

Iatrogenic Causes of Male Infertility
Wednesday, April 30, 2003; 8:55 a.m.
Reviewed by Peter Schlegel, M.D.

The second infertility Plenary session talk on Wednesday was provided by Dr. Christopher Schrepferman. In this presentation, Dr. Schrepferman highlighted the effects of treatment of testicular cancer, inguinal and scrotal surgery, as well as medications on male fertility.

It was pointed out that testicular cancer affects primarily younger men and is associated with a high cure rate. Although 50% of men have an abnormal semen analysis at the time of diagnosis, sperm banking is possible for most men. In azoospermic men, testicular biopsy may be used for sperm extraction before intensive chemotherapy. The direct effect of testicular tumors on spermatogenesis is reflected by the fact that up to 70-75% of men are fertile after orchiectomy alone. Chemotherapy can affect spermatogenesis as well. After BEP, most men become azoospermic, but only 25% remain azoospermic and 50% are normal after 5 years. The role of testicular microdissection with sperm retrieval was discussed, with pregnancy rates of 20-33% reported by several groups. The effects of retroperitoneal lymph node dissection on sympathetic function and antegrade ejaculation was overviewed, including the common need for electroejaculation to allow sperm acquisition for many of these men. Because sperm quality is often poor for these patients, assisted reproduction is often needed with fresh or frozen electroejaculates.

Dr. Schrepferman also overviewed the potential adverse effects of inguinal and scrotal surgery on male fertility. During herniorrhaphy, especially in children, arterial damage, crush injury to the vas or vasal transection can all occur. Up to 10-12% of unilateral hernia repairs in the pediatric population may have vasal injury with production of antisperm antibodies or compromise of sperm concentration. After bilateral repairs, up to 2% of patients may be azoospermic, and with prolonged obstruction of the vas, secondary epididymal obstruction could occur. More recently, it has been noted that mesh placement may be associated with vasal or arterial compromise due to fibrosis. It is not yet clear how often the spermatic cord is affected by use of mesh, nor whether this risk is any different than that with standard repairs. The safety of laparoscopic repairs with mesh has not yet been compared to that of open surgery.

After varicocelectomy with a microscope, arterial injury is rare, and some arterial injuries may be microsurgically repaired. When multiple arteries are present, it was noted that no repair could be needed. During orchidopexy, arterial ligation may be intentionally performed, and the paratesticular structures are at risk because of the "looping vas" often present as well as variable epididymal anatomy. Finally, pexing sutures may compromise and obstruct the epididymis if not carefully placed. Spermatocelectomy and hydrocele repairs can also directly injure or obstruct the epididymis, and Dr. Schrepferman counseled that repair of such conditions is usually not warranted for men who are interested in future fertility, as they are often not very symptomatic.

Microsurgical reconstruction of obstructions is possible in the majority of patients with an iatrogenically obstructed vas or epididymis, whereas sperm retrieval with IVF is an option as well.

Medications that can affect sperm transport include selective serotonin reuptake antagonists, which are commonly used for depression and other psychiatric conditions, as well as alpha-adrenergic blockers. Decreased sperm production is associated with use of chemotherapeutic agents, certain antibiotics, anti-inflammatories (azulfidine, colchicine), histamine (H2) blockers such as cimetidine and hormonal therapies. The ad-

verse action of exogenous testosterone on spermatogenesis was carefully emphasized in Dr. Schrepferman's discussion. In summary, this talk included emphasis on banking sperm, minimization of surgical and medical morbidity, as well as the uses of assisted reproduction and microsurgery to treat abnormalities resulting from iatrogenically-induced male infertility. ◆

Highlights from the State-of-the-Art Lecture

Cost Comparisons of Infertility Treatment
Wednesday, April 30, 2003; 9:15 a.m.
Reviewed by Stan Honig, M.D.

In the era of ICSI, competing costs of treatments for male reproduction play a major role in the decision making process of patients, health care providers and populations.

This state-of-the-art lecture reviewed varicocele associated infertility, obstruction, and cost effects of a delay in diagnosis of a testis tumor as part of a male infertility evaluation.

The published literature supports varicocele repair vs. in vitro fertilization with or without ICSI. From a patient perspective, it is still more cost effective to proceed with varicocele repair as compared to hyperstimulation and intrauterine insemination, but from a health care perspective, the costs are very similar.

With respect to obstruction, based on published data (all from urologists), reconstruction appears always to be more cost effective as compared to sperm retrieval and IVF/ICSI. Even when complex reconstruction (epididymovasostomy) is necessary and in cases with female partners of advanced age, published data support reconstruction as the more COST effective option. Most papers report lower MESA/ICSI pregnancy rates than one might expect in 2003, and therefore one must individualize their local costs to counsel their patients.

Finally, the costs of a delay in diagnosis of a testis tumor are devastating emotionally and financially. Higher stage tumors will require more treatment (chemotherapy vs. radiation) and closer follow-up and likely higher level assisted reproductive techniques to achieve a pregnancy. All these add up to a four-fold higher cost for the health care system in taking care of the patient who is bypassed early for ART as opposed to being evaluated early by a urologist in the treatment algorithm.

In summary, the urologist still has an important role in the cost effective treatment of patients with male factor infertility. A more detailed review of these data may be found in the November 2002 book of Urologic Clinics of North America. ◆

Highlights from the Discussed Poster Session

Infertility: Physiology, Pathophysiology, Basic Research
Wednesday, April 30, 2003; 8:00 a.m. – 12:00 p.m.
Reviewed by Dolores Lamb, Ph.D.

In the poster session "Infertility: Physiology, Pathophysiology, Basic Research," there were several important areas of research presented. Several studies focused on the use of molecular technologies to assess testicular function and semen parameters. Analysis of germ cell specific gene expression was used by Schrader, et al., (#1542), Naughton, et al, (#1550), Hayashi, et al., (#1577) and the presence or absence of haploid expressed genes provided insight into whether maturation arrest was present. C-ret immunoreactivity was absent in men with maturation arrest and Naughton, et al., suggested that this might be contributory to the pathology observed. Similarly, Hayashi, et al., (#1577) assessed the expression of Notch 1 and Jagged and found it absent in testis biopsies of men with maturation arrest. The work of Schrader, et al., suggested that analysis of telomerase, cyclin A1, and RBMY1 may aid in determination of the presence of small foci of spermatogenesis in the Sertoli cell only testis biopsy, although presently it is unclear whether this approach will be superior to routine pathological assessment.

Other studies focused on apoptosis and specific apoptosis related gene expression both in the testis and sperm (although sperm are not transcriptionally active). Apoptosis was increased after a variety of pathologic events such as varicocele, heat exposure, oxidative stress, cryopreservation of sperm (#1559, 1560, 1562, 1563, 1564, 1568, 1571, 1581). Interestingly, although oxidative stress is known to damage DNA, Matschke, et al., (#1566) did not find any increase in DNA damage in the sperm of smokers as compared to non-smokers.

Finally, research advances in the areas of stem cell technologies suggest that it is possible to transplant function Leydig cell progenitors in mice (Lo, et al., #1544). Most interesting were the attempts to perform gene therapy (#1536, Goda, et al., ; 1554, Kojima, et al.,). These studies predict interesting technological advances that may be applicable to the human in the future. ◆

Highlights from the Moderated Poster Session

Infertility Evaluation
Wednesday, April 30, 2003; 10:00 a.m. – 12:00 p.m.
Reviewed by Peter Schlegel, M.D.

The poster session on Wednesday at the AUA unfortunately conflicted with the "discussed" poster session, limiting attendance by those interested in this field. A brief summary of the presented abstracts follows.

Hopps et al. from New York (1685) reported on the clinical characteristics of 78 men with deletions involving segments of the Y chromosome. Those men with microdeletions involving the complete AZFa or AZFb regions were all azoospermic, and none of the men biopsied or who underwent TESE had sperm found. Most men with AZFc deletions were azoospermic, but nearly 75% had sperm found with TESE, as has previously been reported by others.

Lo et al. from Baylor (1686) reported on clinical characteristics of patients with sperm DNA damage, as analyzed by Comet assay. Patients with increased DNA damage had decreased sperm density and total motile sperm as well as total sperm count. No relationship between DNA damage and white blood cells or antisperm antibodies were seen.

Schrader et al. from Germany reported on a real-time RT-PCR technique to detect the presence of hTERT (expressed throughout spermatogenesis) or cyclin A1 (expressed only in spermatocytes) and correlated these results with histologic analysis. They found excellent correlation. This technique could be easily applied on FNA samples and may improve sensitivity of these approaches to detect sites of sperm production within the testis.

Corea et al from Providence examined azoospermic (cryptozoospermic) semen samples and reported that if sperm were presented in semen, then they could be detected with 1000g centrifugation force. Even centrifugation at 3000g did not pellet all spermatozoa in semen samples.

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Schiff et al from New York (1689) reported on a series of men with clinical varicoceles who underwent repair. For men with veins greater than 3 mm in size and reversal of flow on Doppler ultrasound, the greatest improvements in semen parameters was seen postoperatively.

Tash et al from New York (1690) took observations from 3 men with segmental agenesis of the vas deferens. Within the lumen of isolated vasal segments, "toothpaste-like" creamy fluid was seen, confirming that such findings in the testicular end of the vas at attempted vasectomy reversal reflect only vasal epithelial material, not sperm components.

Schoor et al from Chicago (1691) reported on a series of patients with previously repaired cryptorchidism who presented for infertility evaluation. A bimodal distribution of sperm production was seen, with those boys who had early repair (between ages 2-5) and late repair (ages 9-11) the only ones with sperm in the ejaculate. All other patients were azoospermic. Their findings still support early repair of cryptorchidism.

Sigman et al from Providence (1692) reported on a series of men who provided semen samples produced at home vs. those provided in the office. They found no significant differences in semen parameters for these two different cohorts of patients, suggesting that collection at home is acceptable, if the specimens are maintained at body temperature.

Pasqualotto et al from Sao Paulo, Brazil, reported on the effects of age on hormone levels, semen characteristics and testicular volume for a series of men scheduled for vasectomy. Serum FSH levels tended to increase, with decreased semen volume for men as they aged. No significant differences in sperm concentration or serum testosterone were seen, possibly because few elderly (>70 yo) men were studied.

Blumenfeld et al from Toronto (1694) reported on changes in sperm DNA integrity for patients after varicocelectomy. Although a small series, a distinct decrease in DNA fragmentation was observed after treatment. The test method used for detection of DNA integrity is similar (acid-induced denaturation, followed by acridine orange treatment and flow cytometry) to that used in the SCSA test.

Lima et al from Sao Paulo, Brazil (1695) reported increased expression of Hsp-70-2 (a heat shock protein, whose expression is associated with heat-related injury) in spermatozoa of adolescent boys with varicocele. This type of test requires RNA extraction from spermatozoa, a process that is technically challenging.

Spaine et al from Sao Paulo (1696) reported on sperm production in a series of testicular cancer patients who underwent orchiectomy alone, chemotherapy or radiation. After orchiectomy alone, sperm concentrations increased. Interestingly, 3 patients who had sperm in the ejaculate after orchiectomy, became azoospermic after radiation therapy to the retroperitoneum alone. This observation emphasizes the importance of cryopreservafor men with germ cell tumors.

Chuang et al from Baylor (1697) reported that sperm bound to hyaluronic acid (a substance found in abundance in zona pellucida and reported to have an ability to "select" sperm of normal morphology) did not have better DNA integrity than sperm from the initial semen specimen. Sperm with normal morphology also tend to have less cytoplasm, a marker for ROS production. Taken together with their other abstract, these findings may suggest that ROS is not the only factor involved with increased DNA fragmentation, at least as measured with the Comet assay.

Rofein & Gilbert from New York (1698) showed in their laboratory specimens that sperm maintained their viability despite relatively long periods of cryopreservation. Freeze-thaw was associated with decreased viability, but viability was not progressively lost with longer duration of freezing.

Gupta et al from Cleveland (1699) reported on semen analysis characteristics for 693 patients with male factor infertility at Cleveland Clinic. A surprising proportion of men had "normal" semen analyses despite a male factor being present.

Nishida et al from Japan (1700) reported on inter- and intra- observer variation in the detection of varicocele by physical examination. Determination of testicular volume and the presence or absence of varicocele was highly variable between different examiners, emphasizing the potential value of the other abstracts from this section for the clinical diagnosis of varicocele.

Schiff et al from New York (1701) reported on correlation between testicular volume measured by ultrasound or orchidometer by one experienced examiner. A high correlation was seen.

Zahalsky et al from New York (1702) reported on a new maneuver ("The Nagler Maneuver") for detection of varicocele. Patients are asked to push out their abdominal muscles against the examiners hand. This approach was found to be more effective in inducing reversal of flow, and had flow of higher velocity on Doppler ultrasound, than valsalva maneuver alone.

Ishikawa et al from Kobe, Japan (1703) reported on the effects of chemotherapy on sperm production in a series of men treated for testicular cancer. No clear dose-effect relationship between cumulative cis-platinum dose and azoospermia was seen. Older patients appeared to be more likely to be azoospermic than those treated at a younger age.

Sandlow et al from Iowa (1704) clarified the relationship between pyriform morphology and varicoceles. Pyriform morphology is the term used with strict criteria analysis to refer to what was previously called "tapered forms" with WHO analysis. Patients who had decreased pyriform morphology appeared to have the best semen analysis response to varicocele repair. ◆

Take Home Messages

Thursday, May 1, 2003

By Larry Lipshultz (Reprinted in *AUA News*)

This year, the area of male reproductive failure, or infertility, was well represented both quantitatively and qualitatively. Two hundred and two abstracts from over 50 countries were submitted in this subspecialty, and a total of 82 were selected for presentation. In other words, 40% of submitted titles were chosen for presentation in the areas of pathophysiology/basic research, evaluation, and treatment of the infertile male. Some of the most interesting, innovative, and clinically relevant studies are reviewed here.

Gene therapy and stem cell transplantation led the way in basic research studies of male infertility. Gida et al., using a recombinant adenoviral vector, demonstrated successful transduction of rat germ cells from iatrogenic cryptorchid animals with hepatocyte growth factor (HGF). After correction of surgically induced cryptorchidism, the testes containing successfully transduced cells demonstrate more rapid recovery of spermatogenesis. Of importance was the observation that stem cell research may allow future replacement of defective testicular cell types. Lo et al. isolated mouse Leydig cells using the vital dye, Hoescht 33342, and dual wavelength flow cytometry. These cells were then successfully transplanted into a sterile mouse model with a microinjection technique. These two studies suggest that gene therapy and stem cell transplantation may have a role in the future treatment of infertile men.

Insight into the pathophysiology of varicoceles in infertile men was gained from the work of Bertolla et al. and Chen et al. Bertolla et al., using a Comet assay, found that men with varicoceles have a greater level of DNA damage in their semen than controls. Chen demonstrated a significant decrease in oxidative stress in the semen of men after varicocele repair; suggesting that DNA damage is associated with oxidative stress and may play an important role in impaired sperm function in varicocele patients.

Although a previous prospective study failed to show impairment of sperm production with 1-mg doses of finasteride, an interesting series presented by Glina et al. described three infertile men who had poor but reversible sperm production while taking this drug. Each of these patients had concomitant factors, in addition to taking finasteride, that might impair sperm production. With the withdrawal of finasteride, each had an improvement in semen parameters: specifically, sperm concentration. This series suggests an interesting theory that patients with decreased fertility may be predisposed to a "two-hit" impairment of sperm production; however, more prospective analysis will be needed to confirm these results.

In the category of evaluation, several important abstracts merit review. Lo et al. measured the association between DNA fragmentation within sperm and other important parameters in the semen analysis: sperm density, motility, strict morphology, reactive oxygen species (oxidative stress), antisperm antibodies, and white blood cells. When a single-cell gel electrophoresis technique (Comet assay) was used, 24% of the infertile men studied demonstrated increased DNA fragmentation. However, this impairment of DNA integrity correlated statistically only with impaired sperm density and showed a trend toward higher follicle-stimulating hormone (FSH) concentrations. This association, therefore, points toward a primary testicular etiology for this DNA damage.

Blumenfeld, Jarvie, and Willis also looked at DNA damage as it reflected changes following varicocele repair. These authors found that six months after varicocele correction, DNA fragmentation, as measured by flow cytometry of acridine-orange-treated spermatozoa, had significantly decreased ($p = 0.05$), and they suggested that the varicocele repair was actually able, in some instances, to lower DNA fragmentation rates.

Azoospermia is an important and often difficult to treat problem in the infertile male. However, Corea et al. report that the diagnosis of azoospermia was dependent on the force of centrifugation when used to critically analyze grossly azoospermic semen specimens. The authors found that if there are low numbers of sperm in the seminal plasma, these sperm will be optimally pelleted using 1000 g or greater for 15 minutes. A force of 3000 g, however, will not remove all sperm from a sample with identifiable sperm in the fluid phase and, therefore, cannot be used as a quantitative technique.

Azoospermia in the fluid found during a vasectomy reversal is frequently an enigmatic problem; i.e., does this indicate a truly obstructive segment still attached to the epididymis, or one reflecting fluid formed from degenerated sperm? Tash demonstrated in a group of patients with what the authors termed "segmental vassal dysplasia" in which neither the testicular or abdominal ends were patent, that the intravasal fluid had the appearance of toothpaste. This study clearly demonstrated that vasal paste-like fluid is derived from the vasal epithelium alone and not from degenerating sperm.

While it is accepted currently that the increase of maternal age will produce predictable changes in ovarian quality, there is little information on the fate of spermatogenesis or the function of the hypothalamic-pituitary-gonadal (HPG) axis in the aging male. Pasqualatto and colleagues helped to further define changes in the aging male by measuring the effect of age on hormone levels, semen characteristics, and testicular volume in four groups of men (24 to 50 years of age) undergoing vasectomy. The authors found no age-dependent changes in luteinizing hormone (LH) or testosterone levels or in testicular volume, but noted that sperm motility, prolactin levels, and FSH levels tended to change in conjunction with the aging process. The question remains, however, whether these changes are clinically, as well as statistically, significant.

In an age of increased technological advances in molecular biology, Schrader et al. presented an intriguing and apparent clinical advancement in classifying testis biopsies on the basis of the expression of cyclin A1 (CcnA1) and human telomerase reverse transcriptase (hTERT). These markers are expressed at different concentrations in the various subtypes of testicular failure. The authors accurately predicted Sertoli cell only and early and late maturation arrest, as well as normal spermatogenesis, using these molecular markers. The expression of these two markers not only was accurate in 99% of investigated tissue, but the assay could also be completed in as little as 30 to 40 minutes.

In the area of therapy, several important observations have been made. Lisi et al. revisited the question of offering only vasovasostomy for vasectomy reversal. A review of 22 patients requiring redo reversals found that more than half of the original failures were associated with unrecognized epididymal obstruction. Clearly, epididymal obstruction must be considered during initial reversal in many patients. Offering vasovasostomy as the only method of reconstruction may be reasonable for a man with favorable characteristics, such as a short interval since vasectomy, long testicular vasal remnant, and the presence of a granuloma. As these authors demonstrate, in the individual lacking positive prognostic findings, however, the ability to perform an epididymovasostomy at the time of initial reversal has the potential to prevent failures before they occur.

Dohle et al. present compelling evidence to support the role of varicocele repair in improving pregnancy rates. Patients with ultrasound-confirmed varicoceles and oligospermia were randomized to receive either varicocele repair or no treatment. The men who underwent repair had significant improvement in sperm density and motility. More importantly, spontaneous pregnancies occurred in 36% of the treated versus 9% of the control couples. Although the numbers in this study are not large, the significant effect on pregnancy rate is impressive in this randomized, prospective study!

The ethical dilemma of postmortem sperm procurement was approached in a commendable manner by Tash et al. through the application of specific, institution-based guidelines. Implied consent previous to sudden death, plus availability of suitable cryopreservation facilities, and a mandatory one-year quarantine period to allow for counseling after a bereavement period were the guidelines to be satisfied in order to proceed with sperm procurement. Over an eight-year period 4 of 22 deceased men were candidates for retrieval. Only one wife subsequently went on to utilize the acquired sperm for an in vitro fertilization (IVF) cycle. These data illustrate how a strict, guideline-based system can clarify and assist in decision making in the difficult situation of postmortem retrieval inquiry.

Transurethral resection of the ejaculatory duct (TUR-ED) has been established as effective therapy for distal ejaculatory duct obstruction. Kendirci et al. questioned whether outcome after TUR-ED correlated with pathology found at the time of resec-

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tion. They found ejaculatory duct obstruction due to midline prostatic cysts responded most favorably to TUR-ED, whereas in men with ejaculatory duct calcification, improvement in total motile count was significantly less dramatic. These findings have obvious prognostic relevance if only calcifications can be documented preoperatively in the man with ejaculatory duct obstruction.

All of these innovative studies, in addition to many not mentioned here, provide us with improved accuracy and more effective scientific techniques for evaluation of the subfertile male. While the routine semen analysis remains important, it clearly represents only the first step in a much more scientific and sophisticated approach to the accurate evaluation and management of male infertility. ◆

S S M R

MARK YOUR CALENDARS!

59th Annual Meeting of the American Society for Reproductive Medicine
October 11 – 15, 2003
Henry B. Gonzalez Convention Center
San Antonio, Texas
Contact: ASRM
Phone: (205) 978-5000 Fax: (205) 978-5005 E-mail: asrm@asrm.org
Website: http://www.asrm.org/Professionals/Meetings/annualmeeting.html

29th Annual Meeting of the American Society of Andrology
April 17 – 20, 2004
Hyatt Regency Baltimore
Baltimore, Maryland

American Urological Association Annual Meeting
May 8 – 13, 2004
San Francisco, California

SSMR Meeting at the AUA Annual Meeting
May 8, 2004
San Francisco, California
1:00 p.m. – 5:00 p.m.

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Saturday, May 8 – Wednesday, May 12, 2004
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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. 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 SSMR Traveling Fellowship functions is expected, as outlined in the attached schedule.

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SSMR Traveling Fellowship Program 2004

Dear Urology Residency Directors and SSMR Members:

The Society for the Study of Male Reproduction (SSMR) is proud to announce the Fourth Annual SSMR Traveling Fellowship Program, which will take place in conjunction with the 2004 AUA meeting in San Francisco this year.

The SSMR is an AUA-affiliated subspecialty society whose mission is to promote the advancement of the science and treatment of male reproduction disorders, through education of practitioners, public education, and informational exchange of research and new advances through meetings. Currently, there are insufficient numbers of male fertility specialists to serve the needs of the population. The SSMR is committed to cultivating interest in male infertility treatment careers in trainees.

Our previous program at last year's AUA was a huge success, and we wish to build upon that success. Our goal is to present residents in training with the opportunity, while attending the AUA meeting, to have a more intensive exposure to male reproduction issues. The Fellowship Program will include attendance at the SSMR educational program and complimentary SSMR banquet participation. Fellows will also attend an AUA post-graduate course in male infertility, the infertility podium and poster sessions, as well as a symposium with fellowship directors and junior faculty members on how to prepare for a future successful career as a male reproduction specialist. The program will allow significant contact between Fellows and leaders in the field and will conclude with a closing cocktail party attended by the officers and board of directors of the SSMR and other prominent fertility specialists.

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 Saturday afternoon until Wednesday evening will be required.

Meeting expenses covered by the program include airfare, hotel accommodations, SSMR meeting and banquet, tuition for the post-graduate course, all special lectures, and the closing cocktail party. 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, 2004.** The awards will be announced by February 15, 2004.

We hope you will consider supporting this program through the application of trainees in your program. We look forward to another successful SSMR Traveling Fellowship!
Sincerely,

Jay Sandlow, M.D.
Director SSMR Traveling
Fellowship Program
Associate Professor of Urology
Medical College of Wisconsin
Milwaukee, WI ◆

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