NEWS

SSMR

SOCIETY FOR THE STUDY OF MALE REPRODUCTION

SSMR NEWSLETTER FEBRUARY 2004

PRESIDENT'S MESSAGE

ROBERT OATES, MD

I hope all of you had a wonderful holiday season and I look forward to seeing you at this year's AUA and SSMR scientific session. San Francisco is a fantastic city and the SSMR scientific session and business meeting will once again be held, on Saturday, May 8, 2004, from 1:00 p.m. – 5:30 p.m. As you are aware, the stated goal of our Society is "to encourage the study, to elevate the practice, and to improve the quality of care of the subfertile male." This year's effort, as directed by Program Chairman Mark Sigman, addresses each of these goals in a timely and directed fashion. The first half of the program focuses on both the clinical and basic science aspects of in-vitro fertilization. We start with Marcel Cedars reviewing for us and updating our knowledge base regarding what we need to know about ovulation induction (what are the medications used, what are the regimens being employed, etc). Because male infertility is often treated in conjunction with IVF therapies, we certainly need to be up-to-speed on what our Reproductive Endocrinology colleagues are doing to prepare the partners of our patients. After ample time to ask Marcel questions, Vaness Rawe will speak to us about the early events of fertilization and embryo development – I am sure some of the videos she will present will be worth the price of admission (free for non-members). We hope Vaness will be able to shed some light on one of our most vexing clinical problems – when there is failure of fertilization or poor embryo development, is it the sperm's fault, an oocyte issue, or a combination of both?

Following questions and a break, we will launch into our strictly clinical half of the program. How many of you have had the thought, "should I use this sperm test; when should I use that sperm test; will it give me helpful clinical information; is it ready for clinical prime-time,

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etc.?" Mark will moderate an excellent panel of clinicians (Harris Nagler, Craig Neiderberger and Mike Witt) whose charge it is to help us answer these, and many more, questions in as unbiased a manner as possible. Sperm chromatin assays, acrosome assays, sperm penetration assays, antisperm antibody assays, semen volume and pH, fructose are just some of the items on the agenda. We welcome your comments and experience. Finally, Peter Chan will give us a flavor for the different techniques and strategies involved in TESE and testis tissue processing. Is there one best (or better) way to process, a best (or better) solution for extraction, an improved method of cryopreservation are just a few of the issues he will discuss with us. We need to learn as much as we can about this so that we can have an active role in this most important laboratory exercise.

I wish to thank all of you who e-mailed me earlier this year with suggestions for the 2004 program. The Board of Directors took your thoughts into account when formulating the program and we hope we have met your challenge of an exciting, informative and educational meeting. Shortly after the business meeting, we will head off to the Carnelian Room at the Bank of America World Headquarters Building for our annual reception and banquet. I truly hope all of you can attend, as it is an opportunity to have fine food and drink with great friends and colleagues. This year's banquet has been organized by one of our "local" members, Dr. Paul Turek and Debbie Roller of W.J. Weiser and Associates, and I have no doubt that it will be a perfect venue. Transportation will leave from the Argent Hotel at 6:00 p.m. for cocktails beginning at 6:30 p.m. Dinner and entertainment start at 7:30 p.m. and the dress code is relaxed (sport coats for men and "semi-dressy" for women). Please reserve your spot early, as I anticipate a great turnout.

Included in this newsletter are the summaries of the many sessions of interest to our membership at the recent 2003 ASRM meeting. The board of directors and a few other dedicated individuals have worked hard put all of this together for you. A special thanks to Craig Neiderberger for his efforts. Included as well is a listing of the presentations at this year's AUA that I thought would appropriate for all of you. See you this spring!◆

REVIEW OF ASRM 2003

SATURDAY, OCTOBER 11, 2003, AND SUNDAY, OCTOBER 12, 2003

Full Weekend Course –
"Gamete Development, Genetics, and Testing in Male Reproductive Failure"

Faculty:
Paul Turek, MD, Chair
Keith Jarvi, MD
Renee Martin, PhD
Renee Reijo-Pera, PhD

Overview by Paul Turek, MD

Prior to the start of the ASRM meeting, Dr. Paul Turek from UCSF chaired the two-day SMRU postgraduate course that focused on male genetic infertility. With a slant emphasizing the history and developmental aspects of reproductive genetics, Dr. Turek and his colleague Dr. Renee Reijo Pera from San Francisco, along with Dr. Renee Martin from Calgary and Dr. Keith Jarvi from Toronto, Canada, covered the spectrum of infertility genetics in a cohesive and very informative lecture program. The first day of the course focused on how a sperm is made and included information on genes involved with sex determination, meiosis and spermatogenesis as well as the how chromosomes behave during meiosis and the critical role of imprinting in reproduction. Currently understood pituitary-gonadal axis and growth hormone axis genes were also reviewed, often in the context of animal model knockouts and the effect on clinical phenotype. The day finished with lectures on cystic fibrosis and androgen receptor genetics and syndromes that present with reproductive dysfunction. The second day of the course focused on current and future genetic testing for male genetic infertility and current and future treatments such as germ cell transplantation, in vitro germ cell maturation and a summary of the world experience with sperm retrieval techniques in non-obstructive azoospermia.

In all, the course was a refreshing and exhilarating tour of our current understanding and of future potential areas of research in the field of genetic infertility. Some of the salient points in the course are outlined below:

1. From Dr. Reijo Peras lecture on sex determination, it became clear that in addition to the SRY, many other genes are involved in determining "maleness," in the embryo including several genes downstream to SRY such as SOX9 and DAX-1 in the male, and other "anti-testis" genes in the female gonad such as WT1. Indeed the variable expression of a number of these genes may account for cases of XX, SRY-Neg, sex-reversed females.

2. From a discussion on the genetics of the Y chromosome, it was suggested that about 25 of 1000 human reproductive genes are known, but far fewer are well characterized. The palindromic or "mirrorlike" nature of the spermatogenesis genes on the Y chromosome was discussed, and the theory that the Y chromosome is susceptible to mutations in the AZF regions due to ancestral proviral DNA insertions in these locations was explained.

3. The epigenetic programming that characterizes imprinting was described as essential for male germ line, embryo and fetal development by Dr. Reijo Pera. This process of methylation of certain genes is thought to occur in clusters, and may alter the frequency of meiotic recombination occurring in genes near these clusters. Imprinting is now thought to involve 100 genes, of which about 65 are described. The controversial relationship between defective imprinting with ICSI and recently observed birth defects such as Beckwith-Weidemann and Angelmann syndromes was also reviewed.

4. Dr. Renee Martin discussed the chromosomal findings in the blood and sperm of both fertile and infertile men. In general, chromosomal abnormalities in human are quite common, especially when compared to other mammals, and are estimated to occur in 20-50% of all conceptions. In normal men, about 1-2% of sperm have numerical and 7-14% have structural chromosomal anomalies by most analytic methods. In contrast, infertile men with a normal somatic karyotype harbor a 4-fold increase in numerical abnormalities of sperm. In an analysis of different subsets of infertile men, including men with oligospermia, asthenozoospermia and teratozoospermia, no differences are found in the incidence of chromosomal 13, X and Y abnormalities. This suggests that being infertile in general and not just having oligospermia or azoospermia puts men at higher risk of harboring sperm chromosomal abnormalities. In addition, no particular features of sperm strict morphology except

amorphous heads with multi-flagellated tails and globozoospermia are associated with higher incidences of sperm chromosomal anomalies on FISH.

5. In a fascinating lecture, Dr. Martin discussed how errors of meiosis and recombination occur more frequently in chromosomes with smaller numbers of gene-repair clusters or "recombination nodules," which includes chromosomes 21, X and Y. Indeed, recombination errors in these highly susceptible chromosomes may help explain the higher incidence of sex chromosomal aneuploidy in the sperm of infertile men and may also underlie the increased incidence of ICSI offspring that harbor sex chromosomal abnormalities.

6. A discussion of current understanding of the genes involved with sperm motility (200-300 potential genes) and reproductive syndromes concluded that genes governing sperm motion dynamics and mitochondrial function are likely to play significant roles in male infertility.

7. Dr. Keith Jarvi discussed the basic science of sperm chromatin structure and the how susceptibility of sperm to DNA denaturation might be increased with elevated oxidation, apoptosis or defective protamine gene complex formation in sperm. Approximately 10% and 22% of fertile and infertile men, respectively, have high DNA damage rates by sperm chromatin structure assays. In addition, these findings tend to be very reproducible in a single individual over short time frames (days-weeks) but may vary quite widely over longer time frames (months). The relationship between abnormal chromatin structure and poor fertility in vivo and in vitro studies was also described along with the fact that a DNA damage rate of 30% or more in a semen analysis portends poor fertility outcomes (despite normal IVF fertilization rates) in infertile couples in data from 2 independent centers.

8. The deficiencies of CFTR gene testing in men with congenital absence of the vas deferens (CAVD) was discussed in detail, and included data suggesting that up to 50% of mutations are missed in these men when more extensive gene mutation testing instead of common mutations panels (25-87 mutations testes) is used. One reason for this is that CAVD patients tend NOT to harbor the same common mutations as men with actual cystic fibrosis, for which the common mutation panels were designed. Based on his research, Dr. Jarvi recommended CFTR and 5T testing in CAVD, idiopathic obstruction and ejaculatory duct obstruction cases of infertility and suggested (controversially) that men with "sperm abnormalities" on semen analysis also be considered for such testing.

9. In an inspired lecture, Dr. Reijo Pera asked the attendees to consider a whole different approach to the genetic explanation of the complex trait of infertility. She suggested that since "99.99%" of our genes are shared among us (despite our obvious differences), that maybe the critical differences in our genetic constitutions are better described by examining the single nucleotide polymorphisms (SNPs) that characterize each of us, and that are likely to provide a better genetic fingerprint of a single individual.

10. A lecture by Dr. Turek on the current state of affairs with in vitro and in vivo germ cell transplantation suggested that the advances needed to make this therapy a possibility in humans will likely be forthcoming sooner rather than later, as the required research appears to be mainly evolutionary rather than revolutionary in extent. The course ended with a review of the world experience with microdissection TESE and FNA mapping followed by directed TESE by Dr. Turek. In general, despite some differences from center to center, microdissection increases sperm detection in nonobstructive azoospermia (NOA) by 30-50% over multibiopsy TESE. In addition, on (unweighted) average about 50% of microdissected NOA patients will have sperm and about 50% of FNA mapped patients will have sperm for ICSI.

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MONDAY, OCTOBER 13, 2003

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, PhD

Overview by Dolores Lamb, PhD

The Bruce Stewart Memorial Lecture was presented by Dolores J. Lamb, PhD, and was entitled, "The New Genetics of Male Infertility in the Era of ICSI." Today, at least one-quarter (and perhaps as much as one-half) of all male infertility is diagnosed as idiopathic reflecting our poor understanding of the mechanisms regulating spermatogenesis, sperm maturation and transport through the genital tract and the early steps of fertilization and embryonic development. Accordingly, we are unable to properly diagnose these patients. Concerns have been raised that much of what we diagnose as idiopathic infertility may have a genetic basis and thus, there is the possibility that the offspring of the severe male factor couple conceived by ICSI may be at risk.

The initial portion of the lecture focused on our current understanding of the genetic basis of male infertility. Chromosomal abnormalities (numerical and structural) account for a significant amount of azoospermia. These include syndromes such as Klinefelter (XXY), as well as translocation, inversions and deletions (including the Y chromosome micro deletions). Other genetic causes of male infertility, such as gene mutations are slow being identified and include abnormalities such as congenital bilateral absence of the vas deferens (due to mutation of the gene associated with cystic fibrosis).

Recent experimental data from Dr. Lamb's laboratory was presented to show that approximately 40% of men with Sertoli cell only syndrome have evidence of defective DNA repair leading to genomic instability. This instability was evident not only in the sperm and germ cells of the testis, but also in the somatic cells and results suggest that the Sertoli cell only patients may be at risk of cancer development that may be associated with this generalized gnomic instability. The deficient DNA repair also lead to increased length of specific triplet repeats associated with several triplet repeat diseases (myotonic dystrophy and SCA-2). Of greatest concern was myotonic dystrophy with 4% of men evaluated for Y chromosome micro deletions exhibiting triplet repeat expansions in the mild to moderate severity disease range (a 64-fold increase over the general population). Instability of triplet repeat length was also found in the sperm of the severe oligospermic male and this suggests that the offspring conceived by ICSI may be at risk of a triplet repeat disease.

Obviously, even with the most advanced genetic testing available today, there are no guarantees of a perfect baby. Nevertheless, it is important that the severe male factor couples planning to achieve a pregnancy with ICSI understand that because we do not understand the causes of their infertility, there may be as yet unknown genetic risks to their offspring.

SMRU Traveling Scholar Abstracts

Overview by Robert Brannigan, MD

The 2003 Annual Meeting of the ASRM marks the first time that the SMRU Traveling Scholarship award recipients' abstracts were highlighted in a special podium presentation session. This year there were a total of eight award recipients, and five of them were selected to give oral presentation at this special session. Attendance at the session was outstanding, highlighting the support for and interest in research by younger investigators.

Lo et al. from Baylor and the University of Louisville (#O-9) reported on de novo testosterone production in a luteinizing hormone receptor knockout mouse after transplantation of Leydig stem cells harvested from ROSA 26 cryptorchid mice testes. These cells were stained using a Hoechst vital dye and separated by flow cytometry prior to transplantation. Serum testosterone levels rose in a time dependent fashion from a baseline of < 20 ng/dL to 48 ng/dL five months post-transplant in the mouse receiving the sorted side population Hoechst dim cells. In contrast, testosterone levels did not rise in the knockout control or in the mouse receiving nonsorted testicular cells. In summary, this is the first report of successful functional transplantation of Leydig cells in a hypogonadal recipient. The authors hypothesize that the delay in the time to rise of testosterone reflects the need for the transplanted progenitor cells to proliferate and differentiate into mature steroidogenic cells in the recipient mouse. They add that it is likely these cells, rather than mature transplanted cells, that are responsible for testosterone synthesis in the recipient animals.

Stuart et al. from the University of Illinois at Chicago (#O-10) presented their work on evaluation of men with unilateral or bilateral undescended testes: does age of correction make a difference? The study was a retrospective review of data from four different clinics (2 in the US, 1 in Egypt, and 1 in Europe). Physical exam findings, endocrine testing results, and semen analysis parameters were analyzed, and patients were stratified by age at time of correction and also by unilateral or bilateral cryptorchidism. The authors reported several interesting findings. They found that even when corrected peripubertally, sperm may be present in the ejaculate of men with bilateral undescended testes. Of note, the authors found a bimodal distribution of sperm present in the ejaculate of those corrected before 5 years of age and then again in men corrected between the ages of 9-13 years. Furthermore, no men in this study with bilateral cryptorchidism who underwent repair after 13 years of age were found to have sperm present in the ejaculate. During the discussion, the authors noted that none of these testes were retractile preoperatively, and they added that the bimodal semen analysis distribution, with more deficient parameters found for patients with cryptorchidism corrected between 5-8 years of age, warrants further investigation.

Grotas et al. from the University of Miami (#O-11) reported on a comparison of ejaculatory success rates and sperm parameters in patients with acute versus chronic spinal cord injury (SCI). This study was a retrospective chart and database review of 2623 ejaculation trials performed on 486 patients participating in the Miami Project Male Fertility Research Program from 2/02 to 3/03. Several parameters were assessed, including ejaculatory success rate with penile vibratory stimulation (PVS), ejaculatory success rate with electroejaculation (EEJ), % of positive ejaculation trials with sperm present in the semen, mean total sperm count in sperm-positive trials per time interval, and mean % sperm motility in sperm-positive trials per time interval. The authors found no successful PVS trials within the first 3 months post injury, and PVS success rates varied from 60-70% after 13-18 months. In summary, the authors found that although ejaculates with sperm may be seen with PVS at any time after 3 months, it is probably best to wait until 12 months post-injury to attempt PVS, at which time response rates are more consistent. EEJ trials were very successful at all time points, with 84% success in the first 3 months to

almost 100% by 19-24 months. The authors note that although semen can be reliably obtained with EEJ at all time points post-injury, sperm parameters with this method will also be most consistent at least 12 months after the injury. These findings should be taken into consideration when counseling patients with spinal cord injury about treatment to restore their fertility. During the discussion, the issue was raised that urologists are often called to collect sperm for cryopreservation from affected patients shortly after spinal cord injury. This presentation, in contrast, lends further support to the concept that it is indeed advisable to wait at least several months before attempting sperm retrieval.

Khaira et al. from the University of Michigan (#O-12) presented their findings that epididymal obstruction results in isolated sperm heads in post-vasectomy rats. The study was a prospective, randomized animal model experiment using rat vasectomy and epididymal obstruction subjects. All animals underwent bilateral vasectomy at the start of the study, and unilateral epididymal obstruction was created via microsurgical ligation of the mid-corporal epididymis at week 4. The animals were then sacrificed at 1, 2, 4, 8, 12, and 22 weeks later.

Concurrent Session – Male Reproduction and Urology Abstracts and Lectures

Overview by Craig Niederberger, MD

K. Danziger and co-authors investigated the standard screen for cystic fibrosis mutations in men with congenital absence of the vas deferens. As frequencies of mutations may differ between ethnic subpopulations, the common mutation panel may be insufficient. Describing a DNA sequence method which focuses on sequence anomalies noted on gel electrophoresis, the authors found mutations of which only 25% would be identified with the traditional mutation panel. Interestingly, 3 of 5 mutations identified in female partners would not have been identified with the traditional mutation panel.

F. Pasqualotto and co-authors studied the effect of varicocelectomy on serum hormonal levels in infertile males with clinical varicoceles, stratifying their analysis based on seminal parameter outcomes subsequent to varicocelectomy. The investigators did not find alterations in testosterone, LH and FSH after varicocelectomy, regardless of seminal outcome, although the power of the study was substantially limited by the small study size.

G. Christensen and colleagues investigated the incidence of 2 candidate genes for male infertility, the meiotic factor SPO11 and the polyamine metabolic factor EIF5a2, expressed in testis. Of 192 azoospermic or severely oligospermic males screened, 18 polymorphisms and 2 mutations were noted in SPO11, and 15 polymorphisms and 1 mutation were found in EIF5a2. Despite the relatively low incidence, polymorphisms and mutations in these genes may account for a small discrete population of infertile males.

D. Johnson and co-authors described a semen collection technique with a novel container designed to preserve semen quality for artificial insemination. Within the container is a warmed, osmotically balanced media, and the semen is funneled into a small volume, reducing the ratio of surface area to volume. The authors previously demonstrated prolongation of seminal quality in a canine model, and extended their findings in the human, finding a statistically significant prolongation of seminal quality using the device.

M. Zahalsky and H. Nagler evaluated the surgical risk to the epididymis during hydrocelectomy and spermatocelectomy in 338 patients during a 13-year period. The authors found the risk of epididymal injury to be 5.6% during hydrocelectomy and 17% during spermatocelectomy, allowing surgeons to more accurately assess the risk to the epididymis during these procedures.

M. Morshedi and co-authors investigated capsase activity in human spermatozoa. The authors demonstrated increased capsase activity under apoptotic induction in semen, and found higher capsase activity in the higher motility fraction of subfertile males without identified bulk seminal parameter abnormalities when compared to donor controls, suggesting capsase activity as a marker in subfertile males warranting further investigation.

F. Calzi and co-authors investigated the relationship of mitochondrial ferritin (MtF) content and sperm motility. The investigators first identified mitochondrial (as opposed to cytosolic) ferritin in human semen samples, extending previous studies demonstrating MtF in mouse testis. The authors also observed decreased MtF content in asthenospermic semen samples when compared to normospermic controls, thus identifying another marker warranting further investigation in subfertile males.

J. Park and co-authors used a microarray system to screen for genes with differential expression during spermatogenesis, identifying 170 genes with greater expression in pachytene spermatocytes, and 350 genes with greater expression in round spermatids. This kind of screen points to the importance of current and future work elucidating the complex pathway of genetic molecular events resulting in spermatogenesis.

Finally, Rebecca Sokol addressed in the minisymposium the question of whether sperm counts are historically declining. Beginning with the well cited Carlsen meta-analysis published in 1992 in the *British Medical Journal*, Dr. Sokol presented an exhaustive review of the methodological and statistical criticisms of the Carlsen study, and the U.S. data. Most of the U.S. studies that were constructed as well as possible given the nature of historical retrospective data suggested that either sperm counts are not changing, or as curve-fitting the Carlsen data suggests, if there was a decline in the farther past, counts have been increasing in the recent past. Dr. Sokol concluded with an analysis of possible geographic variation in semen analysis in the United States.

Poster Reception

Overview by Peter Kolettis, MD

Anderson et al demonstrated that pregnancy rates and implantation potential are not affected by reducing the number of embryos transferred. By transferring an average of 2.3 rather than 2.8 embryos, the pregnancy rate did not change (31%) and the rate of high order multiples (> 3 sacs) was reduced from 13.5% to 4.2% (P = 0.009). Powers et al demonstrated a high association between abnormal DNA condensation and low fertilization rate in conventional IVF. Flow cytometric analysis was used to measure DNA condensation. A higher proportion of patients with < 40% fertilization had abnormal percentages (<65%) of decondensation compared to those with > 40% fertilization.

Fretz et al demonstrated that repair of clinically significant varicoceles was associated with a 23% pregnancy rate even when there was no improvement in seminal parameters. This suggests that varicocele correction may lead to some type of qualitative improvement, such as improved sperm function. Importantly, this study lacked controls so a controlled study would be required to better understand this phenomenon. Hopps et al reported a series of 8 men with iatrogenic injury to the epididymis. In 86% of cases, sperm returned to the semen after microsurgical reconstruction. Only one natural pregnancy occurred in this small series. Thus, after re-

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construction these patients at least have the potential to conceive naturally although they may ultimately still require assisted reproduction. Paduch and Fuchs reviewed the experience with more than 2200 vasectomy reversals performed by Fuchs. The overall pregnancy rate was 61.4%. Both vasovasostomy and vasoepididymostomy were performed with local anesthetic with remarkable efficiency (average operative times were 76 and 106 minutes) and reasonable cost ($3500 total cost to patient). Interestingly, absorbable suture, (10-0 and 9-0 Dexon) are currently used.

Burkman et al demonstrated that marijuana smokers appear to have decreased fertility potential. Use of marijuana was associated with a decreased semen volume and total motile sperm count in the population of men studied. Kort et al demonstrated that high body mass index (BMI) sperm DNA fragmentation index. As the BMI increased above 25, the DFI also increased. They concluded that obese men should be encouraged to lose weight prior to any ART procedure. Katagiri et al concluded that men with severe oligospermia or azoospermia had longer trinucleotide repeat length found in their androgen receptor (AR) gene. This suggests that an abnormal AR gene may be associated with impaired spermatogenesis.

Suh et al demonstrated in mice that high dose diethylstilbestrol (DES) exposure decreased combined testicular/epididymal weight but had no apparent effect on sperm function of in vitro fertilizing capability. Interestingly, higher phytoestrogen intake appeared to be associated with improved sperm capacitation and acrosome reaction. There is some evidence that cigarette smoking is associated with impaired fertility. In a study by Hallak et al. fertile men were evaluated and there were no apparent differences detected in sperm concentration, motility, and hormone levels between nonsmokers and smokers. Importantly, only fertile men were evaluated so this selection bias might prevent an effect from being demonstrated.

Kort et al evaluated men with a high body mass index (> 25) and found that there was an inverse relationship between BMI and total numbers of normal motile sperm. As noted by the authors, additional studies are needed to clarify the relationship between BMI and measures of fertility potential such as those measured in this study and in their other study (see poster 333). Keel examined a phenomenon understood by most fertility specialists, that is, that semen parameters can vary substantially over time. This has important implications for trying to determine a man's fertility potential based on one or even multiple semen analysis. In addition, studies that report improved semen parameters with some form of treatment must have appropriate controls and allow for this known significant degree of variability.

TUESDAY, OCTOBER 14, 2003

SMRU Workshop – "Genetic Evaluation of Male and Female Reproductive Failure"

Faculty:
Peter N. Schlegel, MD, Chair
Lawrence C. Layman, MD
Paul G. McDonough, MD
Robert D. Oates, MD

Overview by Peter N. Schlegel, MD

A comprehensive overview of genetic defects that can contribute to male and female infertility was provided in this Workshop at the ASRM Annual Meeting. Dr. Paul McDonough discussed the myriad genetic causes of female gonadal failure, and Dr. Lawrence Layman discussed the genetics of hypogonadotropic hypogonadism in females and males. He overviewed the phenotypic presentation of this syndrome as well as the many gene mutations/deletions that have been identified as causes, including genes that act on the hypothalamus (KAL1, FGFR1, LEP, LEPR, NROBI), as well as pituitary genes (GNRHR, HESX1, PROP1, FSHB, LHB). Many of these genetic defects have been elucidated in single individuals or small cohorts of patients, but the corresponding phenotypes provide interesting insight into genetic action.

Dr. Robert Oates then presented a comprehensive and clear discussion of genetic factors that are associated with azoospermia or severely impaired spermatogenesis in the male. The relationship of CF deletions to Wolffian development including congenital bilateral absence of the vas deferens was overviewed as well as appropriate evaluation of men with CBAVD. Female partners need to be tested before assisted reproduction to avoid having an affected child. Counseling of male partners and their families was recommended as well to identify potential genetic conditions in family members.

Evaluation of men with impaired spermatogenesis using Y chromosome microdeletion testing and karyotype analysis was also discussed in detail by Dr. Oates. The newer system for characterizing Y chromosome microdeletions using analysis of the specific sites of palindromic repeat break-points was overviewed, and a comparison to the AZFa, AZFb, and AZFc deletion sites previously described was given. The significance of each type of deletion for spermatogenesis and the importance of understanding the mechanisms of development of Y microdeletions was discussed. The workshop provided an informative state-of-the-art review of existing literature in this rapidly expanding field of importance for clinicians.

Reproductive Biologists Professional Group Workshop – "Future of Spermatogonial Stem Cells and ART"

Faculty:
Gary D. Smith, PhD, Chair
Dolores J. Lamb, PhD
Derek J. McLean, PhD

Overview by Dolores Lamb, PhD

The workshop on "The Future of Spermatogonial Stem Cells and ART" was chaired by Dr. Gary Smith who presented an overview of the properties of stem cells in general (there are embryonic stem cells—the center of considerable controversy today for application in human health research and adult stem cells). Adult spermatogonial stem cells were the focus of this workshop. The existence of a spermatogonial stem cell was first suggested by Huckins, more than 30 years ago. There is a significant need to develop methods for the cryopreservation of spermatogonial stem cells. In the mouse, a simple freezing technique has successfully preserved mouse spermatogonial stem cells, but it is unknown whether human spermatogonial stem cells can be preserved as effectively. Dr. Derek McLean provided insight into current research aimed at the enrichment of spermatogonial stem cells. Successful development of this type of technology will be key to the eventual application of spermatogonial stem cell transplantation in humans because if this application was developed to treat patients post-chemotherapy, it is critical that contaminating cancer cells not be transplanted along with the stem cells. Other future applications will include culture of stem cells, perhaps with the aim of expansion and eventually gene therapy to repair defective genes. Finally, Dr. Dolores Lamb discussed the technique of transplantation and the methods to define the efficacy. Xenografts into surrogate animals has been the topic of extensive investigations, however, as the

genetic disparity between species increases, the ability of the seminiferous tubules to support foreign spermatogenesis declines. This fact, in addition to concerns about the introduction of new viruses has tempered enthusiasm for the future application of this technology in humans. Certainly, it may be useful to preserve some endangered species, such as the Florida Panther. For eventual use in humans, there remain challenges such as the need for improvement in stem cell purification, efficiency of transplantation (colonization) and expansion in vivo. This is a rapidly advancing field and it is hoped that these advances will be realized in the near future.

Concurrent Session – Male Reproduction and Urology Abstracts and Lectures

Overview by Jon L. Pryor, MD

The oral presentations for the Society for Male Reproduction and Urology (SMRU) were held on Tuesday afternoon, October 14, 2003. The session began with Dr. Erik Seaman (O-121) describing a technique to help locate a non-palpable mass during surgery. After delivery of the testis by an inguinal approach, an intra-operative ultrasound was performed to guide the placement of a 25-gauge needle into the mass, which was then injected with indigo carmine. This aided in the identification and excision of the mass after opening the tunica albuginea.

Drs. Raman and Schlegel (O-122) demonstrated that sperm could be retrieved from cryptorchid testes for IVF and ICSI in 35 of 47 TESE attempts (74%). The clinical pregnancy rate of 46% is similar to the non-cryptorchid NOA group. Size of testis and age at orchiopexy were predictors of sperm retrieval. This success rate argues for postpubertal orchiopexy as opposed to prophylactic orchiectomy.

Dr. Bakircioglu et al (O-123) compared a microdissection TESE to a multiple extraction TESE in a non-randomized study of 42 men (updated from abstract submission) with Klinefelters syndrome. 59% of those undergoing microdissection versus 30% undergoing multiple biopsies had sperm retrieved. They found that lower age had a positive effect on sperm recovery, though this was not found by the Cornell group in the Q and A. They also found chromosomal abnormalities in some embryos of those who underwent preimplantation genetic diagnosis (PGD) and therefore recommend PGD in this group to select normal embryos for transfer.

Dr. Lee et al, (O-124) used a collagen gel matrix to demonstrate improved in vitro differentiation of mouse spermatocyte to spermatids compared to a monolayer method.

Drs. Witt and Lotspeich (O-125) showed an 18% incidence of AZF microdeletions in African American men with severe oligospermia (which he defined as less than 10 million sperm per ml) or azoospermia; this is similar to the microdeletion rate reported in other ethnic groups. It was brought up in Q and A that most groups now use less than 5 million sperm per ml as the definition of severe oligospermia and indicator for obtaining genetic tests.

Dr. Pryor et al (O-126) found that carnitine did not improve sperm motility or pregnancy rate in 21 patients randomized to a 24-week trial of placebo versus oral carnitine.

Dr. Bruck et al (O-127) found lower acrosin activity in 5 subjects with spinal cord injury SCI) compared to 7 control subjects; they hypothesize that the lower acrosin activity indicates a lower fertilization capacity in SCI patients.

Dr. Sparks et al (O-128) studied the predictive value of sperm morphology for pregnancy rates in couples undergoing intrauterine inseminations. They have previously shown that IUI is more cost effective than IVF if the total motile sperm count (TMSC) in the neat ample is more than 10 million motile sperm. In this study 238 couples with TMSC greater than 10 million underwent 460 cycles of IUI. Morphology was done using Kruger strict criteria prior to or on the day of the first IUI. Pregnancy rate per couple was 25% and 13% per cycle. There was no difference in pregnancy rate per cycle between sperm morphology groups. Therefore, sperm morphology is not predictive of IUI success rate in those with TMSC greater than 10 million.

The program ended with Dr. Debra Anderson, PhD, presenting a minisymposium entitled "ART for Men with Chronic Viral Infections." She used knowledge learned about minimizing the risk of transmission of HIV in discordant couples (infected man to his non-infected female partner) who are trying to conceive, as a model for how to approach men with other chronic viral infections, such as hepatitis B. With intercourse, there is a 0.1-1% transmission rate of HIV. Early studies where IUI was used showed an increased risk of transmission, as high as 10%. It is thought that this increased risk of transmission occurs from bypassing the immunological barriers in the lower female urogenital tract. In 1994 the ASRM Ethics Committee guidelines stated that HIV+ individuals should be excluded from ART procedures because of this high risk of transmission. However, in 2002 the ASRM Ethics Committee changed their guidelines to HIV+ individuals have the right to be treated with ART. It is primarily the development of effective antiretroviral therapy for HIV and advances in sperm washing techniques to lower HIV levels in the inseminating fraction that has reduced the rate of transmission and resulted in this change from the Ethics Committee. Shedding HIV in semen is intermittent; use of antiretroviral therapy and not obtaining semen for insemination during acute or advanced stages of the disease, and not during times of a secondary infection or inflammation, will lower HIV-1 in semen. Sperm preparation for IUI using a discontinuous gradient and/or swim up will further decrease the viral load in the inseminating fraction. There have been more than 4000 ART attempts in Europe using these techniques and no known transmissions of HIV to date. Future considerations will be use of preimplantation genetic diagnosis prior to embryo transfer, in vivo and in vitro microbials, and vaccinations of donors and recipients. Dr. Anderson thinks these principles (reducing risk factors such as secondary infection, use of antiviral drugs, improved detection techniques, and sperm washing procedures) should be used with IUI regardless of the fertility status to minimize the risk of transmission of HIV in discordant couples who want to conceive.

Poster Reception

Overview by Mark Sigman, MD

IVF Outcome From TESE For NOA

Poster 246 Derkman et al:

Higher miscarriage rate with testicular sperm from NOA than ejaculated sperm with frozen embryo transfer. Delivery rates were the same.

Poster 248 McKenzie et al:

Higher miscarriage rate for male factor ICSI as compared to female factor IVF. Slightly better biochemical pregnancy rate for MF ICSI.

Poster 270 Jeon et al:

A trend of lower fertilization rates, embryo quality, implantation and pregnancy rates was found during ICSI cycles with sperm from NOA patients.

See **ASRM**, page 8

ASRM, cont. from page 7

Klinefelter Syndrome

Poster 254 Verneave et al:

Looked at FSH, LH, T, FSH/LH ratio, T x LH index, testis volume, age, presence of facial hair, and the presence of gynecomastia in Klinefelter patients undergoing TESE. Sperm were recovered in 48% of patients. No parameters predicted the presence of sperm.

Sperm Retrieval

Poster 258 Bibancos de Rosa et al:

Examined the probability of sperm recovery in a mixed group of obstructed (10 patients) and non-obstructed (20 patients) azoospermic men undergoing repeat TESA at 5.7 - 6.8 mo intervals. If sperm were recovered during the first TESA, they would likely be recovered in a 2nd or 3rd attempt (83% - 100% success) in the same testicle. Failures in the first TESA attempt were not studied.

Poster 328 Stuart et al:

Compared sperm retrieval by a standard TESE as compared to micro-TESE in 33 patients with NOA. Sperm were recovered in 30.3% of patients by both methods but higher numbers of sperm per retrieval were obtained by micro-TESE.

Sperm DNA Integrity

Poster 256 Coulam et al:

Compared the percentage of sperm with DNA fragmentation by a sperm DNA integrity assay in couples with and without biochemical pregnancy loss after IVF. A greater percentage of men with pregnancy loss (46% of men) had a high percentage of sperm DNA fragmentation (> 25% of sperm) as compared to couples without pregnancy loss (25% of men). The authors suggest that couples with biochemical pregnancy losses after IVF should have a sperm DNA fragmentation assay.

AZF Deletions

Poster 326 Kaponis et al:

Examined 4 men with AZF deletions and 13 men with obstructed azoospermia. They evaluated Sertoli cell function by measuring testicular ABP (androgen binding protein levels) and evaluated Leydig cell function by measuring intratesticular testosterone levels. No differences were noted between the two groups of patients suggesting no defects in the Sertoli cell and Leyding cell compartments in patients with AZF deletions.

Poster 354 Chuang et al:

Examined DNA from NOA patients for evidence of deletions of individual DAZ gene copies. They found that some patients with normal Y chromosome microdeletion testing by standard STS methods had deletions of some but not all DAZ gene copies.

Ductal Reconstruction

Poster 338 Sandlow and Kolettis:

Examined patency and pregnancy rates following vasovasostomy in the convoluted vas. Patency and pregnancy rates were 97% and 50% when whole sperm were present in the vas fluid, 67% and 67% with sperm parts, and 50% and 25% with clear fluid without sperm.

General Infertility

Poster 342 Lucidi et al:

Compared the semen parameters of men with and without a history of prior fertility. No difference in semen parameters was found indicating that a prior history of fertility does not predict a normal semen analysis.

Poster 386 Stern et al:

Reported the outcomes of pregnancies with sperm sorted for X or Y chromosome content by flow cytometry performed for sex selection. The rate of congenital malformations was 2.4% - comparable to the historical incidence in the general population. When sorted for X bearing sperm, 92.2% of children were female while sorting for Y bearing sperm resulted in males in 80.9% of cases.

Poster 552 Naughton et al:

Reported a correlation between the degree of male sexual dysfunction following radical prostatectomy and female partner sexual dysfunction. This was examined by a questionnaire; however, the response rate was low (10%).

Physiology/Molecular Biology

Poster 346 Turner et al:

Examined the expression of sonic hedgehog pathway genes in adult mouse epididymis. They found that expression of these genes is greater in the epididymis than in the testis or prostate, and that expression increases from proximal to distal epididymis. This suggests that these proteins may play an important role in adult epididymal function.

Poster 400 Rawe et al:

Demonstrated the presence of several actin related proteins in mature human spermatozoa. It is suggested that these proteins may play a role in fertilization.

Poster 4002 Aoki et al:

Examined the relative amounts of protamine-2 in individual spermatozoa from infertile men previously demonstrated to have sperm protamine-2 deficiency. A heterogeneous distribution of protamine-2 was observed in these patients' sperm.

WEDNESDAY, OCTOBER 15, 2003

SMRU Workshop – "New Methodologies for Propagation of Male and Female Germ Cells"

Faculty:
Susan A. Rothman, PhD, Chair
Roger G. Gosden, PhD, DSc
Pasquale Patrizio, MD

Overview by Robert Oates, MD

This workshop addressed recent advances in both female and male germ cell propagation in vivo and in vitro. Male germ transplantation has been investigated extensively in the animal model. However, human experimentation has been far less common and far less successful. As pointed out by the speakers, the need for new technologies to help

identify early germ cells, characterize them, and then purify enriched fraction needs to be further investigated. Once that an enriched fraction is obtained, then those germ cells may either be cryopreserved, cultured or transplanted. What drives these germ cells to undergo both mitosis and meiosis is still to be worked out and will, undoubtedly, be quite complicated biochemically. This will be a crucial finding and discovery as it may allow us to better and more successfully culture these germ cells and perhaps lead to improved results of transplantation. Culture conditions, molecular mechanisms, biochemical parameters, genetic happenings must all be understood and worked out prior to success in this endeavor. Germ cell culture and/or transplantation may be very helpful for a number of human clinical circumstances. These include harvesting of germ cells prior to ablative chemotherapy. As estimated by Dr. Patrizio, there are 6000 cases of testis cancer, 12,000 cases of leukemia, and 20,000 cases of lymphoma each year in the United States. Therefore there exists a tremendous population of men and women who may benefit from germ cell culture and or transplantation should they experience azoospermia/ovarian failure following their chemotherapeutic or radiotherapeutic regimens. As we all know, cryopreservation of a semen specimen should always be offered to men before the initiation of chemotherapy. There are those, however, that are too sick and ill to preserve a semen specimen before starting life-saving chemotherapy. For women, perhaps freezing some oocytes prior to adverse events such as chemotherapy or aging might be a useful as means of preserving their fertility potential. Therefore, although the field is just beginning and some excellent work has been done, there is a long way to go before we can successfully cryopreserve early germ cells, cultured them in vivo, or transfer them/transplant them either to a human or xenograft host. This symposium eloquently introduced us to these possibilities and gave the audience a peek at what the future might bring in this area of clinical and laboratory research.

Concurrent Session – Male Reproduction and Urology Abstracts and Lectures

Overview by Peter N. Schlegel, MD

Hopps et al. led off this session by overviewing the Cornell experience with used of cryopreserved testicular sperm from men with non-obstructive azoospermia (O-238). They found that the majority of men with non-obstructive azoospermia who have testicular sperm frozen (68%) do not have sperm survive freeze-thaw and usable for ICSI. Therefore, they recommended having fresh TESE available for a repeat cycle of ICSI even when cryopreserved testicular sperm are available from this subset of patients.

Martin et al. (O-239) reported on chromosomal pairing and recombination foci in men with non-obstructive azoospermia compared to controls. They identified an individual man with a greatly reduced frequency of recombination associated with impaired sperm production. This appears to be the first infertile man identified as having an arrest in meiosis because of an error in the processing of recombination foci or a defect in the synaptonemal complex leading to incomplete chromosome pairing.

Schiff et al. (O-240) reported on the use of a biomaterial wrap (Alloderm) or sealant (Coseal) used in a rodent model for sutureless vasovasostomy. They found that use of biomaterial or sealant resulted in much shorter operating times, but higher patency rate was seen in control (sutured) anastomoses or those created with biomaterial versus those fashioned with sealant or biomaterial and sealant. They concluded that the biomaterial wrap decreased the number of sutures required and simplified vasovasostomy without compromising surgical outcome.

Russell et al. (O-241) reviewed the subject of having frozen semen samples available from men prior to a programmed IVF cycle. All of us have experienced cases where men are unable to produce a specimen, are unavailable or have unexpected azoospermia on the day of oocyte retrieval. They reported use of frozen semen samples in nearly 14% of cycles, for both planned and unplanned reasons. Their results support having frozen samples available, in large part because of the relatively low cost of cryopreservation.

Goes et al. (O-242) reported on changes in FSH after varicocelectomy. They found that patients with normal FSH levels tend to have improved semen analyses, whereas men with elevated FSH may have increased testicular volume without improvement in semen analysis.

Cooperberg et al. (O-243) discussed the lack of standardization in reading testicular biopsies. Many men with severely impaired sperm production actually have mixed patterns of histology on diagnostic testicular biopsy. They re-reviewed 127 cases where biopsies were performed and found that re-reading these slides resulted in a change of treatment plan for 20 of 39 cases with mixed histologic findings. A standardized approach to histologic analysis by pathologists was recommended. Until that is available, review of biopsy slides by male infertility experts may be very worthwhile.

A study of testicular biopsies from aging men (age 59-102 years) was reported by Dakouane et al. from France. In this report, they found that spermatogenesis was possible until an advanced age (89 years), but an increase in the incidence of post-meiotic aneuploidy was associated with impaired spermatogenesis. Elderly men with preserved spermatogenesis did not have a statistically significant increase in aneuploidy (O-244).

Ahn et al. reported on charges for vasectomy reversal at private practices and academic institutions. They found that the majority of private practices do not offer vasoepididymostomy nor testicular sperm retrieval. The charges for reversal averaged just under $6,500 at private practices and over $10,000 at academic centers. Surgeons' fees were similar in the two settings, but facility fees were higher in the academic setting. Of private practices, 40% offered reversal in an office setting under local anesthesia.

Drs. Nina Desai and Amy Sparks presented a symposium on techniques for cryopreservation of testicular, and percutaneously derived epididymal samples. They addressed issues of testicular sperm quality in men with obstructive vs. non-obstructive azoospermia. Men with non-obstructive azoospermia have sperm that are less likely to survive freeze-thaw and allow lower fertilization and pregnancy rates than for men with obstructive azoospermia. Significant variation in survivability of sperm from men with non-obstructive azoospermia has been reported by different centers, whereas sperm from men with obstructive azoospermia reliably survive freeze-thaw. ◆

Upcoming Events / Sessions of Interest at the 2004 AUA Annual Meeting

May 9 – 13, 2004
San Francisco, California
Submitted by Robert Oates, MD

Sunday, May 9, 2004
Plenary Session: Point-Counterpoint – Should the Adolescent Varicocele be Repaired?
Moderator Laurence Baskin and debaters Evan Kass and David Diamond

Monday, May 10, 2004
Plenary Session: State-of-the-Art Lecture – Stem Cell Transplant in Male Infertility
Presented by Victor Brugh
Plenary Session: State-of-the-Art Lecture – Testicular Microlithiasis
Presented by Raymond Costible
Plenary Session: AUA Update – Defining the Standard for Vasectomy Success
Presented by Harry Fisch
Plenary Session: Panel Discussion – Case Studies in Male Infertility – Azoospermic Men
Moderator Harris Nagler and panelists Jon Pryor, Robert Oates, Craig Neiderberger and Dorrie Lamb
Plenary Session: Panel Discussion – Androgen Replacement in the Aging Male
Moderator Alvaro Morales and panelists Ridwan Shabsigh, Abraham Morgentaler and Cully Carson
Plenary Session: AUA Update – Report on the IOM Study on Assessing the Need for Clinical Trials of Testosterone Treatment
Presented by Darracott Vaughn and the IOM Study Committee

Tuesday, May 11, 2004
Podium Session – Infertility Therapy

Wednesday, May 12, 2004
Discussed Poster Session – Infertility: Physiology, Pathophysiology, Basic Research
Discussed Poster Session – Infertility Evaluation
Highlights from Tuesday – Infertility
Presented by Paul Turek

Thursday, May 13, 2004
Take Home Messages – Infertility
Presented by Gail Prins

Instructional and Postgraduate Courses include…

Sunday, May 9, 2004
Infertility Diagnosis and Treatment
Larry Lipshultz with Paul Turek (12 IC)

Sunday, May 9, 2004
Evaluation and Management of the Infertile Male: What's New and Important
Marc Goldstein with Jon Pryor and Dominick Carbone (22 PG)

Tuesday, May 11, 2004
Vasovasostomy, Vasoepididymostomy and Sperm Retrieval Techniques
Arnold Belker with Chris Schrepferman (46 IC)

Needs and Objectives for the SSMR Program

Needs:
What the Urologist needs to know about ovulation induction:

1. Biology of fertilization and early embryo development.
2. Sperm testing: What is useful and what is useless
3. Testis tissue processing for sperm retrieval: What are the best methods?

Objectives:
At the conclusion of the session, the participant will

1. Be able to list the common ovulation induction regimens.
2. Understand the steps involved in fertilization of human ova.
3. Be able to describe the initial stages of embryo development.
4. Understand the indications for ordering various sperm assays and be able to describe the information gleaned from each assay.
5. Be familiar with different methods of processing testicular tissue for sperm retrieval.

Agenda for SSMR at the AUA

Saturday, May 8, 2004
Hyatt/Plaza Ballroom East
San Francisco, California
1:00 p.m. – 5:30 p.m.

1:00 p.m. **Introduction**
Mark Sigman, MD, Program Chair

1:05 p.m. **What the Urologist Needs to Know About Ovulation Induction**
Marcel Cedars, University of San Francisco
- New medications being used: What are they? How do they work?
- New regimens being used: What are they? How do they work?
- Down regulation: Long, Short, Antagonist regimens
- Monitoring: What do they do?

1:35 p.m. **Q & A**

1:45 p.m. **Biology of Fertilization and Early Embryo Development**
Veness Rawe, Pittsburgh Development Center
- Final stages of oocyte
- Sperm penetration and decondensation
- Early embryo formation to the blastocyst stage: What is the sperm's role?
- If the embryo is poor, is it the sperm's fault and what can be done about it?

2:45 p.m. **Q & A**

3:00 p.m. **Break**

3:30 p.m. **Sperm Testing: What is Useful and What is Useless**
Panel: Harris Nagler, MD, Craig Niederberger, MD, Michael Witt, MD
- Semen volume and pH, Fructose, SPA
- SCSA, Viability, CMPT
- Acrosome Assay, ASA, CASA

4:05 p.m. **Q & A**

4:15 p.m. **Testis Tissue Processing: What Are the Best Methods?**
Peter Chan, MD
- Cryopreservation of tissue vs. cryopreservation of isolated sperm
- Solutions to preserve in
- Solutions to collect in
- Mincing, grinding methods of handling testis tissue

4:50 p.m. **Q & A**

5:00 p.m. **Annual Business Meeting**

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Tentative Agenda for the SSMR Traveling Fellowship Program 2004

May 8 – 13, 2004
San Francisco, California

Saturday, May 8, 2004		
SSMR Annual Meeting:	1:00 p.m. – 5:00 p.m.	(Hyatt/Plaza Ballroom East)
SSMR Annual Banquet:	6:00 p.m. – 11:00 p.m.	(Bank of America World Headquarters Building/ Carnelian Room)
Sunday, May 9, 2004		
Plenary Session – Adolescent Varicoceles:	9:20 a.m. – 9:50 a.m.	(Moscone Center)
Male Infertility Postgraduate Course:	1:30 p.m. – 5:00 p.m.	(Moscone Center)
Monday, May 10, 2004		
Plenary Session – State-of-the-Art lectures, AUA Update:	8:00 a.m. – 12:00 p.m.	(Moscone Center)
Podium Session – Sexual Function/Andrology:	1:00 p.m. – 3:00 p.m.	(Moscone Center)
Endocrine Forum:	1:00 p.m. – 3:30 p.m.	(Moscone Center)
Tuesday, May 11, 2004		
Panel Discussion with infertility experts regarding fellowships, career decisions, etc.:		8:00 a.m. – 10:00 a.m. (Hyatt/Belvidere)
Poster Session – Sexual Function/Andrology:	8:00 a.m. – 12:00 p.m.	(Moscone Center)
Poster Session – Sexual Function/Andrology:	1:00 p.m. – 5:00 p.m.	(Moscone Center)
Infertility Podium Session:	3:30 p.m. – 5:30 p.m.	(Moscone Center)
Cocktail Party:	5:00 p.m. – 7:00 p.m.	(Butron Room at the Hyatt)
Wednesday, May 12, 2004		
Plenary Session – Infertility Highlights:	7:45 a.m.	(Moscone Center)
Infertility Poster Session:	8:00 a.m. – 12:00 p.m.	(Moscone Center)
Infertility Poster Session:	1:00 p.m. – 5:00 p.m.	(Moscone Center)
Thursday, May 13, 2004		
Take Home Messages for Infertility:	8:10 a.m.	(Moscone Center)

Please Note: The dates and times of these activities are tentative, and may change after the final AUA schedule is determined.

Jay Sandlow, MD
Chair, SSMR Traveling Fellowship Award
jsandlow@mail.mcw.edu ◆

SSMR Traveling Fellowship Program 2004

Saturday, May 8 – Thursday, May 13, 2004
San Francisco, CA

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 $1000 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 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, MD
Director SSMR Traveling Fellowship Program
Associate Professor of Urology
Medical College of Wisconsin
Milwaukee, WI
jsandlow@mail.mcw.edu

Application for the SSMR Traveling Fellowship Program 2004

Saturday, May 8 – Thursday, May 13, 2004
San Francisco, CA

Please Print or Type.

Name:_____Degree(s):_____

Work Address:_____

City:_____State:_____Zip:_____

Home Address:_____

City:_____State:_____Zip:_____

Work Phone:_____Home Phone:_____

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. AUA abstract (if submitted)
4. 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.

Signature of Department Chairman:_____

Send (or FAX) completed applications to:

Jay I. Sandlow, MD
Associate Professor of Urology
Medical College of Wisconsin
9200 West Wisconsin Ave.
Milwaukee, WI 53226
FAX: (414) 456-6217

Deadline: February 15, 2004

YOU ARE INVITED TO ATTEND THE 2004 SSMR ANNUAL BANQUET

Saturday, May 8, 2004
Bank of America World Headquarters Building, Carnelian Room
Bay Room, 52nd floor
555 California Street
San Francisco, IL 94104

SSMR colleagues and guests will enjoy a delicious dinner and soothing music while experiencing San Francisco's best panoramic view at the Carnelian Room on top of the Bank of America World Headquarters. The American-continental cuisine is highlighted by Chef David Lawrence and his talented culinarians' use of the best and freshest ingredients available, and the 40,000-bottle wine cellar has been honored with the prestigious Wine Spectator's Grand Award.

Transportation will be provided from the main entrance of the Argent Hotel at 6:00 p.m.

6:30 p.m. – 7:30 p.m. Cocktails
7:30 p.m. – 10:00 p.m. Dinner

*(If you have any dietary needs, please contact the SSMR office at **(847) 517-7225** prior to April 21, 2004.)*

Dress code required:
Men – sport coat
Women – semi-dressy

# of people attending _____ x $80.00 per person = $ _____ (on and before April 21, 2004)

# of people attending _____ x $90.00 per person = $ _____ (after April 21, 2004)

Name:_____

Spouse/Guest(s)_____

Address:_____ ❒ Home ❒ Office

City:_____State:_____Zip:_____

Phone:_____Fax_____E-mail:_____

Method of Payment:

❒ Check (payable to the SSMR) ❒ Visa ❒ MasterCard

Card #:_____ Exp. Date:_____

Signature:_____

Please return this form to the SSMR office no later than April 21, 2004.

SSMR
1111 N. Plaza Drive, Suite 550
Schaumburg, IL 60173
Phone: (847) 517-7225
Fax: (847) 517-7229

MARK YOUR CALENDARS!

S S M R

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

American Urological Association Annual Meeting
May 8 – 13, 2004
Moscone Center
San Francisco, Calif.

SSMR Meeting at the AUA Annual Meeting
May 8, 2004
1:00 p.m. – 5:30 p.m.
Hyatt/Plaza Ballroom East
San Francisco, Calif.

A Special Thanks to the Sponsors of our 2003 Annual Meeting. We look forward to their continued support!

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