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MEN MACHISMO MEDICINE

Objective: The reader of this article will learn some of the causes of male infertility, what tests measure male fertility, and the statistical outcomes of treatment options.

CME

Advances in the Treatment of Male Infertility

by Glenn P. Palmisano, MD, and Connie Brennan

ADVANCES IN INFERTILITY RESEARCH are continuously improving treatment options and success rates for the infertile couple. The most dramatic development has been in the area of male infertility. Only a couple of years ago, the major stumbling block to treatment of the infertile couple was the infertile male. The combined use of intracytoplasmic sperm injection (ICSI) and sperm aspiration has revolutionized the way we now look at and treat male factor infertility.

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Semen Analysis

One of the first tests performed to determine male fertility potential is semen analysis. This procedure measures eight parameters of sperm function: concentration, volume, motility, progression, velocity, linearity, viability, and morphology. Each has a range of normal values. The World Health Organization defines normal semen parameters as follows:

Volume: ..... ≥2.0 mL
Sperm Concentration: ..... ≥20 million/mL
Motility: ..... ≥50% with forward progression
Morphology: ..... ≥30% normal.

Even when collected under ideal circumstances, the parameters will vary considerably between specimens from any individual. The most critical factors affecting sperm concentration, motility, and morphology are usually the abstinence interval and coital frequency. Other factors that may alter the ejaculate are febrile illnesses, alcohol, drugs, medication, systemic disease, prolonged increased scrotal temperatures, and stress. Interestingly, while cigarette smoking remarkably affects female fecundity, there has been no significant association found in males.[1]

There is often much anxiety expressed by both partners when an abnormal semen analysis is reported. There is fear regarding the cause and reversibility of the condition. Fortunately, since the process of spermatogenesis is completed approximately every 3 months, sperm quality can be improved by elimination or treatment of these factors during that interval. The male partner is often not present during the educational counseling which takes place within the physician's office. He may have been reluctant to reveal an accurate social history either on the fertility questionnaire or to his partner. For this reason, it is important to offer the female patient some printed educational material that she can take home for him. Those patients with repeated abnormal semen analysis are referred to a urologist for further follow up. After treatment, semen analysis can be repeated. Two to three semen samples will give a better indication of sperm count and semen quality.

Intracytoplasmic Sperm Injection (ICSI)

For those patients with persistent male factor infertility after urologic evaluation and treatment, the options available are ever increasing. ICSI has revolutionized infertility treatment for the patient with poor motility or morphology. During ICSI, micropipettes are used to inject the eggs with a single sperm while being visualized under a microscope. This method allows couples with moderate to severe male factor infertility remarkable success in achieving pregnancy. Until now, the presence of male factor infertility has decreased the success rate of all treatments.

Recent research indicates that using ICSI in conjunction with in vitro fertilization (IVF) may attain pregnancy rates for couples with male factor infertility that are comparable to the success rates of conventional IVF without the male factor.[2] This new technology for male factor infertility

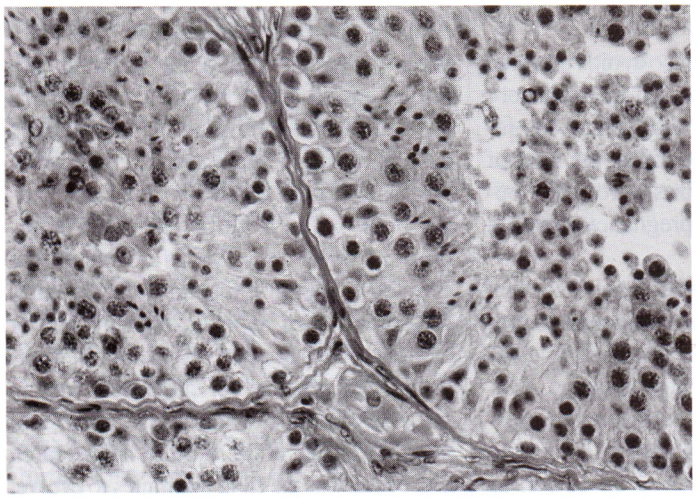


Figure 1 – A histologic slide showing a normal testicle.

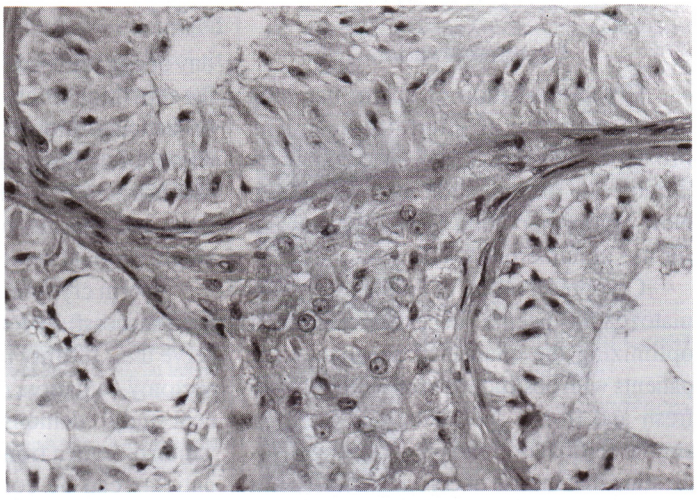


Figure 2 – A histologic slide showing Sertoli cell only picture.

makes pregnancy possible for couples who have had repeated failures at IVF or who have been excluded from IVF because of inadequate sperm count or motility.

Despite the criticism about the lack of natural selection while breaking the zona pellucida and the cytoplasmic membrane with the injection pipette, there has been no increased incidence of malformations, chromosomal abnormalities[3] or pregnancy loss.[4]

Other new applications for treatment include electroejaculation for men with spinal cord damage, microsurgical epididymal sperm aspiration (MESA) for non-reconstructable obstructive azoospermia, and testicular sperm extraction (TESE) in cases of severe spermatogenic defects. These latter two cases, which were previously considered hopeless, when combined with ICSI share a comparable fertilization rate with those for whom ejaculated spermatozoa are used. The fertilization rates were similar with testicular biopsy spermatozoa and epididymal spermatozoa when used in conjunction with ICSI. The findings demonstrate that testicular spermatozoa have gained full maturity and initiate normal fertilization and that the epididymis is not necessary for fertilization.[5] One case study in Australia concluded that testicular aspiration produced a higher quantity and quality of spermatozoa than electro- or vibro-ejaculation.[6]

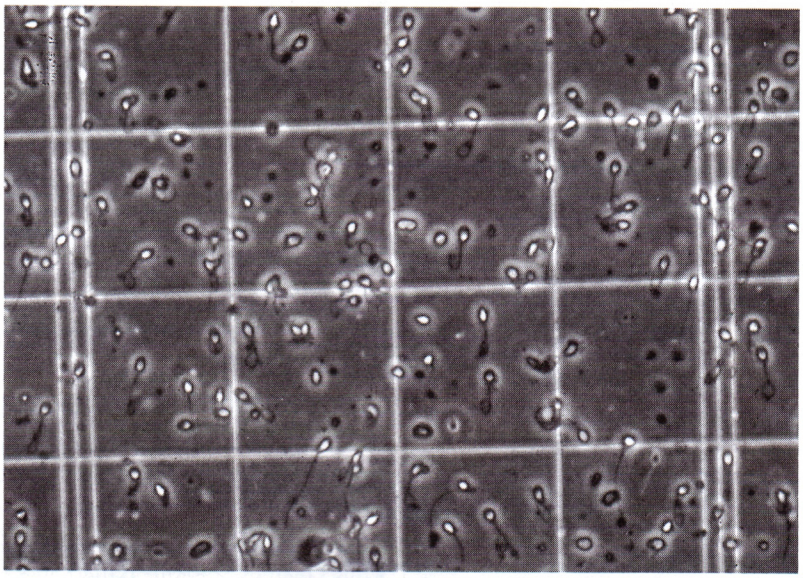


Figure 3 – A normal semen specimen seen under the microscope through a Makler counting chamber.

Sperm cryopreservation has also been used successfully for men who want to preserve their fertility prior to undergoing vasectomy, radiation, or chemotherapy.

Cryopreservation

Cryopreservation of sperm has long been a mainstay of infertility treatment. Frozen donor sperm has been available for intrauterine insemination for many years. Now cryopreservation is being expanded for use in numerous ways.

Cryopreservation of epididymal spermatozoa has been a successful method of optimizing the chance of pregnancy for patients with obstructive azoospermia. Both fresh and frozen spermatozoa resulted in similar fertilization and pregnancy rates, indicating that the use of cryopreserved sperm does not compromise treatment outcomes. Assessment of sperm vitality before freezing is beneficial and recommended, as sperm vitality of less than 20% typically shows poor outcomes in subsequent ICSI cycles.[7] Due to the low number and motility of testicular spermatozoa, cryopreservation is not yet feasible.[8]

Sperm cryopreservation also avoids the logistical problem of coordination of egg retrieval and sperm aspiration. It prevents the abandonment of a complete IVF cycle in the event that the male partner is unable to produce a semen specimen on the day of egg retrieval.[9] It also avoids the need for repetition of epididymal microsurgery or testicular biopsy. The simultaneous retrieval of epididymal sperm at the time of reconstruction maximizes a couple's options and chances for pregnancy within a single surgical setting.[10]

Sperm cryopreservation has also been used successfully for men who want to preserve their fertility prior to undergoing vasectomy, radiation, or chemotherapy. A recent study[11] demonstrated that cryopreservation of semen from adolsecent oncologic patients can be considered an option as well. While the serum values for luteinizing and follicle stimulating hormones were significantly lower in adolescents than in adults, the testosterone serum levels and testicular volumes were similar to those in adult men. Sperm concentrations, motility, and morphology in the adolescent patients did not show significant differences compared with adults. The question of fertility is often beyond consideration when the young patient's life is acutely threatened. However, improved survival rates increasingly prompt the question of quality of life after therapy, including fertility.

Autoimmune Disorders

Research is ongoing in the treatment of immunologic causes of infertility. Once again, ICSI with antibody-free sperm obtained by separating techniques may prove to be the most effective treatment in severe cases of sperm autoimmunity.[12] An association between certain autoimmune conditions and recurrent pregnancy loss (RPL) has been well established. RPL is defined as three or more spontaneous consecutive pregnancy losses fathered by the same partner.[13] In women with suspected autoimmune disorders, suppression of the overactive immune response during early pregnancy with aspirin, heparin, and/or corticosteroids appears promising. Because the precise reasons for pregnancy loss in these disorders are unknown, treatment remains controversial. Additional research is necessary as the field continues to evolve.

Pharmaceutical companies are cur-

The 1994 ART registry for the US and Canada reported IVF success rates (expressed as deliveries per egg retrieval) as 21.1%, up from 18.6% in 1993.

rently researching recombinant forms of FSH and LH. The current gonadotropic medications are urinary products whose potency may vary slightly from one batch to another. The new recombinant products will be synthetic and therefore purer and more standardized. They, too, will be able to be injected subcutaneously by the patient. Many experts predict that eventually most of the drugs used in fertility treatment will be recombinant products, synthesized in the laboratory.

Other exciting prospects on the horizon are the possibilities of gene transfer for the treatment of certain genetic diseases and diagnostic applications of embryonal biopsy.[14] These new technologies have also generated serious ethical and legal issues. Ethical guidelines and appropriate legislation with contributions from the medical and scientific community are gradually being established worldwide.

Statistics of Success

The most recent national data summary for all IVF-related procedures show gradual increases in success rates for most of the assisted reproductive technology (ART) treatments.[15] The 1994 ART registry for the US and Canada reported IVF success rates (expressed as deliveries per egg retrieval) as 21.1%, up from 18.6% in 1993. The report confirms previous findings of disappointingly low success rates for women over 40 (excluding donor egg IVF). In a comparison of women under 40 to those 40 and older who underwent stimulated IVF cycles, the differences are dramatic: 24.5% deliveries per retrieval in the younger group compared to 9.0% in the older group. The rates of success are further compromised by the presence of male factor infertility. In women under 40 with male factor present, the success rate was 20.2% compared to 8.5% in women over 40 with male factor present. Other encouraging statistics show that the majority of births were singletons (63.7%), followed by twins (28.3%), triplets (5.9%), and 0.6% higher order multiple deliveries.

Gamete intrafallopian transfer (GIFT) and zygote intrafallopian transfer (ZIFT) rates also rose. From 1993 to 1994, GIFT went from 28.1% to 28.5% deliveries per retrieval; ZIFT, from 24.4% to 29.1%.

The highest success rate (46.8%) was for donor egg IVF. The younger age of most egg donors probably accounts for these results and underscores the advantage of younger eggs.

Rates for birth defects and miscarriage remain comparable to those for the general population.

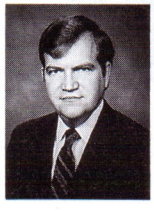
Due to the fact that ICSI was not widely used in IVF programs until late '94 or early '95, national statistics are not yet available for use of this technique. However, Reproductive Biology Associates in Atlanta reported a 30.8% success rate for ICSI for women under the age of 37 with male factor infertility during the period of September 1994 - July 1995. For women over age 37 with male factor infertility, the success rate dropped to 14.9%.[16]

Conclusion

The future of infertility treatment is promising. Success rates continue to climb. Ongoing research has developed new techniques and pharmacology. Those who were once excluded from the experience of parenthood now have new hope. Yet, despite the enthusiasm for and success of ICSI, the need still exists for continued intensive research at the molecular level. It is still necessary for men to undergo continued investigations and testing so that scientists can better understand and possibly cure the underlying genetic causes of male infertility.

References

1. Bolumar F, Olsen J, Boldsen J. Smoking reduces fecundity: a European multicenter study on infertility and subfecundity. The European Study Group on Infertility and Subfecundity. Am J Epidemiol 1996 March 15; 143 (6): 578-87.
2. Silber, Sherman J. A Modern Approach to Male Infertility. Insights into Infertility 1997; spring newsletter p. 10-12.
3. Kupker W, al-Hasani S, Diedrich K. Andrologia 1996; 28 Suppl 1:37-42.
4. Coulam CB, Opsahl MS, Sherins RJ, Thorsell LP, Dorfmann A, Krysa L, Fugger E, Schulman JD. Comparisons of pregnancy loss patterns after intracytoplasmic sperm injection and other assisted reproductive technologies. Fertility and Sterility 1996 June; 65 (6): 1157-62.
5. Ubaldi F, Camus M, Tournaye H, Clasen K, Nagy Z, Smitz J, Van Steirteghem A, Devroey P. Results of microsurgical epididymal sperm aspiration (MESA) and testicular sperm extraction (TESE) in azoospermic men using intracytoplasmic sperm injection (ICSI). Andrologia 1996; 28 Suppl 1 (): 71-5.
6. Watkins W, Lim T, Bourne H, Baker HW, Wutthiphan B. Testicular aspiration of sperm for intracytoplasmic sperm injection; an alternative treatment to electroemission; case report. Spinal Cord 1996 Nov; 34 (11): 696-8.
7. Holden CA, Fuscaldo GF, Jackson P, Cato A, Southwick GJ, Hauser R, Temple-Smith PD, McLachlan RI. Frozen-thawed epididymal spermatozoa for intracytoplasmic sperm injection. Fertility and Sterility 1997 January; 67 (1): 81-7.
8. Silber SJ, Van Steirteghem AC, Liu J, Nagy Z, Tournaye H, Devroey P. High fertilization and pregnancy rate after intracytoplasmic sperm injection with spermatozoa obtained from testicle biopsy. Human Reproduction 1995; 10 (1): 148-52.
9. Watkins W, Bourne H, Nieto F, Gronow M, Baker G. Testicular aspiration of sperm for intracytoplasmic sperm injection: a novel treatment for ejaculatory failure on the day of oocyte retrieval. Fertility and Sterility 1996 October; 66 (4): 660-1.
10. Matthews GJ, Goldstein M. A simplified method of epididymal sperm aspiration. Urology 1996 January; 47 (1): 123-5.
11. Kliesch S, Behre HM, Jurgens H, Nieschlag E. Cryopreservation of semen from adolescent patients with malignancies. Med Pediatr Oncol 1996 January; 26 (1): 20-7.
12. Marshburn P. Antisperm antibodies and infertility. Infertility and Reproductive Medicine Clinics of North America 1997 April; 8 (2): 243-66.
13. Kutteh W, Stovall D, Scott J. The immunologic diagnosis and treatment of recurrent pregnancy loss. Infertility and Reproductive Medicine Clinics of North America 1997 April; 8 (2): 267-87.
14. Kim MH. Current trends in human IVF and other assisted reproductive technologies. Yonsei Med J 1990 June; 31 (2): 91-7.
15. Assisted reproductive technology in the United States and Canada: 1994 results generated from the American Society for Reproductive Medicine/Society for Assisted Reproductive Technology Registry. Fertility and Sterility 1996 Nov; 66 (5): 697-705.
16. Reproductive Biology Associates, Atlanta, GA. Cumulative Statistics for 9/94 - 7/95.



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