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UROLOGY BOARD REVIEW MANUAL

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Male Fertility Issues

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Chapter 1—Infertility

INTRODUCTION

Infertility has become an increasingly common problem among couples, particularly those older than 35 years, with one in five couples experiencing some form of infertility.^{1–5} Increased media attention to the tremendous advances in assisted reproductive medicine has heightened the general population’s awareness of infertility and available treatments and, subsequently, has led to an increase in the number of couples seeking evaluation and treatment.

Unlike most patient complaints, the clinical approach to infertility involves the diagnosis and treatment of a couple rather than an individual. Male factor infertility is involved in approximately 50% of couples experiencing infertility, and 20% of all infertility cases are solely due to the male factor.⁶ Prior to the advent of intracytoplasmic sperm injection (ICSI), the prognosis for couples with severe male factor infertility was poor. With ICSI, couples that were traditionally considered sterile are now able to conceive biologic children.⁷ ICSI has dramatically increased the success rate of in vitro fertilization (IVF) when very few sperm are available.^{8,9} However, much of this success comes at the expense of added cost and morbidity associated with assisted reproductive techniques such as IVF.^{10,11}

It is interesting to note that when many studies refer to advances in the treatment of male factor infertility, they are referring to the treatment of the male gamete, not the person.¹² The increase in pregnancy rate is due, in part, to the fact that ICSI/IVF is being used to overcome gamete inadequacy rather than anatomic abnormalities that prevented pregnancy. Additionally, as ICSI availability continues to increase, it has been suggested that the indications for its use be broadened beyond severe male factor infertility to include such conditions as borderline findings on seminal fluid analysis (SFA) or unexplained infertility.^{13–15}

The increasing success rates associated with IVF may persuade some patients and clinicians to forego male

infertility evaluation beyond SFA and proceed directly to treatment of the gametes with IVF.¹⁶ Although it is reassuring to both patient and physician that fertilization can be achieved with ICSI, fertilization is not an exclusive indicator that the DNA in the sperm is intact. Furthermore, it is possible for existing genetic defects to be passed on by ICSI. It is critical that all parties involved with infertility treatment recognize that infertility is a complex issue involving both partners and occasionally is a harbinger of a more serious underlying disorder.^{17,18} The use of IVF (with or without ICSI) in the absence of evaluation and treatment of the male partner may lead to the underlying cause of the male factor being undiagnosed and untreated. In this era of cost containment, evaluation and treatment of the cause of infertility often is more cost-effective than directly proceeding to assisted reproductive techniques.^{10,11,19,20}

NORMAL SPERMATOGENESIS

Spermatogenesis is the highly organized and progressive maturation of immature germ cells to their final form as mature spermatozoa (**Figure 1**). During the early stages of spermatogenesis, the processes of mitosis and meiosis are important for cell renewal as well as cell maturation. Mitosis is responsible for effectively replenishing immature germ cells, whereas meiosis is involved in the maturation of germ cells.

The most immature form of germ cell is called a spermatogonium. There are two main types of spermatogonia—Type A and Type B. Type A spermatogonia tend to be self-renewing cells as well as cells that differentiate into Type B spermatogonia. Type B cells subsequently undergo meiosis to become spermatocytes. Spermatocytes undergo five phases of differentiation: preleptotene, leptotene, zygotene, pachytene, and diplotene. Genetic recombination, or crossing over, typically occurs during the pachytene phase. During the diplotene phase, the chromosomes separate and the spermatocyte then