Infertility: A Family Practice Approach

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DR. KEITH FREY (*Assistant Professor, Division of Family Medicine*): I would like to welcome you to this Grand Rounds presentation on infertility. Dr. Klein will begin with a case presentation of a couple from the Family Medicine Center. I will review the evaluation at the primary care level. Dr. Dodson will provide an overview of the infertility consultation from a subspecialist's perspective. Dr. Andolsek will discuss the psychological considerations in infertility and continuity of care.

CASE PRESENTATION

DR. JONATHAN KLEIN (*Resident in Family Practice*): Mr. and Mrs. M. were referred to Dr. Frey in July 1986 for further evaluation of their longstanding infertility. The couple had been married for four and one-half years and had been having unprotected intercourse for the last four years. Results of a prior infertility evaluation with Mrs. M. in 1984 included a normal complete blood count, normal thyroid functions, a negative VDRL, basal body temperatures consistent with ovulation, and a normal Papanicolaou smear. A postcoital test performed in February 1984 (day 18 of her cycle) revealed "hostile" cervical mucus. No cause was established or treatment prescribed.

Dr. Frey's medical history notes Mrs. M. to be 30 years of age, with menarche at age 13 years. Her menses had been regular with 28-day cycles. Oral contraceptive had been discontinued in 1983. She had no prior pregnancies. An ovarian cyst was diagnosed by laparoscopy in 1974. Past medical illnesses included two urinary tract infections and an episode of presumed pelvic inflammatory disease that was treated with tetracycline in November 1981.

The physical examination was entirely normal. Dr. Frey's infertility evaluation included the following normal laboratory tests: urinalysis, complete blood count, VDRL, and Papanicolaou smear. Basal body temperatures were consistent with ovulation. A hysterosalpingogram revealed bilateral tubal obstruction with left hydrosalpinx.

Mr. M. is a 28-year-old man who had not fathered a child previously. Previous medical illnesses included mild renal insufficiency that was presumed secondary to acute tubular necrosis, which required hospitalization in 1984 and 1985. His review of systems was otherwise negative. Physical examination was significant for a left varicocele. Laboratory evaluation revealed a creatinine level of 194 μmol/L (2.2 mg/dL), proteinuria (1+), and a normal complete blood count. Two semen analyses were performed. Each had adequate volume and normal percentages of normal forms with normal motility. The sperm counts, however, were 700,000/mL and 30,000,000/mL, respectively. At this point in the evaluation Mr. M. was referred to a urologist for consideration of a varicocelectomy and Mrs. M. to a gynecologist for laparoscopy.

DR. FREY: We selected this couple for several reasons. Their situation underscores the necessity of a comprehensive evaluation done in a timely fashion. At least two infertility factors were present, reinforcing the need for comprehensive evaluation of the couple. Couples can be evaluated initially in a family practice setting with consultants selected as specific problems are identified.

ROLE OF FAMILY PHYSICIAN

Infertility is defined as one year of unprotected intercourse in which a pregnancy has not been achieved. Using this definition, approximately 15 to 17 percent of couples in the United States are infertile.[1,2] The family physician is a natural entry point in the health care system for these couples. Typically, the family physician will have been providing primary care to them for some time.

A family physician with an interest in, and an understanding of, normal human reproduction and the common causes of infertility can provide an initial evaluation of such a couple. We also have an important role in the continuity of care. As problems beyond our expertise are identified, a consultation becomes necessary. The continuity of care will be crucial as the couple works their way through the medical system with its embarrassing and

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often painful procedures. The family physician can provide support, direction, and interpretation for such couples.

It is important to anticipate the common issues likely to be present in an infertile couple before they are seen. Often the couple is quite frustrated, having tried to achieve a pregnancy over an extended period. Reminders of their failure are constant in their lives: a monthly menstrual period, questions from well-intentioned friends and relatives, pregnancies of friends and co-workers.

Couples who present for infertility evaluations may be anxious, angry, or depressed. Exploring the support they provide for each other and that which they receive from their support systems at large is an essential step in the early evaluation. A comprehensive evaluation of both partners is essential. This initial evaluation can be performed easily and appropriately in the family physician's office.

DIAGNOSTIC EVALUATION

Let me focus first on the workup on the man. A complete history is very important and should evaluate fertility in previous relationships, the current sexual history, and a detailed review of systems. Specific attention is paid to the genitourinary tract, previous surgery, and prior infectious diseases. An occupational history should evaluate potential chemical, thermal, or radiation exposure. A complete physical examination is performed with particular attention to the genitourinary tract. The examination includes noting urethral meatus location, testicular presence and size, presence of a varicocele (examined with the patient supine, standing, and during a Valsalva maneuver), and performing a prostate examination.

The laboratory evaluation includes a complete blood count, urinalysis, urine culture if indicated, VDRL, and two semen analyses. The semen analysis should include a sperm count, semen volume, and evaluation of sperm form, motility, and liquidity. The sample should be obtained by masturbation after at least a two-day abstinence, and delivered to the laboratory promptly. The male partner's evaluation is concluded at this point if the history, physical examination, and laboratory values are all within normal limits.

The evaluation of the female partner requires the same detail in history taking. This history should focus on previous pelvic surgery, pelvic infections, and a thorough description of her menstrual cycles. Are the menses regular? Of what interval and length of flow? Are there associated moliminal symptoms? The previous contraceptive history and current sexual history should be noted. Coital frequency and timing during the menstrual cycle should be reviewed, as well as postcoital body position

(to keep the semen pool in contact with the cervix). A complete physical examination is mandatory, including a thorough pelvic examination. Attention should focus on the normality of the anatomy, and any evidence of scarring or infection should be noted. An initial laboratory evaluation includes a complete blood count, urinalysis, urine culture if indicated, Papanicolaou smear, and VDRL. Basal body temperatures (taken orally with a basal body thermometer) can be initiated to confirm ovulation, to assess luteal phase length, and to time subsequent diagnostic tests.

After the initial history, physical, and laboratory evaluation, any subsequent workup is individualized. The majority of female patients will require a luteal serum progesterone level (to confirm ovulation and luteal adequacy) and a postcoital test (to assess cervical mucus and sperm interaction). The fallopian tubes can be evaluated by hysterosalpingography or laparoscopy, depending upon the patient's previous history. An endometrial biopsy may be necessary to confirm a suspected luteal phase abnormality.

While this initial infertility evaluation can be performed by the family physician, two points should be emphasized. First, the primary care physician should have a good working relationship with at least one gynecologist with expertise in infertility. Such a relationship requires good communication and a knowledge of the consultant's approach and philosophy toward infertility. Second, the infertile couple deserves a comprehensive, yet timely, primary care evaluation. Once the initial evaluation is completed, prompt consultation with an appropriate gynecologist, while receiving ongoing support and primary care, is essential.

DR. WILLIAM DODSON (*Assistant Professor, Department of Obstetrics and Gynecology, Division of Reproductive Endocrinology and Infertility*): The goals of the primary care provider are to provide efficient diagnostic algorithms, assist the infertile couple in formulating reasonable treatment expectations, communicate effectively with consultants, assist with implementing treatment, and provide continuing health maintenance, often forgotten by couples and physicians during the lengthy diagnostic and therapeutic processes. The goals of the infertility consultant are to ensure that no areas of infertility have been left unexplored, to provide a more accurate description of the abnormal factors encountered during the infertility survey, to implement secondary and tertiary care when necessary, and to communicate effectively with the referring physician.

There is neither general agreement regarding the details of what an infertility survey comprises, nor general accord regarding the diagnostic or therapeutic algorithms for a particular infertile couple. All couples do not have the same cause of infertility; therefore, some individualization of diagnostic and therapeutic maneuvers is necessary so that redundant or ineffectual tests are avoided and that irrelevant treatment is not undertaken. Of utmost importance is the effective communication between the consultant and the family physician. It is desirable for a family physician to nurture a professional relationship with one or two consultants. This relationship will foster more effective communication, from which the infertile couple can only benefit.

PREVALENCE

A recent population-based study of the causes of infertility within a specialist infertility practice in England revealed that 10 percent of all new gynecology visits and 22 percent of all attendances at local gynecology clinics were for evaluation and treatment of infertility. The incidence of infertility of the couples in the district studied was estimated to be 17 percent.[2] Familiarity with the causes and treatments of infertility is therefore essential for family physicians providing care for the reproductive-aged couple. The couple presented today illustrates several basic principles of the evaluation of infertility. First, common problems are encountered commonly. Second, multifactorial causes of infertility occur in 15 percent of infertile couples, and third, it is imperative that infertile couples receive prompt and efficient comprehensive care furnished by a team of primary care providers and specialists.

CAUSE

The most common diagnostic category seen in the British study was "unexplained" infertility, which occurred in 28 percent of couples. Second only to "unexplained" infertility was male factor infertility, which was seen in 26 percent of couples in the British study, and in the couple presented today. Male factor infertility includes oligospermia or azospermia, disorders of sperm function or motility (asthenospermia), and abnormalities of sperm morphology (teratospermia). Naturally there is a spectrum of severity of abnormalities. The most commonly encountered cause of male infertility is a varicocele formation. Male infertility associated with serum antisperm antibodies is also commonly encountered; however, the role of immune dysfunction in male infertility is not well established.

Infertility associated with tubal damage or adnexal adhesions was encountered in 14 percent of infertile couples in the British study. As in the case of male infertility, the spectrum of severity is wide, ranging from a few, filmy ovarian adhesions to bilateral tubal occlusion, as in this

case. Tubal obstruction can result from acute salpingitis caused by multiple organisms, including Neisseria gonorrheae, Chlamydia trachomatis, and presumed secondary invaders, most commonly from the Enterobacteriaceae family. An unremarkable history of acute salpingitis, however, does not eliminate the possibility of damaged oviducts, in that many cases of tubal occlusion are encountered in which no episodes of salpingitis are recalled. Other causes of anatomic distortion of adnexal structures capable of interfering with ovum pickup and gamete and embryo transport include endometriosis and previous adnexal surgery. Unlike tubal occlusion that is due to salpingitis, these causes do not typically injure the endosalpinx; however, extrinsic adhesions can impair tubal function, preventing intrauterine pregnancy.

Other potential causes of infertility were explored in this couple and found to be absent. These diagnostic categories include ovulatory failure, endometriosis, and cervical mucus abnormalities. Ovulatory dysfunction was encountered in 21 percent of infertile couples, ranging in severity from luteal phase defects to chronic anovulation. In this couple normal ovulatory function was suggested by a history of regular menses of normal intermenstrual interval and moliminal symptoms, biphasic basal body temperatures, and a normal midluteal serum progesterone level.

Endometriosis, encountered in 6 to 20 percent of infertile women,[2] is thought to arise from endometrial implantation from retrograde menstruation. Endometriosis can be detected only by direct visualization of the pelvic peritoneum. Tubal occlusion may prevent endometriosis in this patient by prohibiting retrograde menstruation. Cervical mucus abnormalities are encountered uncommonly. For couples in whom the male partner has sperm density or function abnormalities, determination of the quality of cervical mucus may be irrelevant, made possible only with the aid of in vitro cervical mucus cross match.

Even in the cases of infertile couples with established causes of infertility, such as the present couple, a survey of the causes of infertility should be completed if the couple desires treatment. For example, this couple had more than one significant infertility factor. If the evaluation of the cause of infertility had been set aside after the male or tubal-factor had been identified, the other factor would not have been discovered.

Implementing a comprehensive survey is important for several reasons, particularly when subfertility factors are encountered. First, the survey will more likely be without incompleted components. Second, the survey will be done over a shorter period of time, thereby avoiding the grueling pursuit of diagnostic tests that interfere with the routine of the couple. Third, the survey will screen for multifactorial causes of infertility, which can be treated simultaneously rather than serially, thus reducing the burden of infertility diagnosis and therapy borne by the infertile couple. A comprehensive survey should consist of at least one semen analysis, a properly timed postcoital test, a hysterosalpingogram or hysteroscopy, laparoscopy, and midluteal serum progesterone test or endometrial biopsy.

MANAGEMENT

Therapeutic options for disorders of fertility have been increasing in number over the last 20 years. With the advent of in vitro fertilization and embryo transfer, gamete intrafallopian transfer, and intrauterine insemination during superovulation, even the most difficult cases of infertility are now amenable to treatment.[3] Gamete donation has enabled men and women with abnormal gonad function to become parents. Unfortunately, the number of options for diagnosis and treatment has become so great that it is possible for an infertile couple to spend years and thousands of dollars exploring diagnostic and therapeutic options in the pursuit of an elusive pregnancy.[4] Prevention of the frustration of multiple failures requires careful individualization of therapy with regard for the treatment goals of that particular couple.

DR. KATHRYN ANDOLSEK (*Assistant Professor, Division of Family Medicine*): My goal is to discuss the psychological issues couples such as Mr. and Mrs. M. experience. One individual expressed some of these issues very poignantly: "My infertility is a blow to my self-esteem, a violation of my privacy, an assault on my sexuality, a final exam on my ability to cope, an affront to my sense of justice, a painful reminder that nothing can be taken for granted. My infertility is a break in the continuity of life. It is above all, a wound to my body, to my psyche, to my soul."[5] The feelings are intense. Infertility is an experience of loss that differs from other loss experiences. I will discuss the ways in which infertility differs and discuss specific provider strategies that I hope you will find useful as you care for couples with infertility.

The family physician should be aware that the workup, diagnosis, and even treatment of infertility can all precipitate intense emotional issues.[6–9] We are in a unique position to identify and assist couples to work through these issues. Our medical care can involve both partners in the infertility workup, thus allowing us to focus continually on couple issues as well as on individual ones. The first stage that couples usually pass through is the shock of discovering their infertility. This shock is followed closely by disbelief and denial as they struggle to explain their infertility. Infertility is frequently encountered relatively early in married life and often is the first stressful event a couple must face together. The process of resolution can be the blueprint for handling future conflict. An attempt to find an explanation may result in "blaming" one or

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the other. Medical providers can contribute inadvertently to this tendency to place blame through their word choice in explaining diagnoses. (Such comments as "your tubal disease is likely due to wearing an IUD so many years" may be true, perhaps, but send a powerful message of responsibility to the female partner.) The couple may experience guilt, especially over past sexual issues. There may be self-doubt and anger. The family physician should get each member of the couple to label his or her feelings and help each understand his or her individual coping strategies. Both partners may need practice developing an adaptive "couple-coping" style. We need to help them build on their intimacy and avoid misinterpretations that can erode it.

The second common stage the couple experiences is mourning the "loss" of the child. This stage is more difficult than with other grief experiences, such as the loss of a child to death. In infertility the loss is not visible or tangible. The child, after all, has never been conceived. The individual and couple mourn lost expectations and lost experiences. Their grieving lacks an endpoint. There is no funeral; their grief is not public. While grieving, they still have hope for a cure. Friends and family may be unaware of their loss or may even contribute to the reminders of their infertility; depression commonly occurs. Infertility creates stress both from the loss of a major life experience and the prolonged series of hassels (evaluation and treatment).

With infertility there are many losses. There may be the loss of the marital relationship (real or imagined). There is a perception of loss of health; one or both partners may feel damaged or defective. This feeling can be exacerbated if the physician prescribes medicine or surgery. There is loss of status—loss of being a parent. There may be lost self-confidence or loss of self-esteem. There is a loss of fantasy, of what parenting and the child would be like. They may be shocked at their anger toward other pregnant couples and at the same time feel bad that they have these feelings. As we help couples discover, articulate, and work through these issues, it is important also that we help them arrive at some understanding of their motives in wanting to parent. They may need help generating options and testing the acceptability of these options. Finally, there is a need to explore with the couple the sexual issues common in infertility.[7] There may be physical changes from the infertility problem itself, such as pelvic pain secondary to pelvic adhesions. The couple may focus so much on sex for procreation that it interferes with the spontaneous nature of the sexual relationship. The numerous psychological issues discussed, altered body image, feeling defective, perhaps feeling physically and sexually unattractive, guilt, and anger, can all affect the sexual relationship.

With this brief understanding of some of the psychological issues, we can develop specific behavior strategies:

1. Evaluate and treat the couple as a couple when at all possible.
2. Discuss the nature of the psychological issues involved.
3. Help the couple understand their motives for parenting—their desire to parent, to experience a pregnancy, to meet the expectations of others, to create genetic continuity—and help them share these motives.
4. Encourage the couple to discuss their expectations and feelings and to grieve.
5. Discuss the sexual issues. Encourage the couple to nuture their marriage and intimacy; they will need its strength to address these stresses.
6. Proceed with evaluation and therapy at a rate with which the couple is comfortable.
7. Help the couple broaden their support systems, including the self-help groups such as Resolve, Inc.

None of these issues are easy. As family physicians, we are in a unique position to assist these couples, both medically and psychologically, as their infertility is addressed.

DR. FREY: In conclusion, it may be of interest to provide follow-up on our couple. Mrs. M. underwent laparoscopy for her abnormal hysterosalpingogram. The findings included adhesions requiring subsequent lysis at laparoscopy and bilateral fimbroplasty. She had an unremarkable postoperative course. Mr. M. was referred to a urologist and his varicocelectomy surgery is currently pending. It is anticipated that the couple will be placed on clomiphene therapy, and a successful pregnancy is hoped to be achieved in the near future.

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