The Subfertility Handbook
A Clinician's Guide

Edited by Gab Kovacs
This helpful and practical handbook will be an essential resource for all clinicians dealing with problems of subfertility. It provides a comprehensive approach to infertility, starting with the initial history taking and dealing with the diagnostic techniques of ultrasound and surgery, as well as all forms of therapy, including ovulation induction, infertility surgery, andrology, donor insemination and reproductive technologies. The authors are experienced members of the Monash University affiliated Reproductive Medicine Clinics – one of the world’s pioneering centres in IVF technology. They have distilled a wealth of expertise and ‘hands on’ experience in this area to provide an invaluable guide to all those involved in the treatment of infertility, from gynaecologists to physicians and postgraduate students specializing in reproductive medicine.
The subfertility handbook: a clinician’s guide
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The subfertility handbook: a clinician’s guide

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1

Introduction

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Infertility is a problem that affects many couples. Most adults have life plans that include children. When efforts to have children are unsuccessful, feelings of helplessness, frustration and despair are common. It is often at this point that many couples seek help from a Clinician. The Clinician's role is not only to help define the couple's problem, but also to be sympathetic and considerate to their emotional needs at this most difficult time. An understanding of the epidemiology, as well as of the historical aspects of the treatment of infertility, will be extremely helpful in achieving this goal.

Infertility is defined as the state in which a couple, desirous of a child, cannot conceive after 12 months of unprotected intercourse (Mueller and Daling, 1989; Thonneau et al., 1991). This is taken as being abnormal as 90% of couples will conceive within that time (Tietze, 1956; 1968). Infertility is either primary, when no pregnancy has ever occurred, or secondary, where there has been a pregnancy, regardless of the outcome (Thonneau et al., 1991). The ratio of patients presenting with primary and secondary infertility has remained remarkably stable with 67–71% of patients with infertility presenting with primary infertility and 29–33% presenting with secondary infertility (Hull et al., 1985; Templeton, Fraser and Thompson, 1991; Thonneau et al., 1991).

To understand infertility better, it is important to appreciate the epidemiological term, fecundity (Spira, 1986; Jansen, 1993). The fecundity of a couple is measured by their fecundability, i.e. the monthly probability of conception without the use of any contraception (Jansen, 1993). A couple is subfecund when there is an involuntarily long interval between births or until first conception. When the fecundability of the couple is zero, for whatever reason, the couple is infecund, or sterile (Jansen, 1993). The rate of sterility is believed to be 3–5% but the true incidence is unknown (Spira, 1986; Jansen, 1993). The reason for this may be that more couples have been inquiring about
infertility and requesting medical assistance in order to have a child. There has been no general increase in the prevalence of infertility, and the increase in demand for treatment appears to have been generated by greater expectations (Aral and Cates, 1983; Templeton, Fraser and Thompson, 1991). This in turn has been partly generated by the increased media focus on the new medical procedures and technologies available for achieving pregnancy.

The fecundability rate amongst young couples who discontinue contraception in order to become pregnant is quoted to range from 25% to 36% (Cramer, Walker and Schiff, 1979; Harlap and Baras, 1984; Spira, 1986). For many years, the incidence of infertility was thought by many to be 10%, but a number of excellent recent studies give a clear indication as to the true figure, which ranges from 13.5% to 18.4% (Hull et al., 1985; Thonneau et al., 1991), and translates to one in seven women. These studies have demonstrated that infertility is a real health problem because of its prevalence (Thonneau et al., 1991). Clinicians, both in general practice and in specialist gynaecological practice, will regularly encounter couples presenting with these problems.

In women, the main causes of infertility — accounting for 50% of cases — are ovulation disorders and tubal damage (Spira, 1986; Thonneau et al., 1991). Some of the rarer causes of infertility include endometriosis, hyperprolactinaemia and genital tract disorders (Thonneau et al., 1991). In men, the main causes of infertility are oligospermia, asthenozoospermia, teratospermia and azoospermia, which account for 20–25% of cases (Thonneau et al., 1991). In 18% of couples, no cause is found (Spira, 1986), and 3% of couples in this group will conceive each month without assisted reproductive techniques (Barnea, Holford and McInnes, 1989; Hull et al., 1985; Deaton et al., 1990). Combined causes of infertility can be found in 10–30% of couples (Hull et al, 1985; Thonneau et al., 1991; Jones and Toner, 1993). It is therefore very important to investigate both partners, and one must never assume that infertility is exclusively a female or a male problem.

Female risk factors of infertility

A number of factors have been identified as increasing the risk of becoming infertile, especially in women. Two of the major risk factors associated with female infertility are pelvic inflammatory disease and sexually transmitted diseases. The number of reported cases of the former has been increasing over the past two decades (Curran, 1980; Westrom, 1980). Damaged fallopian tubes are the major cause of infertility, and two organisms, Neisseria gonorrhoea and Chlamydia trachomatis, are responsible for the majority of cases
(Mueller and Daling, 1989). The risk of becoming infertile increases with each successive episode of pelvic inflammatory disease and increases with the severity of each episode (Westrom, 1975; 1980). Pelvic inflammatory disease can be a silent process, particularly when due to *Chlamydia trachomatis*. Its long term effects are the same as pelvic inflammatory disease, which is symptomatic and requires medical intervention (Rosenfeld *et al.*, 1983). The risk of pelvic inflammatory disease is increased in women who contract a sexually transmitted disease when using an IUD.

Pelvic surgery, including surgery for appendicitis (Mueller and Daling, 1989), is associated with an increased risk of infertility (Thonneau *et al.*, 1991), although this risk may be reduced by the increasing use of laparoscopic surgery which has a lower postoperative adhesion rate. Ectopic pregnancy is associated with an increased risk of tubal infertility (Mueller *et al.*, 1987), but this may be due to the pre-existing conditions that lead to the ectopic pregnancy rather than to the surgery itself. Induced abortion, if followed by infection, may lead to tubal disease and infertility. However, in well-designed studies, there appeared to be no increased risk of tubal infertility in a population for whom abortions were performed safely under appropriate sterile conditions with proper medical supervision (Daling *et al.*, 1985).

Cigarette smoking is becoming more prevalent amongst teenage girls and young adult women. Recent controlled studies suggest that women who smoke have an increased risk of infertility due to tubal disease and to abnormalities of cervical mucus (Phipps, Cramer and Schiff, 1987). The relationship between age and fertility is not so clear cut. Many women are now delaying the age at which they have their first child, and it appears that fertility may reduce with increase in age, particularly for women over 35 years (Spira, 1986).

**Male risk factors of infertility**

There are also a number of risk factors associated with male infertility. Sexually transmitted diseases are an important risk factor for male as well as for female infertility, most commonly those caused by *Neisseria gonorrhoea* and *Chlamydia trachomatis*. These organisms can cause changes in semen quality and, if left untreated, an infection may result in blockage of the vas deferens or seminal vesicles (Megory *et al.*, 1987). Mumps orchitis is rare in men in their reproductive years, but approximately 30% of men with orchitis will become azoospermic. The presence of a varicocele, a history of inguinal hernia surgery, and vesicular damage due to torsion or trauma may all lead to infertility. The relationship of male infertility with cigarette smoking is controversial. There are conflicting reports from studies, some showing an increased
risk of infertility (Wentz, 1986) and others showing no adverse effects from smoking (Vogt, Heller and Borelli, 1986).

Emotional experiences and infertility

Infertility is a major life crisis for most couples. People usually assume that they are fertile and when they want to conceive, they will be able to. The emotional experience passes through several phases, beginning with disbelief and denial, moving into frustration and, only after a considerable time, to acceptance (Jones and Toner, 1993). The physician who sees couples with infertility needs to communicate to them an awareness of their emotional crisis. It is difficult to ascertain from the literature what couples’ expectations are, but from our own experience at Monash IVF, we find them to be extremely high. With constant media coverage of medical ‘miracles’ – test tube babies – most couples expect instant success. It is important that the treating physician, in conjunction with a specially trained counsellor, goes through both the positive aspects of assisted reproductive technology as well as some of the negative aspects with which each couple may have to deal.

Couples will feel pressure, frustration, and often loneliness as their friends begin to have children. They feel that they are failures. They become tired, feel shocked and dismayed. Issues in the household often take on a greater importance than they would in ‘normal’ circumstances when couples are not under this stress. Couples may also feel a loss of control, particularly when enrolled in an in-vitro fertilization (IVF) programme. With time and counselling, a number of these hurdles can be overcome. Couples become more realistic, they often show a greater ability to empathize with other people’s problems and realize that not every aspect can be controlled (Stens, 1989; Lewis, 1989; Goldman, 1989; Bohm, 1989; Stuart, 1989; Winkler, 1989; Lene, 1989; Oberauer, 1989; Kozolanka, 1989; Domar et al., 1992).

Historical aspects of infertility: A brief overview

The emotional rollercoaster which is associated with infertility has been with us for as long as the problem has existed. The treatment of this problem, however, has changed dramatically over the past 50 years, and many of these changes have culminated in the modern techniques used for assisted reproduction. It has been in the second half of this century that the most dramatic advances in the management of the infertile couple have been made. Even in the 1950s, certain clinicians recognized the contributions that veterinary medicine could make to the field of human reproduction. At this time, there were
four separate areas of progress in the management of infertility. Firstly, the ability to diagnose tubal patency (Rubin, 1950); secondly, the study of spermatozoa, which included the establishment of standards of normal semen analysis, artificial insemination using donated or husband’s sperm and cryopreservation of sperm (Page and Houlding, 1951). The first guidelines were set down for donor insemination, and involved using donors who were syphilis negative, free of disease and whose mental behaviour was of unquestionable normality (Shields, 1950). The third area of progress involved the increase in the state of knowledge regarding sex hormones and, finally, there was an improvement in the methods used to determine the timing of ovulation. The phenomenon of Spinbarkeit was described and was used to determine ovulation and to improve the results of artificial insemination (Cohen, Stein and Kay, 1956). The first wedge resections of polycystic ovaries were described (Stein and Leventhal, 1935; Stein and Cohen, 1939) and gonadotrophins were extracted from a human menopausal era. In the 1970s, artificial insemination using frozen, banked, donor sperm steadily became more widely practised.

In 1951, Hellman described delicate instruments and suture materials to aid in tubal surgery, and these were widely adapted in the 1960s. However, these techniques were not to become successful until the 1970s, when microsurgical techniques were established.

Microsurgical techniques which had initially been developed for the repair of blood vessels, were applied to tubal surgery. Research began into applying these techniques to tubal anastomoses with significant improvements on the previously poor results (Paterson and Wood, 1974; Gomel, 1977). At the same time, laparoscopy was being used for diagnostic purposes, and it was really at this time that the era of minimally invasive surgery began (Smith and Dillon, 1970). All these changes occurred virtually hand-in-hand with the development of IVF, and dramatically lessened the need for tubal reconstructive surgery. The first successful live birth through IVF was reported by Steptoe and Edwards in 1978. At the same time as all of these new reproductive technologies were developing, marked advances were being made in laboratory techniques as radio-immunoassays were developed for human chorionic gonadotrophin (hCG) and luteinizing hormone (LH) as well as oestrogen. Radio-immunoassay to detect prolactin was also developed and the aetiology of the amenorrhoea–galactorrhoea syndrome became clear. It was at this stage that bromocriptine also became available and revolutionized treatment (Jewelewicz and Zimmerman, 1978). Gonadotrophin-releasing hormone (GnRH) was also identified in the early 1970s, and is now one of the most commonly used drugs for ovulation induction and its analogues for ovarian suppression.
In the 1980s, there was a surge in the technological advance for the clinical practice of endocrinology and infertility. During this decade, IVF became a practical and available treatment for infertility. Initially, oocyte retrieval was performed laparoscopically, but this has now been superseded by transvaginal ultrasound guided oocyte pick up. Other techniques such as gamete intrafallopian transfer (GIFT) and IVF using natural cycles were developed and now offer more options to the IVF patient.

The last 50 years of progress in managing the infertile couple have provided options where no treatment would have been available in the past. The development of procedures, techniques, drugs and laboratory assays which has occurred during this time has laid the foundation for modern fertility management. Help can now be offered where none was available before (Chen and Wallach, 1994).

**Conclusion**

Infertility is such a common problem that nearly every general practitioner and gynaecologist will be confronted by it. An understanding of its prevalence and epidemiology, as well as an appreciation of the emotional strain that couples experience during this difficult time, are important. They will not only help with the medical aspects of treatment, but will allow patients to be treated with respect, dignity and kindness through this extremely difficult and stressful period in their lives.

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