

Mental health aspects of women's reproductive health (Organizzazione Mondiale della Sanità, 2009)

Chapter 8

Infertility and assisted reproduction

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Estimating the prevalence of fertility difficulties, infertility or involuntary childlessness is hampered by variations in the definitions of these conditions (Schmidt & Munster, 1995; Kols & Nguyen, 1997). The central difficulty is in defining both the population with compromised fertility and the appropriate comparison population. The former may be conceptualized as either individuals or couples who are unable to conceive after a specified period of regular unprotected sexual intercourse or those seeking medical assistance in order to conceive. The specified time of trying to conceive has varied from 12 months to more than 24 months. Some studies have included people with primary infertility (the inability to conceive at all), secondary infertility (those who have at least one living child but are unable to conceive again), and sub-fecundity (the capacity to conceive but not to sustain a pregnancy to term). The comparison populations have sometimes included those who have never tried to conceive and large groups of young women who may not yet have tried to conceive.

The definition of infertility has a significant impact on clinical outcomes, including those reported in research studies. Definitions vary in terms of whether the condition is identified by self-report, or based on a life calendar of reproductive events, a physician consultation or a physician diagnosis. Infertility can be regarded as a heterogeneous group of health problems, influenced by a range of risk factors (Marchbanks et al., 1989).

It has been estimated, on the basis of investigations in several clinical services, that 8–12% of women in North America are unable to conceive spontaneously (Beral et al., 1994). Postal surveys of a national sample in Australia suggest that the equivalent figure there is 15% (Australian Bureau of Statistics, 2004). Kols & Nguyen (1997) summarized the available estimates of infertility in developing countries, and found wide variations, e.g. 11–20% in sub-Saharan Africa and 14–32% in Namibia. There have been relatively few population-based investigations of the prevalence of fertility difficulties in developing countries. While this reflects local research capacity, it is also argued that it reflects predominant concerns about overpopulation and the costs of unrestrained fertility in these areas (Inhorn & Buss, 1994). Most women with infertility live in the developing world, and have limited access to diagnostic tests or treatment and, often, no access to assisted reproductive technologies (Fathalla, 1992; Vayena, Rowe & Griffin, 2002).

A population survey in Gambia, using randomly selected census areas, found that primary infertility was relatively uncommon (3%), but secondary infertility following the birth of at least one child was more common (6%) (Sundby, Mbogge & Sonko, 1998). Half of those

affected had not sought treatment and both investigative testing and treatment were limited. Larsen (2000) used linked population census data, which included childbirth history, to examine infertility in 28 African countries. Primary infertility was assumed in those who had been married for at least seven years without having a child, and secondary infertility in those aged 20–44 years whose most recent birth was more than five years ago. Primary infertility was low (less than 3% in the countries surveyed), but there was a wide range in secondary infertility (5–23%). In a survey using random sampling in a rural community in Nigeria, the prevalence of primary infertility was 9.2% and of secondary infertility 21.1% (Adetoro & Ebomoyi, 1991). In a single survey of one urban region in Viet Nam, 5.7% of couples were reported to be infertile (Thwaites, 2002). In countries where treatment for reproductive tract infections is not widely available, more than 30% of women develop secondary infertility caused by tubal occlusion resulting from infection (Vayena, Rowe & Peterson, 2002).

In reviewing prevalence surveys, Schmidt & Munster (1995) found that current and lifetime prevalence of infertility ranged from 3.6% to 32.6%. They concluded that, overall, about 24% of the global population experiences either primary or secondary infertility, and that about 15% of the population of reproductive age will seek medical assistance to conceive.

Causes of infertility

Male and female factors are each believed to account for 40% of cases of infertility; the remaining 20% are either unexplained – so-called idiopathic infertility – or of shared etiology. In women, the most common causes of fertility difficulties are obstructed fallopian tubes and ovulation dysfunction, while in men low sperm viability and dysfunction of sperm motility are most common (Johnson & Everitt, 2000). It has been suggested that 5% of infertility is caused by constitutional problems, including genetic conditions, anatomical defects, and endocrinological or immunological dysfunction (Kols & Nguyen, 1997). The balance is attributable to infection, unhygienic health care practices, particularly in obstetrics, and exposure to environmental toxins. Reproductive tract infections, especially sexually transmitted infections, are the predominant cause of infertility, leading to the formation of scar tissue which obstructs the fallopian tubes (Kols & Nguyen, 1997). In a case control study of 60 women with infertility and 53 matched controls in Ile-Ife, Nigeria (Okonofua et al., 1997), the infertile group had higher rates of *Neisseria gonorrhoeae* antibodies and of a history of other sexually transmitted infections than the controls. Infections secondary to abortion or childbirth are also implicated (Kols & Nguyen, 1997; Sundby, Mboge & Sonko, 1998).

In a comparison of consecutive women presenting with fertility problems and female hospital workers in Nigeria, Aghanwa et al. (1999) found that the patients were significantly more likely to be married to polygamous men and to have had an abortion. It has also been suggested that inappropriate treatment of undiagnosed conditions, including curettage in Gambia (Sundby, Mboge & Sonko, 1998) and cervical electrocauterization in Egypt (Inhorn & Buss, 1994) may contribute to infertility. Female fertility may be reduced following genital mutilation, as a result of chronic pelvic infections leading to obstruction of the fallopian tubes, or because narrowing of the introitus may lead to the anus or urethra being used for intercourse (Ng, 2000). Normal vaginal intercourse may be impossible if the introitus is narrowed through infibulation (Okonofua et al., 2002). Female genital schistosomiasis, which is common in sub-Saharan Africa, leads to granulomatous inflammation of the cervix and increases the likelihood of other reproductive tract infections (Poggensee et al., 2001; Poggensee & Feldmeier, 2001). Infectious causes appear to be

less common in male factor infertility, but parasitic infections (including schistosomiasis, which damages the male genital tract) have been implicated in some countries (Kols & Nguyen, 1997). In developing countries, occupational exposure, for example to heavy metals, biological metabolites, pesticides and heat, may also contribute to infertility (Inhorn & Buss, 1994; Kols & Nguyen, 1997). The assessment of male factors is limited because many men refuse to participate in studies, which may mean that cause is misattributed (Aghanwa et al., 1999).

In groups with limited education, poor access to services or little general knowledge of physiological functioning, superstitious attribution is common. Anthropological investigations of women in Botswana (Upton, 2001), southern Nigeria (Koster-Oyekan, 1999) and Mozambique (Mariano, 2004), using in-depth interviews and field observations, concluded that women are usually regarded as responsible for infertility. In these investigations, infertility was attributed to: transgression of sexual taboos or rituals relating to burial of a dead child; supernatural factors, including witchcraft or a curse by ancestors or deities; and prior abortions or use of orthodox contraceptives (Koster-Oyekan, 1999; Upton, 2001). Egyptian women of low socioeconomic status living in rural areas, who cannot conceive, are regarded as having been subjected to *kabsa*, or the constraint of reproductive capacity by exposure to contaminated individuals (Inhorn, 1994). Upton (2001) and Mariano (2004) identified a contemporary paradox in some African countries, where men in poor rural communities migrate to urban areas to work and are absent for prolonged periods, but their wives are still expected to have children and are responsible when this does not occur. People who cannot have children may be stigmatized and socially marginalized in strongly pro-natal settings. Infertility exerts a significant adverse effect on the mental health of couples who want to have children.

Psychological causation of infertility?

There has been a long-standing belief that female infertility, particularly of unknown etiology, is attributable to psychological factors – so-called “psychogenic infertility”. This has commonly been defined as fertility difficulties for which no organic cause can be identified and in which psychological mechanisms are assumed to be operating. Studies have attempted to find personality or psychiatric factors that would explain infertility. Almost all have focused on women, and most have made retrospective attribution of the observed differences between fertile and infertile women (usually those seeking treatment) to pre-existing factors. The issues proposed as etiologically involved have included uncertain gender identity, external locus of control, infertility as a defence against inner conflicts, ambivalence about having children, psychiatric symptoms, in particular, depression and anxiety, marital problems “masquerading as infertility” and sexual dysfunction (Callan & Hennessey, 1988b; Moller & Fallstrom, 1991; Greil, 1997).

There have been no population-based prospective studies that have followed women from adolescence and investigated pre-existing psychological differences between fertile and infertile groups. However, a number of cohort comparison studies have used more adequate methodology, including systematic sampling, adequate sample size and standardized measures. These studies have found no significant difference in rates of psychiatric illness, other psychopathology or personality factors between presumed fertile groups and those seeking infertility treatment, or between infertile groups and population norms, or between groups with infertility of different origin and duration (Edelmann et al., 1991; Downey & McKinney, 1992; Visser et al., 1994). It has been argued that women who seek treatment may be psychologically robust and not representative of the population with fertility difficulties, but this assertion has not been tested (Eugster & Vingerhoest,

1999). The observed differences in mood and self-regard between fertile and infertile groups are more accurately regarded as secondary to the infertility, rather than etiologically involved (Edelmann et al., 1991; Downey & McKinney, 1992; Eugster & Vingerhoest, 1999). As understanding of the complex physiology and biology of reproduction has grown over the past three decades, the proportion of infertility attributed to unexplained origins has decreased from about 50% of cases to between 5% and 15% (Moller & Fallstrom, 1991). One of the criticisms of efforts to ascribe infertility to psychological factors is that they have led to misattribution of responsibility and “blaming” of victims, especially women; little research has investigated this hypothesis in recent years. While agreeing with this view, some authors have argued that certain psychiatric illnesses and behaviours make individuals more vulnerable to infertility and that these should continue to be investigated (Rosenthal & Goldfarb, 1997).

In particular, the severe weight loss associated with the eating disorder, anorexia nervosa, can lead to suppression of ovulation; cigarette smoking, and alcohol and drug use, can also lead to decreased fertility. Sexual difficulties, especially erectile dysfunction and vaginismus, can impair the completion of intercourse (Rosenthal & Goldfarb, 1997). The links between behavioural factors and fertility pathology were examined in a substantial epidemiological study, which found that, while there were few differences between fertile and infertile women, tubal obstruction was associated with a higher incidence of previous sexually transmitted disease. Women with this condition had a lower age of sexual debut and more sexual partners, were more likely to have used an intrauterine contraceptive device, and were less likely to have used condoms than those with other fertility difficulties (Beral et al., 1994). The study also found that obesity was associated with polycystic ovarian disease (Beral et al., 1994). The contribution to fertility difficulties of a delay in the age of marriage and reproduction has been identified as a concern in many industrialized countries, but the complex social and economic factors involved are not well understood (Rosenthal & Goldfarb, 1997).

Psychological impact of infertility

By definition, infertility can be identified only when it has lasted at least a year. The experience and eventual diagnostic confirmation of infertility can have a profound psychological impact (Menning, 1982), which has been conceptualized and assessed in different ways.

Psychiatric illness or normal psychological reaction to an abnormal circumstance?

There is debate about whether the psychological disturbance observable in people with infertility is more accurately conceptualized as a psychiatric illness or as an intense psychological reaction to abnormal personal circumstances. High rates of clinically significant symptoms of depression and anxiety have been reported in surveys of cohorts of women and, to a lesser extent, men seeking fertility treatment (Beaurepaire et al., 1994). More than 20% of women attending an infertility support group reported that they had experienced episodic suicidal ideation (Kerr, Brown & Balen, 1999). However, the labelling of these conditions as psychiatric illness has been criticized, because psychiatric symptom checklists include somatic symptoms (e.g. “Something is wrong with my body...”) that are normal among those with infertility. As psychological state is dynamic following diagnosis and during treatment for infertility, it has been argued that a syndrome approach to conceptualization is inaccurate and that a psychological profile, along which individuals are ranged, would be more accurate (Berg & Wilson, 1990). Unlike other adverse life

events, which may have a clear resolution, infertility is regarded as uniquely stressful because it can last for many years and for many will not be resolved (Berg & Wilson, 1990). Berg & Wilson (1990) have identified an infertility strain profile, characterized by increased anxiety, irritability, profound sadness, self-blame, lowered energy levels, social isolation and heightened interpersonal sensitivity. Almost all women presenting for treatment have been found to demonstrate some of these features (Berg & Wilson, 1990).

Two approaches have been taken to describing the psychological sequelae of infertility (Greil, 1997). The first is qualitative investigation and clinical description of the experiential responses to infertility. In this approach, infertility is described as a profound life crisis or existential blow and a number of common themes are identified (Menning, 1982; Mahlstedt, 1985). Guilt is prominent among women, together with fears that earlier sexual experiences, the use of contraceptives, or delaying procreation while pursuing professional goals has compromised fertility (Mahlstedt, 1985). Other less rational beliefs – of being punished for past misdeeds or of intrinsic unworthiness – have also been reported, particularly if infertility is of unexplained origin. The frustration associated with being unable to control conception and physiological functioning commonly leads to feelings of anger (Becker, 1994). This may be directed towards a number of people, including the infertile partner, friends and associates who have been able to conceive easily, and people who offer unsolicited advice (Mahlstedt, 1985).

Reaction to infertility is also conceptualized as grief, including for many intangible or disenfranchised losses (Menning, 1982). The losses include: the experiences of pregnancy, childbirth and breastfeeding; the children and grandchildren who will not exist; a generation and genetic continuity; the state of parenthood and the activities and relationships it entails; and an element of adult and gender identity which will never be realized and is substituted with a flawed infertile identity (Menning, 1982; Olshansky, 1987; Dunnington & Glazer, 1991; Nachtigall, Becker & Wizny, 1992). In addition, individuals may fear losing significant relationships, in particular with the partner, physical attractiveness, or a positive sexual relationship (Mahlstedt, 1985; Nachtigall, Becker & Wizny, 1992). Some may offer to allow their spouse to partner someone else in order to have a child. Fertility difficulties can exert a pervasive negative effect on quality of life, compromising planning and commitment to other life activities. The effect is observable in both men and women, but more so in women (Abbey, Andrews & Halman, 1992).

Quantitative investigations have used psychometric measures, standardized in general populations, to examine whether the incidence of particular symptoms or syndromes is different in infertile and presumed fertile populations (Greil, 1997). This approach has two potential limitations. First, standardized measures of psychological dysfunction may not be sufficiently sensitive to capture the complexities of the infertility experience (Greil, 1997). Second, the group of women who experience infertility is heterogeneous, in both gynaecological and socioeconomic terms, and it is unlikely that any control or comparison group can be matched in these terms and in length of time to conceive (Hearn et al., 1987). Despite these limitations, there has been substantial research comparing infertile women and couples with presumed fertile controls or already pregnant women. Perhaps because of the limitations, the findings are inconsistent.

Significantly higher levels of depressive symptoms have been found among women seeking treatment for infertility than in presumed fertile controls (Bernstein, Potts & Mattox, 1985; Berg & Wilson, 1990; Domar et al., 1992; Beaurepaire et al., 1994). However, other investigators have reported no significant differences in levels of depression between infertile and comparison groups (Connolly et al., 1992; Downey & McKinney, 1992; Hynes et al., 1992). It has been suggested that there are, nevertheless, differences in distress

between the two groups, but that the severity of this distress is not clinically significant (Greil, 1997). This is supported by the findings of significantly more nonspecific emotional distress (Moller & Fallstrom, 1991) and less life satisfaction and happiness (Callan & Hennessey, 1988b) in infertile populations. More severe depression is associated with increasing age and being childless (Morrow, Thoreson & Penney, 1995). The findings regarding anxiety are similar, with some studies finding significantly higher levels among infertile groups (Beaurepaire et al., 1994; Visser et al., 1994), and others finding no differences from controls (Connolly et al., 1992).

However, Connolly et al. (1992) acknowledge that individuals have differing degrees of dispositional anxiety and that these may lead to varying anxious responses to infertility. Lower levels of self-esteem and self-regard have been reported, although the differences remain within a normal range (Callan & Hennessey, 1988b; Edelman et al., 1991; Hynes et al., 1992; Nachtigall, Becker & Wizny, 1992; Beaurepaire et al., 1994). Similarly, heightened guilt and self-blame are common, but not pathological (Bernstein, Potts & Mattox, 1985; Morrow, Thoreson & Penney, 1995).

There have been few systematic studies of the psychological impact of infertility in developing countries, and relatively little is known about the psychological functioning of women with fertility difficulties in these settings. This situation has been described as reflecting the eurocentric focus of most research in this field (Inhorn & Buss, 1994). In a single study, Aghanwa, Dare & Ogunniyi, (1999) reported that 29.7% of infertile patients in Nigeria were depressed or had an anxiety disorder, compared with 2.7% of fertile non matched hospital staff controls.

It has been suggested that in highly pro-natalist societies, where women may have few occupational choices and motherhood is the only identifier of adult status, infertility is highly stigmatizing (Inhorn, 2003; Koster-Oyekan, 1999; Mariano, 2004; Upton, 2001). The inability to have children damages both cultural and adult identity, and the attribution of responsibility leads to social rejection and marginalization. Infertile women may have their gender identity questioned, experience social exclusion, be suspected of having evil potential and be subject to harassment, especially from their in-laws (Koster-Oyekan, 1999; Upton, 2001). In settings where women are subordinated, they are highly likely to be blamed for infertility (Mariano, 2004). They may be divorced because of their failure to bear children, which itself is highly stigmatizing, or their husband may marry a second wife (Koster-Oyekan, 1999; Mariano, 2004; Upton, 2001). Divorced and childless women are highly vulnerable when old, because adult children are the usual primary supporters of older people. Given the very limited access to assisted reproductive treatments in these settings, infertility has been described as leading to profound human suffering (Inhorn, 2003). Upton (2001) has argued that the presumption that infertility is rare in countries with high fertility rates, and the inaccurate understanding of its determinants, have led to the condition being "invisible" to policy-makers. As a result, there has been insufficient consideration of the psychological and social costs to women of infertility in these contexts.

Gender differences in the psychological sequelae of infertility

Although infertility exerts adverse psychological effects on both men and women, there is evidence that they react differently (Abbey, Andrews 133 & Halman, 1991; Nachtigall, Becker & Wizny, 1992; Cook, 1993). Women have been found to experience more emotional distress and depressive symptoms associated with infertility than men, except in cases of male factor infertility where the degree of distress is similar (Nachtigall, Becker & Wizny, 1992; Beaurepaire, et al., 1994; Morrow, Thoreson & Penney, 1995). Similarly, there are adverse effects on the gender identity of all women with infertility regardless of

the etiological factor; but male gender identity is adversely affected only by male factors (Nachtigall, Becker & Wizny, 1992). Even when male factors are implicated, women experience more guilt and self-blame than their male partners (Abbey, Andrews & Halman, 1991). This may be because, even when male factors are involved, most of the investigation and treatments focus on the female partner. Women's lives are more disrupted by infertility than men's (Abbey, Andrews & Halman, 1991). It also appears that the loss of sex role identity and the experiences of childbirth and parenthood is more profound for women than for men (Abbey, Andrews & Halman, 1991; Nachtigall, Becker & Wizny, 1992; Cook, 1993). Both men and women are more likely to believe that the woman is responsible if unexplained or combined factors are etiologically involved (Abbey, Andrews & Halman, 1991). Men are more likely than women to experience infertility as a sign of compromised potency and sexual adequacy (Nachtigall, Becker & Wizny, 1992). Individuals respond to disturbing life events in different ways. Women who are able to take an active part in seeking information and making decisions about treatment have lower levels of depression and attract more social support than those who passively submit to medical recommendations (Woods, Olshansky & Draye, 1991). Individuals with high self-esteem and dispositional optimism are better protected against severe depression (Litt et al., 1992). Denial and avoidance are elements of a normal response to adverse experiences, including infertility (Menning, 1982). Some individuals may appear to be more persistently unaffected emotionally by the diagnosis of infertility, but denial is not an effective defence against severe emotional distress. Individuals who use avoidant coping and deny the emotional impact of infertility may seek multiple medical opinions, in order to find an optimistic assessment. They are at higher risk of becoming depressed and may also be vulnerable to exploitation by extravagant claims for treatments, including those for which there is scant scientific evidence (Woods, Olshansky & Draye, 1991; Litt et al., 1992; Morrow, Thoreson & Penney, 1995).

Impact of infertility and infertility treatment on the marital relationship

Infertility can exert adverse effects on the emotional and sexual relationship between partners (Andrews, Abbey & Halman, 1992; Greil, 1997; Eugster & Vingerhoest, 1999; Hart, 2002). Guilt and inexpressible blame can have insidious effects on intimacy. The infertile partner may fear rejection or may feel obliged to offer the other a divorce so that he or she can achieve genetic parenthood with someone else (Hart, 2002). The expression of anger and frustration about the predicament may be constrained in order to protect the infertile partner (Hart, 2002). Sexual spontaneity can be impaired by the need for sexual intercourse to be carefully timed and by the clinical scrutiny to which the relationship is subjected. Both partners may experience emotional pain seeing other couples with children (Hart, 2002). However, systematic psychometric investigations have revealed few differences in quality of marital relationship between infertile and comparison groups. Rather they suggest that marital intimacy and cohesion can be strengthened and enhanced through confronting the experience of infertility together (Dennerstein & Morse, 1988; Berg & Wilson, 1991; Greil, 1997).

Psychological aspects of treatment of infertility using assisted reproductive technology

Psychological sequelae of diagnosis and treatment

In the past 25 years, technologies to treat both male and female infertility have developed rapidly. In industrialized countries with well developed infertility treatment services, it is

estimated that more than 60% of couples with fertility difficulties will seek treatment (Dawson, 1994).

Although the need for assisted reproductive technologies in poor countries is high, the public provision of these highly sophisticated services has to be weighed against the competing demands of major infectious and chronic disease burdens, and limited obstetric and perinatal health services (Vayena, Rowe & Griffin, 2002; WHO, 2003). Private infertility treatment services are 134 being established in many poor countries, but are likely to be accessible and available only to socioeconomically advantaged groups (Vayena, Rowe & Peterson, 2002; WHO, 2003). Teaching hospitals in some developing countries are starting to offer public infertility treatment services (Vayena, Rowe & Griffin, 2002). Overall, the situation in developing countries varies considerably, in terms of availability of appropriately trained health professionals and essential laboratory services, and it is not possible to generalize (Vayena, Rowe & Griffin, 2002).

Rates of pregnancy and live births following assisted conception depend on the experience of the treating centre (Eugster & Vingerhoest, 1999). While rates continue to improve, on average only 20% of couples conceive at each embryo transfer cycle (Kovacs, MacLachlan & Brehny, 2001). Using life-table calculations to review 4225 couples who had undergone 8207 cycles over six years, Kovacs, MacLachlan & Brehny (2001) reported that half the women became pregnant within three cycles and two-thirds became pregnant over six cycles. There is a theoretical debate about whether infertility should be considered a disease that requires medical treatment or an unfortunate life circumstance on which public resources should not be spent. Bewley (1995) argues that the physical and mental health risks of treating an individual, in whom the expected successful outcome of a living child is low, may outweigh the benefits. Others have suggested that the availability of assisted reproductive technologies means that both patients and clinicians try to seek a cure for the condition, rather than exploring other means of establishing a fulfilling life (Becker & Nachtigall, 1994). Critics assert that women are coerced into participating in and persisting with treatment, rather than making a free choice (Shattuck & Schwarz, 1991).

There is now substantial evidence that the nature and intensity of emotional distress vary over the course of infertility treatment. At diagnosis, symptoms of acute distress may increase; there then appears to be a decrease in symptoms once treatment starts (Beaurepaire et al., 1994). Severity of depression at this stage has been linked to having a confirmed diagnosis and a history of surgery for investigation or treatment of infertility (Domar et al., 1992). The initiation of treatment arouses optimism that the condition may be alleviated. However, there is evidence that women hold unrealistically high expectations at this stage of the likely success of treatment (Callan & Hennessey, 1988a; Beaurepaire et al., 1994; Hammarberg, Astbury & Baker, 2001). Injections, scans, blood tests and waiting to know whether eggs have been fertilized are all regarded as more psychologically than physically demanding (Callan & Hennessey, 1988a; Hammarberg, Astbury & Baker, 2001). There is consistent evidence that the moment of embryo transfer arouses optimism, but that the interval between transfer and pregnancy testing to confirm whether implantation and conception have occurred is highly anxiety arousing (Callan & Hennessey, 1988a; Yong, Martin & Thong, 2000; Franco et al., 2002). The onset of menstruation or a negative pregnancy test leads to intense sadness, despair and a sense of lost control (Litt et al., 1992; Franco et al., 2002). Dispositional optimism and active coping are protective against depression following implantation failure; women who use avoidant coping are generally more distressed (Litt et al., 1992).

Repeated unsuccessful treatment cycles can erode the increase in confidence and hope that comes at the start of treatment. It has been shown that, after two years of

unsuccessful treatment, distress returns to a higher level than before treatment and can develop into chronic and severe depression (Berg & Wilson, 1990; Domar et al., 1992). Optimism gradually diminishes over repeated cycles and few couples persist for more than six (Callan & Hennessey, 1988a; Kovacs, MacLachlan & Brehny, 2001). Making the decision to stop fertility treatment is not straightforward, as there is no clear terminal point if conception has not yet occurred (Covington, 1995). Among other factors, the decision not to attempt another treatment cycle is strongly influenced by social forces, including the opinions of family members and friends (Callan et al., 1988). One qualitative study suggested that a state of dissociation between the physical treatment and its psychological consequences is necessary in order for couples to persist with repeat cycles (Benjamin & Ha'elyon, 2002). The authors argued that this is a response to the violation of privacy and time that diagnosis and treatment involve, and that once this detachment cannot be sustained, individuals cease treatment.

In many settings, the costs of infertility treatment are not subsidized by the state and fall on the individual. This can add substantially to the burden of emotional distress, and have a marked effect on decision-making about persistence with treatment; couples have to weigh the financial costs of diagnostic tests and treatment cycles against their yearning for a child (Abbey, Halman & Andrews, 1992; Franco et al., 2002). It has been asserted that couples cannot make a fully informed choice about participation in infertility treatment, because the risks of procedures (including ovarian hyperstimulation and multiple gestations), the economic costs, the limited success rates, and the possible adverse health effects on women and their offspring are generally understated (Pfeffer, 1991; Collins, 1994). Some support for this view has been provided by evidence that, after prolonged infertility, multiple gestations can be idealized and the associated hazards underestimated (Franco et al., 2002). Couples may actively seek a multiple birth in order to create an instant family (Leiblum, Kemmann & Taska, 1990; Gleicher et al., 1995; Goldfarb et al., 1996). Although couples may have significant fears about fetal well-being and doubts about their own capacity to care for more than one infant, they can feel prohibited from expressing this ambivalence because they consented to the transfer of multiple embryos (Leiblum, Kemmann & Taska, 1990; Gleicher et al., 1995; Goldfarb et al., 1996).

Psychological components of treatment

It has been cogently argued that, given the intensity and severity of distress that can be apparent during treatment, infertility clinicians need to have both medical and psychological skills (Covington, 1995). The promotion of optimism and personal control during treatment reduces psychological distress (Abbey, Halman & Andrews, 1992). As irritability, anxiety and depressive symptoms are most intense during the period between embryo transfer and pregnancy-testing, it has been argued that supportive counselling should be available at this time (Yong, Martin & Thong, 2000).

General social support has been found to have a more positive effect on women's distress than on men's (Abbey, Halman & Andrews, 1992). There have been a number of attempts to relieve the psychological distress of infertility and to examine whether this can increase conception rates. Individual, couple and group therapy approaches have been tried (Hart, 2002). A behavioural group treatment approach, including relaxation training, cognitive therapy, exercise and nutritional counselling, reduced psychological symptoms in women, 34% of whom conceived; however, there was no untreated comparison group (Domar, Seibel & Benson, 1990; Domar, 1994). This psychological improvement was replicated in a subsequent study, (Domar et al., 1992b) but the group did not include women with severe psychological dysfunction. Having a peer counsellor who had experienced

infertility, as well as a group leader, was found to be beneficial (Domar, Seibel & Benson, 1990). Fewer men than women want to participate in self-help support groups, although participation has been shown to provide emotional support and practical information and to reduce social isolation. Men who attended such groups to support their wives ultimately found them personally helpful (Lentner & Glazer, 1991).

Termination of infertility treatment

Not all couples with fertility difficulties will conceive following infertility treatment; significant proportions have to adjust to life without a biological offspring. Long-term follow-up studies have examined women's views about, and recollections of, the experience of infertility treatment. Combining a survey of past patients at a hospital in Oslo, Norway with a medical record audit, Sundby, Olsen & Schei (1994) showed that most women had experienced discontinuity of treatment in the public sector, seeing different doctors at each consultation. One-third had stopped treatment without its being formally documented. Those who had a child were satisfied with their treatment, but less than half who did not conceive were satisfied. Independent of whether a child had been born, 70% were dissatisfied with the emotional support that had been provided by health staff (Sundby, Olsen & Schei, 1994). A follow-up study six years after cessation of treatment found that it was recalled as a traumatic life event. Overall, long-term psychological functioning was in the normal range, with greater well-being among those with a child compared with those without a child. Those with a hostile marital relationship, preexisting psychiatric illness, or low level of education were more vulnerable in the long term. The authors commented that people undergoing infertility treatment should be encouraged, and counselled that psychological stability will eventually be restored and that adoption is often a satisfactory outcome (Sundby, 1992). Similarly, fewer than half the women in a study in Finland were satisfied with their infertility treatment. Dissatisfaction was higher among older women who had not conceived, and the doctor's capacity for empathy and kindness was central to satisfaction (Malin et al., 2001). In an Australian study of 116 women, 2–3 years after ceasing infertility treatment, Hammarberg et al. (2001) found that women who had not conceived were less satisfied with the treatment and clinical care and with their life than those who had a baby.

Psychological aspects of pregnancy, childbirth and the postpartum period after assisted conception

In recent years, the number of children born as a result of assisted reproduction has been increasing. In Australia, for example, 2.5% of live births now follow assisted conception (Waters, Dean & Sullivan, 2006). Pregnancies that have been assisted in this way carry higher risks for both mother and infant. These include increased risk of antepartum haemorrhage, multiple gestation, pregnancy hypertension, caesarean delivery, premature birth, low or very low birth weight, and the infant requiring oxygen at birth (Tallo et al., 1995; Wang et al., 1994; Waters et al., 2006). However, these risks are predominantly those associated with pregnancy at an advanced maternal age and multiple gestations (Olivennes et al., 1993). Many pregnancies following assisted conception are regarded as high risk (Dulude et al., 2002).

Pregnancy

Multiple gestations are more likely following induction of ovulation, or after the transfer of multiple embryos (McKinney & Leary, 1999). Multiple gestations are usually diagnosed

very early after assisted conception, and parents may not think about the possibility of losing one fetus. Grief in those who have a single baby after having lost another fetus during the pregnancy is intense, but can be unrecognized by both health professionals and friends (Kollantai & Fleischer, 2001; Swanson, Pearsall-Jones & Hay, 2002; Fisher & Stocky, 2003). The coincidence of bereavement and pregnancy presents a psychological paradox, which is not easily resolved and may lead to delayed or disturbed grief reactions or disrupt the mother–infant attachment (Bryan & Denton, 2001; Pector & Smith-Levitin, 2002).

Very little is known about the long-term psychological consequences of what is termed planned fetal reduction or selective abortion of one or more fetuses in multiple pregnancy. In a study comparing 42 women who had undergone fetal reduction with women who had conceived a singleton pregnancy after in vitro fertilization (IVF), the rates of depression were equal in those who ultimately had a baby, but was high in those from either group who miscarried the pregnancy. However, many described fetal reduction as extremely stressful, 98% experienced anxiety, 69% sadness and 57% guilt as a result of the procedure. Grief, mourning and underlying feelings of shame were apparent in most (McKinney & Leary, 1999). Perhaps reflecting this, fetal reduction is rarely widely disclosed and may be kept secret. However, it is known that keeping secrets harms family relationships through fear of discovery and mistrust (Covington & Burns, 1999; Bryan, 2002).

Qualitative investigations have reported complicated grief reactions in which multiple disenfranchised losses are experienced (Collopy, 2002). The potential impact on the living infant remains unknown, but the possibility of a “survivor syndrome”, characterized by guilt, perplexity and grief for a lost sibling, has been suggested (Bryan & Denton, 2001; Fisher & Stocky, 2003).

Pregnancies in which a heightened risk to maternal or fetal health is identified are more psychologically distressing (Dulude et al., 2002).

Women who become pregnant following assisted conception have been described as: having heightened anxiety about pregnancy loss and infant health, less self-confidence, and greater difficulty in acknowledging ambivalence, anxiety or sadness; using avoidant coping; becoming hypervigilant; feeling unable to complain or seek support and denying the pregnant state as self-protection against loss (Dunnington & Glazer, 1991; Bernstein, Lewis & Seibel, 1994; van Balen, Naaktgeboren & Trimbos-Kemper, 1996; Covington & Burns, 1999; Eugster & Vingerhoest, 1999; McMahan, 1999; Hjelmstedt et al., 2003). Concern about fetal development is high even in women whose pregnancies are known to be low-risk (Reading, Chang & Kerin, 1989; Gibson et al., 2000b) and preparation of a home environment for the baby is delayed (Dunnington & Glazer, 1991; Bernstein, Lewis & Seibel, 1994). The universal psychological challenge of pregnancy is to form a maternal identity, and this process appears to be more problematic in women who have a history of infertility. The relinquishing of an infertile identity and the adoption of a fertile and maternal one have to happen rapidly, but may in reality be complicated and prolonged (Covington & Burns, 1999; McMahan, 1999). Motherhood following infertility has usually been idealized and the losses and adverse experiences it inevitably entails may be unexpected (Covington & Burns, 1999; McMahan, 1999). Although women report increased anxiety about intrapartum damage to the baby, they have often underestimated the potential risks of childbirth to themselves (Connolly et al., 1992; McMahan, 1999). In contrast, two studies reported no differences in anxiety or depressive symptoms measured with standardized instruments between women who had conceived spontaneously and those who had conceived after IVF (Stanton & Golombok, 1993; Klock & Greenfield, 2000). None of the

studies controlled for the particular effects of multiple gestation, and most studies excluded multiple gestations and women who already had a child.

No differences in the intensity or quality of self-reported maternal-fetal emotional attachment have been reported, although women anticipated that their infants might have more difficulties than those conceived spontaneously. In a single longitudinal study, anxiety was reported to decrease more as pregnancy progressed in those who had had assisted conception than in those who had conceived spontaneously (Stanton & Golombok, 1993; McMahan, 1999; Klock & Greenfield, 2000). It has been suggested that women may need additional support and sensitized care in pregnancy after assisted conception (McMahan et al. 1995; McMahan, 1999; Hjelmstedt et al., 2003).

Childbirth

Although women are at greatly elevated risk of caesarean birth after assisted conception (Wang et al., 1994), there has been little investigation of the interactions between these two procedures. There is consistent evidence that both instrumental intervention in vaginal birth and caesarean surgery are associated with increased anxiety, disappointment, grief and dissatisfaction (Boyce & Todd, 1992; Fisher, Astbury & Smith, 1997). Although mode of delivery does not appear to make an independent contribution to postpartum depression when other risk factors are taken into account (Johnstone et al., 2001), caesarean surgery can induce post-traumatic stress reactions (Fisher, Astbury & Smith, 1997). After caesarean childbirth, the first encounter between mother and infant and the initiation of breastfeeding are disrupted, with adverse effects on maternal confidence that are still measurable eight months later (Rowe-Murray & Fisher, 2001, 2002). In one study, childbirth was reported as “more exceptional” after assisted conception, but this descriptor was not defined and is difficult to interpret (van Balen, Naaktgeboren & Trimbos-Kemper, 1996).

Operative delivery and premature birth are both more common among women with multiple gestation, which occurs in 20% of pregnancies after assisted conception (Barrett & Ritchie, 2002). Premature birth typically involves separation of the mother from her infants, sometimes for prolonged periods. Intense anxiety about the infants' health and development and about the separation is universal, and is more severe among those whose infants are seriously unwell; and the anxiety can persist for up to three years (Singer et al., 1999). When babies are kept in neonatal intensive care units, mothers report uncertainty about whether the health professional or the parent has authority over the baby (Bryan & Denton, 2001; Loo et al., 2003). A cooperative approach to decision-making, respecting parental rights, can be helpful (Carter & Leuthner, 2002). Fear about the infants' health and viability can persist and lead to hypervigilance in relation to infant care, and delayed formation of a secure affectionate emotional attachment (Klock, 2001; Loo et al., 2003). No studies have examined the interacting emotional effects of assisted conception, operative birth, prematurity, neonatal hospitalization and multiple birth. However, the established difficulties are further magnified if the infants are separated, for example by discharge of one infant ahead of another or by care in different hospitals (Bryan & Denton, 2001). Maintaining a supply of breastmilk and establishing breastfeeding are difficult and anxiety-arousing with premature and very low-birthweight infants.

Parenthood after infertility and assisted reproduction

Most of the investigations into the long-term impact of assisted conception have focused on women's capacity to mother, the quality of mother-infant attachment and the

developmental outcomes of the children. Few have focused on maternal mental and physical health in itself.

Descriptive and exploratory studies claim that, after assisted conception, mothers are more likely to be overprotective and to recall infertility as an influential negative life event. Burns (1990) concluded that infertility is not transient, continues after conception and may be experienced as long-term adjustment difficulties in the family. Further, parents may be less conscious of the challenges of parenthood and, although the quality of parenting is high, have to make an extraordinary effort to feel effective. Burns (1990) suggested that parents may have formed unrealistic and “utopian fantasies”, which make it difficult for them to adjust to the unique demands and unavoidable ambivalence of parenting. She also suggested that they are particularly likely to have difficulties separating from their infants and with the developmental process of individuation, and may be less able to foster the child’s capacity for self-sufficiency (Burns, 1990, 1999). In Australia, there is an excess (6.3–9% compared with 1.2–1.7% of live births) of mothers who have experienced fertility difficulties or assisted conception among those admitted to residential early parenting services because of infant sleep or feeding disorders and maternal exhaustion or mild to moderate depression (Barnett et al., 1993; Fisher et al., 2002; Fisher, Hammarberg & Baker, 2005). A group of mothers who were members of an infertility support group were found to confide less and have fewer acquaintances and friendships than a comparison group who had conceived spontaneously (Munro, Ironside & Smith, 1992). Mothers who had had assistance to conceive anticipated that their infants would have more problems and rated their infants as having more difficult temperaments than a group of controls (McMahon et al., 1997). In contrast, Golombok et al. (1995) found no adverse psychological consequences and “superior parenting” among children conceived with assisted reproductive technologies. Systematic investigations have used the Strange Situations Test, which assesses the quality of mother–child attachment through videotaped observations of the mother and child, while playing together and when separated from each other. These studies have found no differences in mother–child attachment between children conceived spontaneously or with assistance, and that most mothers were sensitive and responsive to their children (Gibson et al., 2000a). None of these studies included infants conceived by use of donor gametes or multiple births (Fisher & Stocky, 2003). In reviewing the early studies, McMahon et al. (1995) concluded that there was little evidence of differences in quality of parenting between families formed with assisted conception and others, but conceded that most of the available studies had methodological limitations.

There is consistent evidence that the emotional health of mothers of multiple infants is poorer than that of mothers of single infants, and that they are at higher risk of becoming depressed, anxious and clinically exhausted after childbirth. Hay et al. (1990) found that 29.7% of mothers of 3-month-old twins reported depression (a rate five times higher than among mothers of single 3-month-old infants); 42% had high anxiety (three times higher than among mothers of single infants). Even higher rates of depression have been reported among mothers of triplets. Robin et al. (1991) found that 40% were depressed 4 months postpartum, while Garel, Salobir & Blondel (1997) found that all reported significant distress and a quarter were being treated for depression one year postpartum. Two studies of the health and social circumstances of women admitted to Australian residential early parenting services for treatment of unsettled infant behaviour and maternal exhaustion, anxiety and depression found an excess of mothers with multiple infants (3.7–5%, compared with the general population rate of 1.4%) (Barnett et al., 1993; Fisher et al., 2002). In a longitudinal study of more than 13 000 women who gave birth in one month in 1970, Thorpe et al. (1991) found that, five years after the birth, independent

of other explanatory factors, mothers of twins were three times more likely to be depressed than those with a single child. In a small comparative study, higher parenting stress was associated with having twins, regardless of mode of conception (Cook, Bradley & Golombok, 1998). This effect may lessen as the children grow older. In examining 158 sets of twins entering preschool, Munro, Ironside & Smith (1990) found less psychiatric disturbance among mothers of twins conceived by IVF than mothers of spontaneously conceived twins.

New technologies and their implications

Donated fresh sperm has been used to treat male factor infertility for 100 years. The use of cryopreservation to store sperm for later donation is a newer technological development. The donation of embryos and oocytes has become possible more recently, and involves the donor undergoing a stimulated cycle and the surgical removal of oocytes for either transfer, cryopreservation or fertilization with donated sperm (Barrero, 2002). The new technologies now available to treat fertility difficulties may themselves carry sequelae for mental health, but very little evidence is so far available (Kirby, 1994).

Issues arising with use of the new technologies include: the ethical, legal and psychological complexities of the use of donated genetic material; payments to donors for their genetic material; debates about the maintenance of secrecy and disclosure, and the impact of legislation regarding children's rights to know their biological heritage versus parents' rights to secrecy. Gestational surrogacy and the use of donor gametes lead to complex considerations of what constitutes a parent–infant relationship (Kirkman, 1996, 1999;

Barrero, 2002; Vayena, Rowe & Griffin, 2002). Relatively little is known about the motives and psychological functioning of donors, including those who donate genetic material anonymously (Rosenthal, 1998). However, it has been established that, over time, donors may change their minds about remaining anonymous or allowing their identity to be disclosed to offspring (Blyth, Crawshaw & Daniels, 2004). In general, people conceived from donated genetic material want to know their genetic heritage and the identity of the donor, and believe that secrecy is harmful to individuals and to families (Blyth, Crawshaw & Daniels, 2004).

A shortage of donated eggs places significant limitations on treatment in most settings. In order to donate ova, women have to undergo ovarian stimulation and surgical aspiration, and the number willing to do so is limited (Cleland, 1994; Murray et al., 1994). Depending on local legislation, eggs may be donated by someone known to the recipient or by an anonymous donor, voluntarily or in exchange for payment. In some European countries, a strategy termed egg sharing is available, in which women undergoing fertility treatment requiring ovarian stimulation and oocyte retrieval can donate half the resulting ova anonymously to another couple in exchange for reduced fees and rapid access to treatment (Ahuja et al., 2003). Investigation of the psychological implications of donating ova to other women has only recently begun. However, in-depth interviews with small samples in the United Kingdom have found that the decision to participate as a donor in egg sharing schemes is influenced by the waiting time for treatment, costs of treatment, individual perceptions of the donated gametes as “tissue” or as a “potential baby”, and a complex existential notion of altruism combined with a desire to achieve a personal life goal (Rapport, 2003; Blyth, 2004). There is ongoing debate about the ethics of this option, in particular since the evidence in its favour has been generated to a large extent by providers. The short- and long-term psychological and emotional sequelae have not been examined systematically by independent investigators (Ahuja et al, 2003; Blyth, Crawshaw & Daniels, 2004).

There is debate about whether tissues with reproductive potential should be treated differently from those donated post mortem. Consideration is being given to whether cadavers, aborted fetuses or live donors may be the best source of eggs (Murray et al., 1994). In order to investigate attitudes to this theoretical possibility, women attending for pregnancy termination, contraception or infertility treatment were surveyed. In general, there was strong support for methods to increase the supply of donated ova, from all sources, but women having abortions did not in general support post-mortem donation of ova. Neither potential donors nor potential recipients disapproved of the use of fetal ovarian tissue for research (Murray et al., 1994).

There is wide variation internationally regarding record-keeping and access to records following the use of donated genetic material (Kirby, 1994). There is a need for considered public and expert debate regarding a number of issues, e.g. quality control to protect against consanguinity, legal acknowledgment of the social rather than the genetic parent, and the rights of the children and not just the adults exposed to these procedures. The disposal of, and experimentation on, surplus frozen embryos or other genetic material remain controversial (Kirby, 1994). In considering the allocation of health resources, there is debate about whether individuals should bear the cost or whether it is a social cost to be born publicly. The complex economics of the cost-effectiveness of treatment have to be considered (Kirby, 1994; Neumann, Gharib & Weinstein, 1994).

There is also debate about whether treatment should be offered to all who seek it, or whether there should be criteria for inclusion in treatment programmes. The debate regarding the rights of the child is sometimes used to withhold treatment from post-menopausal women, because of the complex ethics relating to being born to parents who may die before the child reached maturity (Hope, Lockwood & Lockwood, 1995). Older women are generally less likely to conceive, and it has been suggested that health professionals who offer fertility treatment to older women are assisting them to act irresponsibly (Jackson, 1995). There is debate about whether these decisions, especially whether women over 50 years of age should be refused treatment, should be made by an ethics committee (who may not know the individual patient) or by a single clinician (Craft, 1995).

The psychological implications of the preservation of tissue to protect fertility in those undergoing chemotherapy are yet to be investigated.

For many women, being a mother is core to the formation of their adult identity, and the availability of technologies means that some will persevere in their efforts to have a child, even to the extent of putting their own health at risk (Kirkman, 1996). Health professionals face significant difficulties in interpreting social and ethical dilemmas in individual cases. Nurses rated the emotional distress associated with infertility treatment as worse than either patients or physicians did, and patients rated it as worse than physicians did. However, all agreed that infertility treatment was one of the most difficult professional fields in which to practise (Kopitzke et al., 1991). Patients' irritability and frustration may be directed at health professionals, who may be perceived as lacking sensitivity and ability to communicate, or blamed for the limitations of existing knowledge and techniques. Covington (1995) stated that, because of the multiple losses, prolonged treatment, complexities in defining the end of treatment, and high failure rate, all professionals in this field need to integrate psychological with medical care.

The psychosocial sequelae of infertility and the complex psychological responses to technologically assisted conception are central to the health of people facing these life experiences, and should be considered in research and clinical services.

Summary

Future research

1. Causes of infertility differ, and in each country an accurate understanding is needed of the fertility problems of the population.
 2. In most countries, the prevalence, etiology and mental health effects of fertility problems have not been established.
 3. Research is needed into the demand for, and nature of, infertility treatment services in developing countries.
 4. The long-term psychological consequences of infertility, including after the birth of a child, should be investigated.
 5. There is a need for data on the short- and long term psychosocial and medical consequences for both donors and recipients of gametes, including women in egg-sharing programmes.
 6. There is a need for long-term comprehensive follow-up of the physical and mental health of offspring of assisted conception, with disaggregation by method of conception.
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7. Multiple pregnancies, which are more common after assisted conception, carry greater psychological hazards. The interaction between infertility and multiple gestations in influencing perinatal mental health should be clarified.
 8. The short- and long-term psychological effects of fetal reduction in multiple-gestation pregnancy need to be systematically investigated.
 9. The potential of psychological treatments to relieve the distress associated with infertility and assisted reproduction should be investigated in randomized controlled trials.

Policy

1. Attention to population control in countries with high fertility rates should not preclude identification and treatment of infertility.
2. The causes of infertility should be accurately ascertained.
3. Specialized diagnostic and treatment services are needed for people with fertility problems.
4. Infertility services need to have clear policies about disclosure of mode of conception, maintenance of donor registries, and protection of the needs of children conceived by assisted reproduction. These policies should be informed by public and professional debate.

Services

1. Infertility treatment services in all settings need to be based on evidence about local causes and best practice in treatment.
2. Infertility treatment services should include mental health care as a component of routine care.
3. Mental health care should be focused on: assisting the person to make a realistic appraisal of the chance of treatment success; providing emotional support in the interval between embryo transfer and pregnancy testing; and assisting the person to make a clear choice about when to stop treatment.

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