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0521643643 - Infertility in the Modern World: Present and Future Prospects - Edited by

Gillian R. Bentley and C. G. Nicholas Mascie-Taylor

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Introduction

G. R. BENTLEY AND C. G. N. MASCIE-TAYLOR

This book illustrates the ways in which human biology and culture can affect fertility and outlines some of the modern technologies that, at least in the Western world, can alleviate the physiological problems associated with infertility. It results from a Biosocial Society Symposium held in Cambridge, U.K. in May 1998. It is organized into three sections, each containing two chapters. The first section (with chapters by co-authors S. Fishel, K. Dowell and S. Thornton as well as A. H. Bittles and P. L. Matson) covers the more technical and clinical aspects of infertility that are primarily relevant to industrialized nations with access to modern technologies and the research capabilities to address (and often ameliorate) specific issues of infertility. The second section (with chapters by G. R. Bentley, and J. C. and P. Caldwell) deals with environmental aspects of infertility, including the consequences of industrial pollution for human fertility, and the effects of sexually transmitted diseases (STDs) in the area of sub-Saharan Africa. Finally, the third section (with chapters by F. McAllister and L. Clarke, as well as C. J. Patterson and L. V. Friel) addresses the social aspects of infertility and the importance of behaviour in determining infertility.

It is impossible to compute the incidence of human infertility as a raw statistic or to reduce it to a simple figure. Infertility varies from country to country and from cohort to cohort, depending on the sample, the population surveyed, whether males are included together with females, and whether these figures include 'social infertility' (such as childlessness by choice) as opposed to physiological infertility. Mirroring such variance are the different figures offered in the chapters here. For example, J. C. and P. Caldwell, using

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data from noncontracepting, healthy populations with couples who married when young, estimate that sterility from physiological causes other than STDs may be as low as 2%, a figure that is matched in other demographic studies from similar populations (e.g. Early and Peters, 1990; Wood, 1994). In contrast, S. Fishel, K. Dowell and S. Thornton estimate the rate of infertility to be 14% among Western populations, although this figure probably includes women who delay conception until they are older, when subfecundity is likely to be high. In addition, 32% of this rate can be attributed to male-factor infertility. A. H. Bittles and P. L. Matson again give rather different figures for Western countries, namely 5–8% for primary infertility, presumably related to physiological causes.

These figures should be contrasted with rates for primary infertility of 30% in areas of sub-Saharan Africa covered by J. C. and P. Caldwell's chapter, where STDs are an important factor determining this figure. G. R. Bentley informs us that many studies indicate a regional decline in sperm quantity that is reported to be as high as 50%, although how this translates into fecundity and fertility remains unclear. Dealing with the issue of 'social infertility', F. McAllister and L. Clarke cite data indicating that approximately 20% of women born in 1975 in the United Kingdom (U.K.) will remain childless by the end of their reproductive lives, compared with only 11% of women born in 1942. C. J. Patterson and L. V. Friel present new data suggesting that up to 86% of gays and 70% of lesbians in the U.S.A. (using the most conservative definition of 'gay' and 'lesbian') will not have their own biological offspring.

As the previous paragraphs suggest, the causes of infertility are manifold and complex. Infertility is highly variable from region to region depending on a number of biosocial factors, none of which is amenable to a single solution. For example, the infertility of older women in developed countries who have delayed childbirth for a variety of social and economic reasons can be reduced through the use of assisted conception technology. For men and women in same-sex relationships, having biological children may also require the use of techniques adapted from assisted conception technologies, as will individuals afflicted with particular kinds of genetically inherited diseases that affect the reproductive tract. For younger

women with STDs in sub-Saharan Africa, infertility can only be solved by access to (often unavailable) medicines, or in cases of human immunodeficiency virus/acquired immune deficiency syndrome (HIV/AIDS) will probably remain unsolved and end with the premature death of affected individuals. The situation in this part of the world should be compared with that of HIV-infected individuals in industrialized Western countries, where access to new drug-cocktails to counteract the effects of HIV/AIDS have led to considerably extended life-spans and to a greatly improved quality of life. If increasing infertility becomes evident from our polluted world, cleaner and greener policies will have to be implemented to reduce the dangers to human and other populations. For policy-makers concerned with increasing numbers of individuals who remain childless by choice, the institution of specific policies designed to increase the attractiveness and ease of parenting in the modern world may be required. Each of the chapters in this volume offers solutions for the unique problems of infertility.

The two chapters in the first section counterbalance one another. Chapter 2 outlines the kinds of new technologies that can, in many cases, permit infertile individuals to conceive, while Chapter 3 concentrates on genetic causes of infertility that may require reproductive technologies for conception to occur. Chapter 2 thus provides a comprehensive overview of assisted conception technologies currently available to infertile couples. It covers topics such as ovarian stimulation, *in vitro* fertilization (IVF) and intracytoplasmic sperm injection (ICSI), now used routinely for males with exceptionally low sperm counts. The chapter also outlines some of the key areas of future development that are a focus of attention for fertility treatment specialists. One such area is the use of spermatids instead of fully mature spermatozoa for *in vitro* conception. Similarly, another area is to achieve successful *in vitro* maturation of primary (immature) oocytes rather than a fully developed follicle. Such a development would then obviate the need for artificially stimulating ovarian cycles, a procedure that can cause both short- and long-term health risks for the women involved. Instead, a single biopsy sample of ovarian tissue could be taken, which could then provide innumerable oocytes for potential conception. Furthermore,

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if the development of viable embryos *in vitro* could be extended beyond the current limits, it would provide the opportunity for implanting fewer embryos and reduce the risk of multiple conceptions. It would also increase the possibility of genetic analysis from multi-celled embryos to assess potential conditions of risk. Such preimplantation diagnoses offer couples who may produce offspring with inherited diseases the possibility of aborting *in vitro* as opposed to *in utero* at a much later stage of embryonic development.

Other areas of increasing research include further development of cryopreservation technologies, particularly for oocytes as opposed to embryos, and the preservation of testicular and ovarian tissue from patients treated for diseases in childhood (such as cancer) that would otherwise render them sterile. Future technologies may also focus on the donation not just of oocytes but of cytoplasm, which may improve oocyte quality in women, thus preserving the genetic identity of their offspring. Transplantation of the egg nucleus is also theoretically possible and has been used in bovines, albeit with poor results. This new technology may prove beneficial for women who have defective mitochondrial deoxyribonucleic acid (DNA), which affects conception rates.

Chapter 3 concentrates on genetic factors that contribute to human infertility, ranging from conditions that relate to structural defects of the reproductive tract to conditions that result in increased risk of spontaneous abortion including maternal-fetal red cell incompatibility, and maternal-fetal human leukocyte A system (HLA) incompatibility. A. H. Bittles and P. L. Matson specifically clarify how early fetal loss (EFL) among humans (who experience among the highest rates compared to other mammalian species) is related to specific chromosomal problems. Indeed, more than one study suggests that around 78% of all conceptions end in EFL. The rate of genetic abnormality in conceptuses that abort prior to the eighth week of gestation is approximately 66%, with autosomal trisomies accounting for most of these anomalies. In other words, the human system attempts to eliminate potential genetic abnormalities early in the developmental process. The incidence of EFL is also higher among older women, because of the ageing of their oocytes. Those embryos that remain viable and

continue to mature in humans account for a relatively small proportion of conceptions.

Genetic causes of primary infertility range from chromosome numerical disorders such as Turner Syndrome and Klinefelter Syndrome, to structural disorders such as balanced reciprocal X-autosome translocation, or Y chromosome microdeletions. Other genetic disorders can lead to subfertility. These include autosomal dominant disorders such as Noonan Syndrome, and autosomal recessive disorders such as cystic fibrosis – probably one of the most prevalent of genetic problems in modern human populations that can lead to infertility. More rare autosomal recessive conditions include 5- α reductase deficiency documented consistently in only a few human isolates. There are also a number of genetic disorders with incompletely understood modes of inheritance, such as Stein–Leventhal Syndrome. Finally, A. H. Bittles and P. L. Matson briefly discuss the possibility that mutations in the mitochondrial DNA may lead to conditions of male infertility.

A. H. Bittles and P. L. Matson specifically include sections that complement the chapter by S. Fishel, K. Dowell and S. Thornton by focusing on the potential clinical treatments of genetically infertile individuals, and the genetic outcome of progeny conceived using such technologies. Individuals with such genetic abnormalities are, however, a minority of cases of those seeking assisted conception technologies. Similarly, both chapters are complementary in the way in which they deal with the ethical issues surrounding reproductive technologies. S. Fishel, K. Dowell and S. Thornton are understandably greater advocates for forging ahead with new developments, whereas A. H. Bittles and P. L. Matson urge for more caution in adopting reproductive technologies that may have unforeseen consequences. For example, it is not yet resolved whether offspring resulting from some of the newest technologies (including ICSI) might suffer any health effects. Doubts about the health of artificially conceived progeny have also resulted in a current ban on the use of spermatids for conception. Both chapters caution about the need to evaluate causes of azoospermia and oligospermia which, if resulting from genetic abnormalities, might result in offspring who inherit the same condition. S. Fishel,

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K. Dowell and S. Thornton cover some of the ethical areas that surround egg donation and surrogacy, while A. H. Bittles and P. L. Matson have a small section dealing with the potential for inbreeding caused by the possibility of mating by related offspring conceived using sperm from the same anonymous donor. This latter issue also relates to Chapter 7, by C. J. Patterson and L. V. Friel since lesbian women might opt for artificial insemination as a preferable route for conception.

In Chapter 3, A. H. Bittles and P. L. Matson also discuss the significant emotional and physical costs to individuals suffering from conditions such as Klinefelter Syndrome who elect assisted conception. These may include multiple testicular biopsies, pre-implantation diagnoses and so forth. They advocate the need for comprehensive counselling, which should accompany treatments for such individuals. Similarly, women with cystic fibrosis need particular counselling about the risks associated with pregnancy and gestation, as well as the provision of clear information about the usually shortened life expectancies for afflicted individuals. This would necessarily mean arranging for suitable guardians for the offspring of these individuals in the event of their early death.

In the second section, Chapters 4 and 5 deal with environmental aspects of infertility, but differ substantially in the topics under review. Chapter 4 addresses the issue of whether increasing amounts of environmental pollutants are affecting human fertility in subtle ways, whereas Chapter 5 concerns the evident effect of STDs on human fertility in sub-Saharan Africa. Both represent problems that are relatively intractable for different reasons. In the first case, reducing the kinds of environmental pollutants that are implicated as problematic for fertility would require socioeconomic and political adjustments on a scale that would meet with massive public resistance despite increasing public concern about the issues at stake. Solving the second situation in sub-Saharan Africa remains problematic because burgeoning socioeconomic and political problems in this region continue to prevent the distribution of adequate medical care. In addition, the kinds of behavioural adjustments that are needed to reduce transmission rates of HIV/AIDS are understandably difficult to implement.

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During the past eight years increasing attention has been focused on the potential problem of specific environmental pollutants (called xenoestrogens) that mimic the effects of reproductive hormones. It has already been hypothesized that increasing amounts of such substances have contributed to a decline in human sperm quantity and quality, with frightening forecasts for future male fertility. In Chapter 4, G. R. Bentley describes many of the substances that act as xenoestrogens, and covers their effects on different species in the wild and in the laboratory. She also reviews the evidence for the alarmist claims about human sperm counts. Most of the publicity surrounding the purported decline in human sperm quality can be traced to a paper published by Danish researchers in 1992 in the prestigious *British Medical Journal* (Carlsen *et al.*, 1992). The large numbers of criticisms and reanalyses of the data from this paper have not received the same attention. However, G. R. Bentley reviews and collates these many criticisms. This chapter also deals with the possible effects on female reproductive development, a topic that has not been fully addressed in the literature about environmental pollutants. While admitting that xenoestrogens have the potential to affect fertility in many species, she concludes that the current data are misleading. Further studies on these issues are urgently needed.

In Chapter 5, J. C. and P. Caldwell concentrate on infertility in sub-Saharan Africa, which has the highest reported levels of infertility primarily associated with STDs. This includes HIV/AIDS, although historically the most important STDs to affect women in this region are gonorrhoea and chlamydia. Data from as far back as the 1930s onwards have consistently demonstrated a high proportion of infertility in this region of Africa. The depth of the problem is illustrated by recent data from Gabon where a third of the population in one area are childless. The cause of female infertility in 83% of cases here was tubal occlusion, with chlamydia and gonorrhoea probably primarily to blame.

The authors skilfully combine the sociocultural, historical and behavioural aspects of their data to show how circumstances in sub-Saharan Africa have led to the ready transmission and rapid spread of STDs. Systems of marriage, lineage, inheritance, land-rights and

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postpartum sex prohibitions, as well as the relative freedom of women in comparison with those in Eurasia have created a unique system that J. C. and P. Caldwell refer to as the 'sub-Saharan African sexual system'. The advent of colonialism, the increasing migration that occurred for work opportunities, as well as forced labour exacerbated these social conditions. They also point out that the social premium on fertility in sub-Saharan Africa encourages women to seek alternative partners with whom to conceive if they fail to do so with their husbands.

A separate section in Chapter 5 deals with the specific problem of AIDS and infertility in sub-Saharan Africa. It reminds us that two-thirds of all world cases are concentrated in this region, inhabited by only 3% of human populations. Here, as many as 30% of urban groups are affected. Two other factors are critical in determining these high rates. First, unlike in other areas, transmission of HIV/AIDS is primarily heterosexual; second, high rates of other untreated STDs facilitate infection.

The final section of the book focuses on social aspects of infertility. Chapter 6 deals with the issue of childlessness by choice among women and men in the U.K., while the second evaluates the incidence of infertility amongst gays and lesbians mostly from the U.S.A.

F. McAllister and L. Clarke cite data indicating that approximately 20% of women in the U.K. born in 1975 will remain childless by the end of their reproductive lives, compared to only 11% of women born in 1942. They also point out that, although the data are less reliable for men, figures for childlessness may be even higher for this sex. Although these figures seem alarmingly high, F. McAllister and L. Clarke provide us with a historical perspective from which to view them, pointing out that a similar proportion of women remained unmarried and childless in the early 1920s. This trend was sharply reversed in the years following the Second World War. In earlier times, from the sixteenth century onwards, a high proportion of women and men also remained childless, although due to causes somewhat different than those that characterize the patterns seen today. These include a high proportion of individuals who never married and a number of individuals

who married late. This contributed towards a pattern referred to as the 'Western European marriage pattern'.

What, then, are the characteristics of individuals who choose to remain childless in the U.K. today? F. McAllister and L. Clarke point to the many social factors that can contribute to a woman or a man never having children. This includes choice of careers and length of education, delays in marriage, the availability of reliable contraceptives and postponement of first births. Sometimes couples find themselves unwittingly the victims of age-related infecundity, where successful conception becomes increasingly difficult, and where they may be unwilling or unable to avail themselves of emotionally and financially costly assisted reproduction technologies. One of the problems in assessing such data is the paucity of reliable information for men. In addition, both men and women in later life may rationalize their lack of children in terms of desire, whereas a definite decision specifically to remain childless may not have been made.

What is particularly valuable about Chapter 6 is the unique contribution of both quantitative and qualitative data. In the qualitative section of the paper, interviews were conducted with 34 women aged between 33 and 49. These were grouped into categories depending on how firm their 'choice' had been to remain childless. These categories include 'certain,' those who were 'certain now', those who 'accepted' the fact that they were childless, those who were 'ambivalent', and those who felt the decision had been 'forced' on them. Between a third and one-quarter of respondents fitted into the 'certain' category, many of whom had made this decision relatively early in life as a teenager. These respondents tended to focus on the negative aspects of having children, including the loss of freedom and the heavy responsibilities that accompany parenting.

Those who fitted into the second category of respondents who were 'certain now' tended to have their opinion reinforced by their partners, but who otherwise might have been more uncertain. Many of these individuals were in second marriages or relationships. Those who accepted the fact that they were childless had often been forced into that situation by circumstance; many of these

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were women who had never married while young and who were now in their 40s. Many of these had wished for children when they were younger but not in relationships. In contrast, individuals who fell into the 'ambivalent' category either had a problem with infertility or had postponed having children until they felt they were too old to embark on parenthood. Many of these expressed the wish that they had children. Finally, there was a small group who felt the decision had been taken out of their hands. This group included women for whom there was a fertility problem for which a solution was never sought.

It is clear from these data that, in most cases, having a partner and the views of one's partner are crucial aspects in the decision of whether to have children. Childless women were obviously influenced by the perception in their own relationship that the division of labour would be unequal if they had children. Contrary to expectations, few of the childless interviewees listed their career as a major factor in the decision not to have children, thus challenging the stereotype that childless people are wholly career-minded. In fact, some of the older women who formed partnerships later in life took this transition as the moment at which to reduce their hours at work. Many childless individuals also looked forward to an early retirement.

In conclusion, F. McAllister and L. Clarke suggest that couples who are childless by choice do not represent a uniform and anomalous group of rejectionists, but rather nonconformists who accept the dominant paradigm of parenting and for that reason have often chosen to reject the attendant responsibilities. They close their chapter by covering some policy implications. They suggest that if the burden of parenting (particularly for working mothers) was reduced, many individuals and couples might find parenting a more attractive option. In addition, they advocate that health counselling about age-related declines in fertility should become as important as counselling on the problems of teenage pregnancies. They caution, however, that where government policies have been directed towards encouraging fertility in other European countries, such policies have often had little impact on long-term fertility rates.