Sex and reproduction: an evolving relationship

Giuseppe Benagiano¹, Sabina Carrara, and Valentina Filippi

Department of Obstetrics and Gynaecology, Sapienza University, Rome, Italy

¹Correspondence address. 28 chemin des Massettes, 1218 Grand Saconnex, Switzerland. E-mail: giuseppe.benagiano@uniroma1.it

Table of contents

Introduction
Methodology: search strategy
Sex without reproduction
  Fertility control
  Sexuality after menopause
  Sex for pleasure
Reproduction without sex
  Assisted reproduction technology
  Reproduction after menopause
  Reproduction with one or no gametes
Where is sexuality going?

Background: Although sexual activity has, until very recently, been essential to reproduction, this did not preclude the non-reproductive importance of sexual relationships and non-conceptive copulations. Technological advances, however, now allow for both sex without reproduction and reproduction without sex. This review summarizes social and ethical commentaries on the new relationship between sex and reproduction.

Methods: For each main area discussed, a systematic search was made using (depending on the subject) PubMed, Medline, ScienceDirect, classic books, Google and/or religious websites. The search focused on publications between 1975 and 2009, although some materials from the first part of the 20th century were also utilized.

Results: The classic picture of sex for reproduction and bonding between mating partners is increasingly being replaced by reproduction separate from sexual activity. Although not every advance in assisted reproduction produced, per se, a further separation from sexual intercourse, these two fundamental human activities are today increasingly carried out independently, as reproduction is possible, not only without sex, but even through the intervention of more than two partners. The possibility of reproduction with only one or even no gametes, although highly controversial and not yet feasible, is nonetheless being investigated.

Conclusions: Technological advances in the field of reproductive biology have enabled couples considered infertile to conceive and have healthy babies, causing a revolution in culture and customs. Today the independence of sex and reproduction is established and in the future human reproduction may move even further away from the sexual act, an option definitely unacceptable to some ethicists.

Key words: assisted reproduction technology / contraception / reproduction / human sexuality / religious ethics

Introduction

From an evolutionary viewpoint, sexuality has been driven by the imperative to reproduce. During the 20th century, however, reproduction and sexuality began to move independently, and today they can be, in many ways, considered separate, if not independent. This epochal change has been made possible by enormous progress in the understanding of reproductive processes, followed by a newfound ability to modify them. To understand the changing relationship between reproduction and sexuality is imperative to go beyond biology. Anthropological facts, philosophical reflections and ethical norms and religious dictates must also be taken into consideration.
Specifically a review of religious attitudes toward the new horizons of human reproduction is fundamental to the understanding of an evolving human sexuality, because, by and large, religions continue to oppose change in how humans view sexuality. All religions have focused on sexuality and its moral regulation, considering the sacred origin of life—a gift from God—a basic concept and a cornerstone of religiosity. By necessity, the focus here will be limited to the three major monotheistic religions; for details on sexuality and religious ethics, the reader is referred to recently published reviews (Schenker, 2008; Serour, 2008; Benagiano and Mori, 2009).

Finally, although religious ethics have had a major influence on how humans view sexuality, today secular morality is gaining momentum. As pointed out by Holloway (2005), secular ethicists ‘should remain firm in asserting that though our ethics may differ from theirs, it is an ethic, not a lack of one’.

**Methodology: search strategy**

The initial strategy was provided by the Proceedings of a Ford Foundation-sponsored Conference entitled: ‘The evolution of the meaning of sexual intercourse’ (Benagiano et al., 1996).

After this, a search was carried out through major bio-medical data bases: PubMed, Medline, ScienceDirect, for leading articles in each field evaluated:

- **Sexology**: with a focus on sex for pleasure and sexuality after menopause;
- **Reproductive biology**: aiming at an outline of present knowledge in fields such as assisted reproduction and contraception and a discussion of attitudes towards the new horizons opened by technological innovations;
- **Bioethics**: in order to identify the diverse, sometimes opposite, views on the morality of each of the new developments in human reproduction;
- **Religious Ethics**: in an attempt to summarize the position on sexuality and towards reproduction of the three great monotheistic religions.

Given the multiplicity of disciplines involved in the topics reviewed it has been necessary to consult a number of books, such as Religion and the Individual: A Jewish Perspective (Jacobs, 1992); Family Planning in the Legacy of Islam (Omran, 1992); With Pleasure: Thoughts on the Nature of Human Sexuality (Abramson and Pinkerton, 2002); A matter of life (Edwards and Steptoe, 1980); The International Islamic Code for Medical and Health Ethics (Islamic Organization for Medical Sciences, 1983); The future of human reproduction (Harris and Søren, 1998).

Reference to Holy books is as follows:

- Judaism: Holy Scriptures, a Jewish Bible according to the Masoretic text (Tel Aviv: Sinai Publishing, 1979). Babylonian Talmud (Web version last accessed on 2 October 2008).
- Christianity: Holy Gospel according to Matthew (Web version last accessed on 2 October 2008); Holy Bible (Web version last accessed on 2 October 2008);

For specific points not accessible in the scientific literature we utilized Wikipedia and Google and for statements made by religious authorities we visited their websites.

### Sex without reproduction

Female accessibility and a concealed fertile period carried with them a fundamental consequence: the need to avoid, rather than seek conception during intercourse.

In this respect humans have tried to practice contraception ever since they began to leave written records (Campbell and Potts, 2002).

### Fertility control

The importance of controlling fertility as a means to improve the quality of life of people in general and of women in particular was clearly understood well before effective methods became available and population explosion made some form of birth control mandatory. Indeed, besides Malthus (1798), a separation between sex and reproduction were advocated also by Freud (1898).

Purdy (2008) recently pointed out that sexuality focused on reproduction must have frustrated women throughout human history. She believes that it is hardly plausible that women ever lived full happy lives in societies in which their need for sexual satisfaction, their interest in avoiding pain and suffering, and their desire for control over their bodies and lives were routinely ignored. Particularly important, in her view, would have been the attempt to maintain at least the degree of bodily integrity necessary for ensuring healthy intervals between pregnancies. If this is true, then the moment men and women were able to separate with fairly high accuracy the ‘reproductive’ from the ‘non-conceptive’ aspects of reproduction, a real sexual revolution took place.

The first consequence of the new situation was a successful challenge to male supremacy, because the final drive for equality of sexes had to start from the biological phenomenon that caused it in the first place: the difference in reproductive strategies between men and women. To achieve a society of ‘equals’, women had to harmonize their role as mothers with all the other roles they claimed for themselves (Benagiano et al., 2007).

It is important to stress that this new reality benefited every member of a family: properly spacing children improved their survival, since both short and long intervals between pregnancies are associated with an increased risk of adverse perinatal outcomes (World Health Organisation, 2005).

Obviously, the contraceptive revolution could not have gone unchallenged: the idea that evolution, a natural and inevitable phenomenon, moved sexuality away from a condition where non-procreative coital activity was considered a simple by-product with even negative connotations, has been resisted by the advocates of traditional values.

Within Christianity, reactions were much diversified: protestant Churches at first had a critical attitude, but later generally accepted and approved birth spacing through contraception, whereas the Roman Catholic Church remained adamantly opposed to modern contraceptive technology. For details of Christian and Catholic positions on fertility regulation see Benagiano and Mori (2009).

Islam took, from the beginning, a positive position: the vast majority of Scholars studying family planning have justified it on the basis that Islam is a religion of moderation and have invoked the principles of ‘liberty’ or ‘permissibility’—that is, the idea that everything is permissible unless explicitly designated otherwise in Holy Quran or in the Prophet’s tradition (Sunnah) (Roudi-Fahimi, 2004). Indeed, Islam addresses itself to reason and keeps in harmony with man’s natural
character and never seeks to impose undue burdens and intolerable restrictions (Omran, 1992).

Since ancient times, Judaism has taken a detailed position on family planning. First and foremost, as a rule, abstinence because of economic difficulties and inconvenience of child-raising is not acceptable. A man is not allowed to use any method in view of the ban of castration in the Torah (Holy Scriptures, Leviticus 22:24) and the divine commandment: ‘Be fruitful and multiply’ (Holy Scriptures, Genesis 1:28). Therefore, Jewish Law strictly forbids masturbation as well as coitus interruptus. Yet, a woman, under certain conditions, might be allowed to go through ‘pharmacological castration’ since a female is not obligated to fulfill the divine command if severe health problems dictate it (Schenker and Halperin, 1995).

According to most rabbinical authorities condom use may be permitted when contraception is medically indicated, but oral contraceptives are medically contraindicated. In favour of permissibility is the fact that by using spermicides there is no physical occlusion of the natural genital tract and very little interference with cohabitation. With regard to the most common female methods, intrauterine devices and hormonal contraceptives can be utilized if there is an indication (Schenker and Halperin, 1995).

**Sexuality after menopause**

During the second part of the 20th century two major events substantially modified the population pyramid of western countries: an extraordinary increase in life expectancy that—for women—rose well above 80 years; and a decrease in fertility often below replacement levels.

This means that at least in western countries, a large proportion of women may end up spending more years in post-menopause than in any other phase of their life; the so-called ‘post-parental partnership’ is now significantly longer and becoming more and more important, reaching about one third of their lives (Hartman et al., 2004).

This phenomenon has been accompanied by a true revolution: not too long ago, a post-menopausal woman was considered an asexual being for whom sexual desire and sexual activity were no longer relevant and appropriate, whereas today virtually all studies show that the great majority of women and men can remain sexually interested and active until the end of life (World Health Organisation, 2004).

For many women sexuality may become critical at menopausal transition with several factors contributing to shape future sexuality. These may be biological, psychological and socio-relational and they may negatively affect the entire sexual response cycle, inducing significant changes in desire, arousal, orgasm and satisfaction (Nappi, 2007).

Recently a specific disorder named Hypoactive Sexual Desire Disorder (HSDD) has been identified in post-menopausal women (Leiblum et al., 2007); it is important to underline that this pathological condition exists only when decreased sexual desire leads to affliction, lack of sexual satisfaction, worsening of partner relationship and, ultimately, distress. It is interesting to note that the proportion of women with low sexual desire increases with age whereas, the proportion of women actually distressed about their low desire decreases with age. Consequently, the prevalence of HSDD remains essentially constant with age, providing a possible explanation why no association between HSDD and age is often reported in the literature (Hayes et al., 2007).

In summary, there seems to be greater variability of the sexual experience and functioning in midlife and older women, suggesting a higher dependence on basic conditions like general well-being, physical and mental health, quality of relationship, and life situation. In fact, there is growing evidence against a simple model of post-menopause sexuality that depicts women as victims of their bodily and hormonal changes. Instead, life stressors, contextual factors, past sexuality and mental health problems seem more significant predictors of midlife women’s sexual interest than the presence of menopause itself (Prescrire, 2007).

**Sex for pleasure**

The practical possibility to separate sex from reproduction has eased a condition that has always existed among humans: sex purely for pleasure, either outside wedlock or adulterous. Traditional societies, as well as monotheistic religions, have condemned unequivocally this approach, considering pre- and extra-marital sex highly detrimental for societal and marriage stability. At the other extreme are those who insist that the meaning of sexuality is pleasure independent of procreation. No matter what position one takes, it is probable that modern contraception accelerated the ‘sex for pleasure’ process.

There are today scientists who believe not only that sexual activity goes beyond reproduction and the creation of a bond capable of stabilising couples and creating stable families, but indeed that sex is meant to give pleasure by itself. Abramson and Pinkerton (2002) have recently written on the idea that pleasure in sex is a natural phenomenon. After reviewing evidence from physiology, psychology and cultural values they concluded that, although it is undeniable that pleasure originally developed in order to promote procreation, is not an irrelevant by-product of the drive to procreate. They argue that those who have more sex are likely to produce more offspring, and so the genes that make sex pleasurable get passed on. That, however, is not the final word on how evolution operates. Traits that develop in order to meet one’s need can be co-opted to fulfil entirely different purposes. In the case of sexual pleasure, it turns out that it facilitates things such as interpersonal bonding; it promotes interpersonal relationships, and reduces social tensions; exactly as it happens in the great apes. Although Abramson and Pinkerton believe that these may not have been the reasons why sexual pleasure developed, they feel certain that they helped ensure that it stayed with us and spread through the population. Their final challenging conclusion: perhaps today reproduction is simply a by-product of sexual pleasure!

**Reproduction without sex**

It is undeniable that in the modern world, sexual activity will play a decreasing role in reproduction. A number of technological advances have made a reality the almost complete separation of sexuality and reproduction; almost complete in the sense that masturbation is still the preferred, but not the exclusive, modality to obtain male gametes.

**Assisted reproduction technology**

Pregnancy without copulation, considered science fiction only half a century ago, became a reality when Steptoe and Edwards (1978) made possible the extra-corporeal production of embryos to be
transferred directly to the uterus, thus achieving pregnancy without coital activity. These techniques represent an array of modalities today known as Assisted Reproduction Technology (ART) and, in the more complex situations, In Vitro Fertilization (IVF).

A discussion of the technical advances in IVF and ART is outside the scope of this review, especially in view of the many comprehensive reviews on the subject already published (Pandian et al., 2005; Bensdorp et al., 2007; Edwards, 2007).

Although ART profoundly modified the relationship between sexuality and reproduction, many new discoveries and the technical advances they permitted are not per se likely to have a direct effect on sexuality. Nonetheless, they must be mentioned because they will influence the approach that individuals and couples take to parenthood, as well as for the serious ethical issues involved.

**In vitro fertilization**

Achieving human fertilization in vitro represented such a revolutionary social development that, at least at the beginning, the very idea was rejected by most scientists included. On one occasion, a future Nobel Laureate accused Robert Edwards of ‘condoning murder’, whereas the press announcing the birth of Louise Brown was full of allusion to ‘obscene manipulations’ and the creation of ‘Frankenstein babies’ (Edwards and Steptoe, 1980). Initially, the Church of England reacted negatively, although later modified its position and in 1998 its general synod backed away from a controversial declaration that IVF should be restricted to married couples, passing instead an amendment declaring that marriage was ‘the ideal context for the procreation and rearing of children’ (Anglican Journal, 1 January 1998).

An interesting early discussion of the ethics of IVF by a leading Anglican theologian, Dunstan (1986), was published in the very first issue of Human Reproduction, in an attempt to create a dialogue.

Also the Roman Catholic Church reacted in a strong negative way: an ‘Instruction’ from the Congregation for the Doctrine of the Faith (the old ‘Holy Office’) (1987) condemned IVF in all its many forms, leaving ‘in a suspended state’ only the variant called Gamete Intra-Fallopian Transfer, a modality all but abandoned today. The ‘Instruction’ used exactly the same argument already used to ban positive contraception. Pope Benedict XVI (2008), the author as Joseph cardinal Ratzinger of the ‘Instruction’, recently reaffirmed this prohibition: ‘The two fundamental criteria for moral discernment in this field are: (i) unconditional respect for the human being as a person from conception to natural death; (ii) respect for the originality of the transmission of life’.

Likewise, the Committee on Bioethics of the Synod of the Greek Orthodox Church (Nikolaos, 2008) in January 2006 rejected IVF, whereas at the same time stressing that: ‘in no way can the Church be considered as a formalized authority that seeks to regulate or police our life’.

Yet, practicing Catholic and Orthodox couples in their vast majority accept IVF as a legitimate mean to provide them with a child; a child—it must be stressed—who is the biological offspring of both members of the couple.

In Islam, the social status of women, their dignity and self-esteem are closely related to their procreation potential, both for the family and the society as a whole. Therefore, treatment of infertility for married couples is encouraged as it involves preservation of procreation (Gad-el-Hak, 2000). At the same time, transfer of frozen—thawed embryos, or using frozen—thawed spermatozoa after termination of the marriage contract by divorce or death of the husband is forbidden.

Initially, patients and Muslim doctors alike felt that seeking ART was a challenge to God’s will by trying to render barren women fertile. IVF was only widely accepted after prestigious scientific and religious bodies and organizations issued guidelines, which were adopted by Medical Councils and accepted by concerned authorities in different Muslim countries; these principles have controlled practice in ART centres (for details, see Serour, 2008).

Interestingly enough, the Orthodox Christian Churches of Arab-speaking countries have issued rules that are identical to those of the Muslims.

As already stated, Judaism, starting from God’s command in the book of Genesis, has always dictated that having children is mandatory. This is expressed in the Talmudic saying ‘Any man who has no children is considered as dead’ (Babylonian Talmud), which arises from the words of Rachel, who was barren: ‘Give me children or else I die’ (Holy Scriptures, Genesis 30:2). Because of this overarching principle, helping couples to have children is always permitted, especially because in IVF, oocytes and sperm originate from within the couple, and therefore represent a means for husband and wife to fulfill God’s commandment of procreation (Schenker, 2008). It is true that some rabbis take a strict position, namely that legal and biological ties are severed with the removal of the oocyte and this could change the biological and legal status of the child (Schenker, 2005); it is equally true that Jewish majority’s religious point of view, as formulated by the chief Rabbis of Israel, both the one from the Ashkenazi sector of European origin and the one from the Sephardic sector of Oriental origin, support IVF.

Whatever ethical position one takes vis-à-vis ART/IVF, the idea that reproduction can be achieved without a sexual act has today gained momentum throughout society: as sexuality moved away from its conceptive meaning, reproduction took centre stage by making it possible for millions of infertile couples to have children of their own. It was inevitable that in the modern, internet era, the search for a solution to an infertility problem would move on to this new method of communication and indeed, ‘blogging’ has now provided the most popular and heterogeneous outlet for the infertile (Miller, 2008).

**Use of donor gametes**

The expression ‘gamete donation’, implies the provision of either of the germinal cells by a third party. Indeed, ovum and sperm donation have several points in common, and ethically and legally they are usually dealt together. Today an increasing number of countries have opted for the ethical and legal position, first accepted by Sweden (Ministry of Health and Social Affairs, 2003), that citizens have an intrinsic right to know—whenever possible—their biological parents.

However, it is a fact that, traditionally, there has been a strong asymmetry between ‘motherhood’ and ‘fatherhood’ and, as a consequence, between ovum and sperm donation.

Ethically, if we accept the guiding principles of equality and equity between sexes and sexual orientations, then we must apply the same conditions to all. The classic objection to this position is that it ignores the rights and the interest of the new individual to be conceived.

There are people who believe that any form of gamete donation (or, even more, gamete trading) should be always forbidden. This is the case for a number of important religious ethics; the Roman
Catholic and Orthodox Churches whereas totally accepting the idea that a family can be created by adoption and therefore be based on factors other than biological parenthood, have reaffirmed the need to keep the reproductive process firmly anchored to its biological foundation.

Muslim tradition also rejects the idea of gamete donation, since in Islam the basic principle is purity of heredity, therefore, mixing of genes, is never permitted and each child should be the offspring of a known father and mother. Thus, no third party intrusion into the marital functions of sex and procreation can be tolerated. This rule applies to the donation of spermatozoa, oocytes, embryos or even a uterus (Serour and Dickens, 2001).

In Judaism, an interesting position has been taken by Bleich (1991): he argues that ‘parturition, in and of itself, serves to establish a maternal relationship; therefore, the woman who gives birth is the mother of the child’. However, this position is far from being accepted by all (Bick, 1997).

A description of the position of Protestant denominations is more problematic since within Protestant Churches there is a broad range of views about the morality of employing such new technologies (Conference of European Churches, 2003). For this reason, it is not possible to identify a common Protestant moral position about ART (for further details, see Cohen, 2002).

On the other hand, leaving aside ethical positions often based on dogmas, Holy Scriptures and tradition, many bioethicists take the position that there is no reason against gamete donation, which could be seen as a way to help another fellow to become a parent. This appears peculiarly true in the case of women who today tend to postpone childbearing until after their fertility has substantially declined.

Some countries have banned donor gamete utilization in IVF and reasons for such a prohibition range from possible damage to marriage, to dangers to families and children to endangering society at large. These views are open to criticism (Murphy, 2009a), since secular moral philosophy does not require couples to rely on their own gametes to have children. Indeed, families can thrive even if children vary in their genetic relationship with parents, as documented by adoption and ovum donation. This reality further expands the concept of family, transforming it from an institution based on reproductive functions assigned to a man and a woman bound by the exclusivity of matrimony, to a community of affection and profound sentiments. In this new concept, what matters is not the genetic and physiological basis; rather it is the will to have a child and to assume the responsibilities that go with it.

Preimplantation genetic diagnosis and screening

Preimplantation genetic diagnosis (PGD) is a technique aimed at ruling out the presence in an offspring of a specific genetic disease known to exist in one or both parents. The well-established procedure consists of removing one blastomere of a Day 3 embryo (at the 6–10 cell stage of development). In the event of a suspected single gene defect, the blastomere is tested by PCR, whereas if the suspected disorder involves inheritance of a translocation, or when there is a need to exclude sex-linked disorders, then the Fluorescence In-Situ Hybridization (FISH) technique is employed (Sermon et al., 2007). The latter is already being applied to detect (micro) deletions in single blastomeres for cancer predisposing syndromes (Vanneste et al., 2009).

One possible utilization of PGD is gender selection for couples whose offspring are at increased risk of disorders with an unequal sex incidence. In general terms sex pre-selection is strongly discouraged when it is not banned altogether. This, however, is a very specific and numerically restricted option and cannot be excluded a priori. Nonetheless, prior to offering gender selection through PGD a number of factors must be considered. These include: the risk that a child of either sex will be affected by the condition; the overall reduction in risk provided by gender selection; the potential harms of the procedure; the interests of the family and of the child to be born; the seriousness of the condition and the couple’s procreative autonomy (Amor and Cameron, 2008).

Today, although there is a small diagnostic margin of error (1–3%), PGD has become a well established, safe and effective procedure. This led to calls for systematic screening of large categories of embryos, a request that started a controversy continuing to this day. The debate was opened by Robert Winston who, in a highly publicised interview, accused IVF clinics in the UK of being ‘corrupt and greedy’ (The Guardian. 31 May 2007).

A number of scientists joined the debate (Gleicher et al., 2008; Harper et al., 2008) and two editorials in Human Reproduction tried to draw conclusions from available evidence: Fritz (2008), commenting on the data of Staessen et al. (2004), stressed that ‘significantly fewer cycles progressed to transfer in the preimplantation genetic screening (PGS) group (54.7%) than in control group (85.8%)’. Fauser (2008) pointed out that of three randomized-controlled trials (RCT) performed for AMA (Staessen et al., 2004; Stevens et al., 2004; Mastenbroek et al., 2007), the first two evidenced no significant differences, whereas the third actually showed that the PGS group had a significantly lower chance of achieving pregnancy and live birth. In his view, although the Mastenbroek study was strongly criticized on several grounds (Munne et al., 2007), the fact remains that none of the reported RCTs demonstrate a benefit of PGS.

Looking at the future of PGD, Fragogli (2007) noted that new methods are being developed which will enable the assessment of the entire chromosome complement of embryonic blastomeres and that the technique has become very accurate and reliable.

In conclusion, given our present knowledge, the option of a generalized offer of PGS does not seem scientifically, and therefore not ethically, defendable.

The situation is of course very different in the presence of an established inheritable anomaly, though also in this case ethical objections can be raised in terms of calling the intervention ‘eugenic’. Galton (2005) believes that with the availability of PGD and PGS all the old problems of eugenics have resurfaced. In addition, many disabled groups argue that whereas PGS will marginalize them more and more, the assumption that disabled persons are ‘worse off’, that they ‘suffer’, that they have lesser ‘prospects of a happy life’, should be repudiated (MacBride-Johnson, 2004). Obviously, many hold an opposite view. For instance, MacMahan (2005) has argued that ‘the legitimate desire not to pass on their children inheritable negative, or even fatal, traits should be satisfied’.

Going one step forward, recently some disabled (deaf) couples have argued in favour of being able to have children with their same disability, a decision that runs contrary to the current discussion on the ethics of having ‘super children’. Bioethicists have argued against
this option on the ground that disabilities represent an intrinsic disadvantage that cannot be offset by other advantages that a family might offer them (Savulescu, 2002; Murphy, 2009b).

The Catholic Church, through the words of Pope Benedict XVI (2008) remains totally opposed to any form of PGD: ‘the new problems associated, for example, with the freezing of human embryos, with embryonic reduction [selective abortion of medically implanted embryos], with preimplantational diagnosis, with research on embryonic stem cells and with attempts at human cloning, clearly show that with extra-corporeal artificial fertilization, the barrier that served to protect human dignity has been violated’.

Islamic scholars have also condemned PGD because of probability of misuse. For instance a prominent Egyptian Muslim scholar, declared the procedure religiously forbidden because ‘it will lead to creating a market where babies will turn into a commodity. . . . A human being should be dignified, not treated as a spare tool, this is extremely cruel’ (Ghannam, 2009).

More articulate is the position of Judaism as shown by different Responsa; for instance, Popovsky (2007) took a basic cautionary approach and rejected the idea of meddling with natural childbirth, as inconsistent with the ‘core teachings of the Jewish tradition’. In contrast to this position, Reisner and Wind (2008) argued that PGD may be utilized in the fulfillment of a religious dictate not in opposition to it. In the end the Committee on Jewish Law and Standards has been unable to reach consensus on the issue.

Prevention of diseases based on mitochondrial disorders: use of cybrids

Pathogenic mutations may have an exclusive maternal inheritance when they occur in mitochondrial DNA, because mitochondria are located in the cell cytoplasm and during fertilization the sperm contributes almost no cytoplasm to the zygote; mitochondrial disorders seem to affect about 1 in 400 people. These mutations may be asymtomatic, or cause illnesses such as developmental regression, deafness, blindness, neuropathy, diabetes, cardio-myopathy and liver failure. Risk of recurrence is difficult to estimate because both mutant and normal mitochondrial DNA is present.

A classic example of such a condition is the high incidence of 1278InsTATC mutation causing Tay-Sachs disease in Ashkenazi Jews. According to Poulton et al. (2009) four reproductive approaches are currently available: to avoid transmission of mitochondrial diseases: oocyte donation combined with IVF; oocyte sampling to estimate recurrence risk; chorionic villi sampling to genotype the fetus; and preimplantation genetic diagnosis of embryos produced by IVF; so that those with undetectable levels of mutant mitochondrial DNA can be selected for transfer to the uterus.

A recent development, namely the production of hybrid cells obtained combining the nuclear genome from one source with the mitochondrial genome from another, has now offered an entirely new solution: dissociating the genetic contribution of the mitochondrial genome from that of the nuclear genome, thereby creating a cybrid (a word obtained by fusing together the words ‘cytoplasm’ and ‘hybrid’). To prevent mitochondrial disease transmission, a human oocyte is transplanted into an enucleated recipient oocyte from an unrelated human donor; effectively resulting in an embryo with ‘three genetic parents’. A programme of ooplasmic transfer from fertile donors into oocytes of women with recurrent abortion was started at the Institute for Reproductive Medicine and Science of Saint Barnabas in New Jersey in the mid nineties and led to the successful birth of healthy babies (Cohen et al., 1997). At the time, the news was labelled by many scientists as ‘unwelcome’ and criticized as unethical, leading to the US Government refusal to provide funds for any experiment that intentionally or unintentionally alters inherited genes. The criticism and apprehension came from the fact that mixing of ooplasm from two different sources may generate mitochondrial (mt) heteroplasmy in offspring. Indeed, Brenner et al. (2000), examining 13 embryos from two patients and amniotic cells from four patients were able to find, in addition to the recipient maternal mtDNA, a small proportion of donor mitochondria, thus documenting that ooplasmic transfer can result in sustained mtDNA heteroplasmy representing both donor and recipient. Given this situation, it remains to be demonstrated whether the donor mtDNA out-competes the recipient mtDNA in the heteroplasmic offspring. Also to be ascertained is whether the coupling of two distinct genomes accounted for major problems in three products of conception (Spikings et al., 2006).

Today only a limited number of maternal DNA mutations allow reliable predictions, a problematic ‘grey zone’ exists and problems in the interpretation persist. As a consequence, these applications confront both clinical practice and society at large with several ethical questions and issues, such as the acceptability of suboptimal genetic testing, the value and research use of embryos, the evaluation of late abortion, the ethics of PGD for disorders with an incomplete penetrance and variable expression, the possible transfer of embryos with residual health risks, the acceptability of risks and drawbacks of genetic reproductive technology in general, and the scope and limits of reproductive autonomy and professional responsibility (Bredenoord et al., 2008).

Another type of cybrid may be created by transferring a human nucleus into an animal oocyte stripped of its DNA (a process called nuclear transfer). In September 2007 the Human Embryology and Fertilization Authority (2007) of the UK approved the creation of human-animal hybrids containing 99% human DNA; however, they cannot be implanted into humans, and if implanted in animals, have to fulfill animal research regulations.

The very idea of creating minotaurs has been rejected by many, using arguments such as: moral repugnance, the slippery slope, the appeal to ‘nature’, and the unfair distribution of economical resources. Arguing in favour of cybrids research, Camporesi and Boniolo (2008) claimed that, if you start from the premise that research on early human embryos is ethically permissible under some circumstances, then also research on hybrid embryos should be permitted because of the positive consequences in terms of scientific and therapeutic applications (e.g. the derivation of human embryonic stem cells genetically tailored to the somatic cell donor). Such cell lines offer a unique in vitro model both for studies of human pathogenesis and for drug screening and discovery. Research on cybrids also circumvents the problem of scarcity of human oocytes and their ethically dubious donation.

Production of chimeras

In recent years reproductive biologists have identified the presence in one individual of different populations of genetically distinct cells originating from the same zygote, or appearing in women as a
consequence of fetal cell passage during pregnancy. This phenomenon is known as mosaicism. When distinct cell populations originate from different zygotes, the new individual is called a chimera.

They occur naturally in the animal kingdom, but it was the creation, in 2003, by Chinese scientists (Chen et al., 2003) of human-animal chimeras that sparked controversy and outright rejection. The Chinese group successfully fused human cells with rabbit oocytes, proving that human somatic nuclei can, after nuclear transfer, form embryonic stem cells (ntES cells). The derived ntES cells are human-based on karyotype, isogenicity, in situ hybridization, PCR and immunocytochemistry with probes that distinguish between the various species, maintain the capability of sustained growth in an undifferentiated state, form embryoid bodies and, on further induction, give rise to cell types such as neuron and muscle.

Although the publication of these results was accompanied by strong criticism, human-animal chimeras have been routinely produced for decades and are generated daily in biomedical research laboratories throughout the world (Behringer, 2007). They are typically obtained by grafting human cells or tissues orthotopically or heterotopically into an immune-deficient animal.

It is self-evident that, whereas the availability of chimeras will avoid the use of human embryos for certain types of experiments, the procedure creates new ethical issues unimaginable only a decade ago. In this connection, Bobbert (2006), stressed that human-animal chimeras, raise fundamental questions concerning the human being’s self-image, the concept of person, identity and species, and the moral rights and duties that are connected with such concepts. In 2007, the UK became the first country to legislate on the use of chimeras, based on the concept that an embryo possesses a lower status than a child or an adult human; this is the same principle upon which abortion was legalized in 1968 and research on human embryo was authorized in 1990. Research with chimeras, limited to up to 14 days, is not thought to be different than human embryo research, as these cannot be carried out without licence and cannot be implanted (Naren Patel, oral communication).

The new legislation is contained in a Bill extending the regulatory scope of the Human Fertilization and Embryology Authority to cover all human embryos created outside the body, including interspecies embryos, provided that such use is justified as being necessary and desirable, that the proposed use is licensed and appropriate safeguards adopted (United Kingdom, 2008).

Christian groups rejected the idea of allowing the production of such embryos: for example, the Christian Medical Fellowship (2007) stated: ‘Many people already find the production of animal-human hybrids for research morally repugnant, for both religious and ideological reasons. In a multi-faith society we should not be hurriedly embracing technologies about which a significant proportion of the population has severe moral misgivings’.

Genomic imprinting

Imprinting is defined as the ‘Parent-of-origin specific gene expression’ and is determined by epigenetic modification of genes, such that gene transcription is altered whereas the actual gene sequence remains unchanged (Swales and Spears, 2005). As a result of genomic imprinting only one inherited copy of the relevant imprinted gene is expressed in an embryo. The purpose of this reprogramming is to ensure that sex-specific genomic imprinting is initiated; a key point in ensuring normal embryo development after fertilization.

In some cases, errors in genomic imprinting are lethal, whereas in others they lead to developmental disorders and disease. Fear that assisted reproduction techniques, especially ICSI, may cause alterations in genomic imprinting has been raised by the reported occurrence of three children conceived using ICSI with Angelman syndrome, a serious neurological disorder (Cox et al., 2002; Orstavik et al., 2003). A 3–6-fold increase in the occurrence of Beckwith–Wiedemann syndrome, characterized by pre- and post-natal overgrowth and defects of the abdominal wall, has also been reported (DeBaun et al., 2003; Gicquel et al., 2003; Maher et al. 2003).

According to Swales and Spears (2005), potential problems do not end with germ cells, since the preimplantation embryo is also exposed to a period of culture which could again alter the epigenetic reprogramming. Additional evidence of the possible occurrence of errors in genomic imprinting in IVF, comes from studies in which altered spermatozoa have been utilized. According to Marques et al. (2004), although the maternal imprints had been erased from all sperm, the paternally methylated H19 gene was under-methylated in some sperm from the oligozoospermia donors. If sperm used for IVF have lowered global methylation levels, a reduction in pregnancy rates is observed, stressing the importance of normal gamete DNA methylation on embryo development and ultimately ART outcome (Benchajit et al., 2005).

Obviously, fear of altering genomic imprinting speaks in favour of caution in evaluating long-term consequences of ART. This is an ethically relevant point, although we have failed to identify in the published literature ethical debates specifically addressing this point.

Reproduction after menopause

Thanks to ovum donation, the possibility for a woman to bear a child (although not biologically hers) past the natural barrier of menopause has become a reality. Today, healthy post-menopausal women can carry out a pregnancy, often without major problems (Antinori et al., 2003).

This newfound procreative opportunity for women in their fifties and sixties, has been criticized on several grounds. First, it has been argued, post-menopausal mothers may not be able to establish a correct approach to their ‘children/grandchildren’; also, pregnancy in these age brackets may represent a major risk for the future health of prospective mothers; finally, children may be deprived of their parents earlier than necessary. In its defence, proponents point out the major improvement in life expectancy. This argument has been counteracted with the fact that, whereas longevity is a new reality, healthy ageing is still in the making.

Without entering the debate, arguments put forward by opponents seem to have been considered convincing enough, since a number of countries have taken steps to block pregnancy past age 50 (e.g. Germany, Italy, Sweden).

At present, after the menopause ‘true reproduction’ (i.e. producing a child who is genetically the offspring of both components of the couple) is not yet feasible.

At the same time, three entirely different developments may—in the not too distant future—allow post-menopausal women to bear a child of their own. These are oocyte cryopreservation, the discovery of at least some of the factors involved in the aging of ovaries and the possibility of identifying ovarian germ cells in adult ovaries.
A recent paper by a Canadian group (Chian et al., 2008) documents the feasibility of cryopreservation of oocytes by vitrification: obstetric and perinatal outcomes in 165 pregnancies and 200 infants conceived following oocyte vitrification were very encouraging: the mean birthweight and the incidence of congenital anomalies were comparable with that of spontaneous conceptions. The same group has now published the first healthy live birth of a baby conceived from immature oocytes retrieved in a natural menstrual cycle, followed by in vitro maturation and cryopreservation of the oocytes by vitrification (Chian et al., 2009). Obviously, both techniques can be utilized to store ova and therefore allow women to conceive a baby of their own after menopause.

A further research avenue has been opened with the demonstration that a gene, called Bax, expressed in granulosa cells and oocytes, may be central to ovarian cell death (Tilly, 1996). Following-up on that lead, Perez and her group (1999), have shown that Bax-deficient mice possess 3-fold more primordial follicles than their wild-type sisters. A third line of research deals with the identification of germ cells in adult ovaries of mice (Zou et al., 2009).

In general, presently available methods for achieving gestation in menopausal women imply the use of ovum donation and, as such the same ethical considerations already exposed in section ‘Use of donor gametes’ apply. In addition, considerations about an ageing mother and its effect on offspring must also be taken into consideration.

Reproduction with one or no gametes

For a number of years a small group of scientists have attempted human reproductive cloning (i.e. the creation and birth of a cloned person who would be the genetic twin of one born previously) in a variety of forms (Gillott, 2003; Levy and Lotz, 2005; Strong, 2005), although, to this day, no proven success has been obtained. In spite of this lack of success, human reproductive cloning has been heatedly debated.

There is an almost unanimous opposition to human reproductive cloning; coming not only from the public at large, but also from almost every existing institution, national and international. In 1997, World Health Organization General Assembly approved, with only one vote against (Zimbabwe voted against because the wording was not strong enough), banning cloning with the wording: ‘the use of cloning for the replication of human individuals is ethically unacceptable and contrary to human integrity and morality’; all subsequent declarations by national and international bodies go in the same direction. Subsequently, on March 2005 the United Nations General Assembly passed a Resolution that stated ‘Member States are called upon to prohibit all forms of human cloning inasmuch as they are incompatible with human dignity and the protection of human life’.

Biologically, it has been argued that human reproduction by cloning is directly against the evolutionary pathway set for the species. However, widespread opposition on ethical grounds to the cloning of a human individual began years before scientists started cautioning that there are major technical problems to be resolved in order for this procedure to be considered safe enough to be attempted (Benagiano and Primiero, 2002).

Warning that animal studies were all but reassuring, Edwards (2002) stated ‘Cloning is still a matter of argument about animals, where results in most, if not all, species so far cloned by nuclear transfer have been appalling. Perhaps no-one would accept moving to human studies while disasters, evidently due to imprinting, afflict virtually every cloned offspring’. Indeed, especially in ruminants, somatic cell nuclear transfer is frequently associated with pathological changes in the fetal and placental phenotype with significant consequences for development both before and after birth. This is due to the fact that eukaryotic organisms possess a complex apparatus that maintains portions of their genome in a state that is refractory to transcription initiation and this type of DNA is commonly termed heterochromatin (Martin et al., 2005). Cloning can bring about errors in the elaborate apparatus of epigenetic silencing and lead to ‘epimutation’, the abnormal silencing of a gene. As Niemann et al. (2008) have indicated, in reproductive cloning epigenetic reprogramming of the transferred somatic cell nucleus from its differentiated status into the totipotent state of the early embryo can occur. This phenomenon causes an erasure of the gene expression programme of the respective donor cell and of the establishment of the well-orchestrated sequence of expression of an estimated number of 10 000–12 000 genes regulating embryonic and fetal development. Examining the offspring of cloned mice it has been determined that many of the errors seen in cloned animals have epigenetic causes, although it is possible that germ cells are able to correctly undergo genomic imprint reprogramming (Tamashiro et al., 2002).

In spite of all these unresolved issues, the practice of animal cloning continues and expands with several groups reporting improved results. For instance, a Chinese group led by Li Ning in Beijing, has just published what they consider an optimal protocol for the parthenogenetic activation of vitrified bovine oocytes capable of producing hundred of normal animals (Hou et al., 2009).

In 2003, Zavos published what is considered the first ever attempt towards human reproductive cloning: then in 2004 and 2005, Hwang and his group published two reports in which they produced evidence of their advances toward human cloning. It was subsequently revealed that the highly publicized reports of Hwang’s team were not totally truthful (Min, 2005). Since then, no additional reports on the subject have been made available.

Philosophically, the argument against reproductive cloning has been mostly that it is an affront to human dignity, in particular the dignity of the child produced by cloning. An interesting approach is that taken by Mc Dougall (2008), who suggested that, ‘allocating funds to such a pursuit can affront human dignity by diverting resources away from those existing people who lack sufficient health to enable them to exercise basic rights and liberties’.

The few who favour reproductive cloning, do so on the ground that reproductive cloning may be the only option acceptable to ‘those who are both unable to provide sperm or oocytes, and opposed to sperm or oocyte donation or to adoption’. Proponents of reproductive cloning call it ‘reproductive regeneration’ a term that, ironically, perfectly describes why so many find the procedure unacceptable: it negates the very essence of reproduction, which is generation, not regeneration (Benagiano and Primiero, 2002). Because the procedure could help couples when everything else failed, it is deemed to ‘fall within our standard conceptions of family or procreative liberty’ (Robertson, 2000). These arguments have been rebutted by a Commission set up by the President of the USA (President Council of Bioethics, 2002). Clearly, the two camps have staked out totally opposite and conflicting positions regarding the ethics of human reproductive cloning. Yet, Cohen (2004) believes that one day some form of compromise might be found.
One way to circumvent the opposition to cloning, whereas still providing a means to achieve fatherhood for men without male gametes of any type and maturity, has been published in 2006 by Nayernia and his group, utilising bone marrow-derived stem cells trans-differentiating them into male germ cells. Caution has been expressed that these cells cannot as yet be made into functioning sperm and that sperm created from bone stem cells could have undetectable abnormalities that could cause disease in offspring. (Khamisi, 2007). Nonetheless, the same group (Nayernia et al., 2009) has now reported the in vitro derivation of human sperm from embryonic stem cells.

The Catholic and Orthodox Churches, as well as most Protestant denominations have repeatedly indicated their total opposition to human cloning of any kind, labelling this procedure de-humanising and against human dignity, whereas within Islam and Judaism the idea is still debated.

Roman Catholic adamant opposition to human cloning for whatever purpose and in whatever form, has been clearly enunciated since 1997 (Pontifical Academy for Life) and reaffirmed even at the United Nations (Martino, 2001).

Similarly, Orthodox Christian Churches, including the Russian and the Greek, reject human cloning in all circumstances, as an attempt to create human beings in man’s image rather than God’s. If human clones are bred for the egotistical reason of giving one person a second, a third, a hundred or more lives, then a profound moral crisis arises. . . What sort of person would it be, knowing that he, of all people, was somebody’s copy?” (Ethics of human cloning, 2008).

Among Protestants, Evangelical denominations tend to be closely aligned with the Roman Catholic and Orthodox Churches and consider that ‘Cloning is unethical and immoral and shows a complete disregard for the sanctity of human life’ (Evans, 2002).

In principle, Islam also condemns reproductive cloning. In 1983 the Islamic Organization for Medical Sciences (IOMS) convened a seminar on the Islamic view of human reproduction and determined that human cloning was not permissible. At the same time, some authorities are sympathetic to the idea of cloning cells of a childless sterile man if his wife is willing to bear the child (Dickens and Serour, 2001). An interesting aspect of these scholars’ thinking is that the husband’s father would be considered the genetic father of the child, introducing problems of his consent and perhaps of inheritance laws. However, generally it is considered rather premature to recommend departing from the prevailing condemnation of reproductive cloning.

The situation is even more complex within Judaism: whereas the State of Israel has banned twice (in 1998 and 2004) reproductive cloning, some Jewish religious leaders take the position that human reproductive cloning could conceivably be justified in some circumstances. This view is largely based on historical tradition and sacred writings, which largely focus on human destiny (Tanos and Schenker, 1998). Other Jewish authorities oppose the idea for fear that cloning human beings might harm the family by changing the roles and relationships between family members, since religious status is passed down through the mother and tribal designation is passed down through the father. Thus, a child needs both a mother and a father (Schenker, 2008). Some Jewish scholars worry that cloning could reduce human beings to commodities by making it possible to breed clones with certain characteristics, such as physical strength or high intelligence. The Rabbinical Council has affirmed its opposition to reproductive cloning (Tanos and Schenker, 1998).

Where is sexuality going?

Given the rapid evolution in the meanings of sexuality and of modalities to achieve reproduction over the last half-century, it is difficult to predict the direction in which both will move.

Some conclusions, however, can still be drawn. A certain degree of separation between sexuality and reproduction has always existed among humans. What was not available until recently was a set of methods capable of separating these aspects with high efficacy. The discovery of such methods has therefore accelerated a trend already present in a number of cultures (mostly western). Population explosion forced even pro-natalistic cultures, such as those of Africa and Asia to rethink their cultural paradigms and move towards sexuality without reproduction.

Today, whether this is viewed with great favour or dismay, sexuality and reproduction are two separate, although still closely related, human activities. It seems inevitable that, at least in the short-term, this hiatus will increase and, with additional technological advances, reproduction may become—for some at least—a fact of life independent from sexuality.

It is not clear whether the trend towards the separation of sex and reproduction will ever become a mass phenomenon. What seems certain is that—given the economic cost of extracorporeal reproduction—the procedures lumped together under the acronym ART will not, for the foreseeable future, be utilized by the masses.

Widespread utilization, however, is only one side of the coin, since technology will continue to progress and make available, albeit to a privileged few, modalities unthinkable only a decade ago. When, very recently, Pearson (2008) asked a number of top specialists in the field of human reproduction in which direction development will go over the next 30 years, she got amazing answers: germ cells derived from induced pluripotent stem cells; artificial wombs; complete ectogenesis.

A major determinant of future trends is the ethical approach, or rather approaches that will prevail over the next decade or so. As aptly pointed out by Harris and Søren (1998) a constant feature in the ethical debate over reproduction technology has been the conflict between private choice and public regulation. Indeed, each new reproductive technology is of benefit to some people, while at the same time, seems to offend moral sensibilities of others.

In this respect religious ethics have, in monotheistic religions, taken a distinct, if not separate or even opposite courses. Roman Catholicism, Orthodox Churches and some Protestant denominations (especially Evangelical Churches) have staunchly defended the sexual act in its pristine naturality as the only ethical means to reproduce. In contradistinction to this position, some Islamic and Jewish scholars have affirmed the supremacy of child-bearing over sex, to the point of opening a discussion even on reproductive cloning as a last attempt to give a child to a couple.

References


Robertson JA. Why human reproductive cloning should not in all cases be prohibited. NY Univ J Legis Public Policy 2000–2001;4:35–43.


Submitted on October 16, 2008; resubmitted on July 17, 2009; accepted on July 21, 2009.