Assisted reproductive technologies are an integrated part of national strategies addressing demographic and reproductive challenges.

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BACKGROUND: The decline in the total fertility rate in the latter half of the 20th century in many European countries is becoming increasingly important in determining the demographic composition of Europe and its individual member states. This review focuses on discussion surrounding how assisted reproductive technology (ART) can impact declining fertility rates. METHODS: This article summarizes key aspects of presentations given at the ‘State of the ART 2007—ART and Society’ meeting held in Lyon, France, in June 2007. For each topic, searches were conducted in MEDLINE and other databases and the results, alongside unpublished data and personal opinion, were presented to the Workshop Group. Individual subjects were discussed and any disagreements or omissions resolved. RESULTS: Although reduced fertility rates will have an impact on total population number, it is the change in the age structure of the population that is likely to be the most challenging factor faced by the European Union (EU). With evidence suggesting that an ageing population threatens future standards of living and social cohesion, managing demographic change through integrated policy response has become an important component of EU legislation. However, current measures fail to tackle the contribution that ART may play in alleviating falling fertility rates. Indeed, ART can have an important impact on economic and demographic factors, and should be incorporated into a population policy mix. Current barriers to ART include legislative restriction across different EU countries, limited availability to ART and current perception of ART in society. CONCLUSIONS: The inclusion of ART as part of a population policy mix in Europe is justified but must involve better communication among ART professionals, politicians and the general public.

Keywords: assisted reproductive technology; demographics; fertility; infertility; SWOT analysis

Introduction

The privilege to marry and establish a family is considered a fundamental human right (United Nations, 1948). Despite international calls for the prevention and appropriate treatment of infertility, this condition is becoming more and more common in the developed world (United Nations, 1994). The decline in the overall health standard of the population can, at least partially, help explain the increase in infertility, such as the rising prevalence of obesity, which is associated with anovulation and polycystic ovarian syndrome (Nelson and Fleming, 2007), and the escalating incidence of sexually transmitted diseases that affect the reproductive organs; for example, the rise in chlamydia (Low et al., 2007). Furthermore, postponement of having the first child is increasingly becoming common in the developed world, as more people delay starting a family until later in life (Commission of the European Communities, 2005, 2006). Consequently, postponing having a first child may result in ovarian ageing and associated infertility. Recently, the European Union (EU) parliament acknowledged that infertility is one of the causes of demographic decline throughout Europe (European Parliament, 2008). Together, these health and social considerations mean that the number of infertility cases is growing, resulting in a progressive increase in the need for assisted reproductive technology (ART) (Nygren and Andersen, 2001a,b, 2002; Nyboe Andersen et al., 2004; Andersen et al., 2005, 2006, 2007; Center for Disease Control and Prevention, 2006).

The International Committee Monitoring Assisted Reproductive Technologies defines infertility as the ‘failure to conceive after at least 1 year of unprotected coitus’ and ART as ‘all treatments or procedures that include the in vitro handling of human oocytes and sperm or embryos for the purpose of establishing a pregnancy’ (Zegers-Hochschild et al., 2006). This definition of ART, from a patient’s perspective, provides a medical solution for individuals with infertility by allowing them the chance to
start their own family. Beyond the level of the individual patient, however, ART has implications for society as a whole. This is because the clinical definition of infertility does not take into account the ‘social infertility’ encountered by an increasing number of people who, owing to lifestyle or career choices, will turn to ART to conceive when natural fertility has declined. Therefore, it is important to consider this perspective with regard to the wider impact of infertility treatment.

This review focuses on some of the important impacts of ART on society and provides an overview of the presentations given in the ‘State of the ART 2007—ART and Society’ meeting held in Lyon, France, in June 2007. Presenters provided an overview of the results of searches conducted in MEDLINE and other databases, alongside unpublished data and personal opinion, to the Workshop Group. These were discussed and any disagreements or omissions resolved. In this article, we consider the consequences of changing demographics in Europe and the role of ART in addressing the decline in fertility in many European and other developed countries; the perception of ART in society and how this is reflected in ART legislation and availability; and ART strengths, weaknesses, opportunities and threats. Finally, we assess how ART professionals can improve communication of the impact of ART on society in order to dispel widespread misconceptions, such as the use of ART for ‘designer babies’ with specific characteristic traits (e.g. hair colour). This in turn will help to create a political and social environment that enables advances in the field of ART that benefit not only people with infertility, but society as a whole.

**Changing demographics in Europe**

The three drivers of demographic change are fertility, mortality and migration. These factors not only have consequences on population size, but also on its composition by age. Of these, fertility is the main determinant for the future size and composition of the population in Europe (Maccheroni, 2007).

In October 2006, the Commission of the European Communities (CEC) published a new Communication entitled ‘The demographic future of Europe—from challenge to opportunity’ (Commission of the European Communities, 2006). This document highlighted that birth rates in many European countries have decreased to dramatically low levels in recent years. Currently, the average total fertility rate (TFR) for the enlarged EU of 25 countries (EU-25) is only 1.5 births per woman and only a limited increase to 1.6 is projected by 2030. This is well below the replacement rate of 2.1 required to stabilize the population size in the absence of immigration (Commission of the European Communities, 2005, 2006). Despite the fact that young European couples would like to have more children (High Level Group, 2004; D’Addio and D’Ercole, 2005), couples continue to postpone starting a family until later in life due to a variety of economic, educational and social reasons, including expensive housing, job insecurity and lack of welfare incentives (Commission of the European Communities, 2005, 2006, 2007). Potentially, this is a major cause for concern to fertility specialists since postponement will result in some women never getting pregnant. Further, higher age of the mother at first birth is associated with increased serious medical risks for mother and child.

The consequence of a low TFR is a projected shrinkage of the European population from 486.3 million (in 2004) to 472.2 million by 2050 (Commission of the European Communities, 2007). Although in itself, this decrease in the population is not a cause for concern when considering the long time scale involved (>40 years), the age structure of the population will have changed dramatically. The CEC highlighted that ‘demographic ageing is above all the result of significant economic, social and medical progress giving Europeans the opportunity to live a long life in comfort and security that is without precedent in our history’ (Commission of the European Communities, 2006). However, demographic ageing was identified as one of the main challenges that the EU will have to face in coming years (Commission of the European Communities, 2006). Indeed, it has been estimated that one in six Europeans was aged over 65 years in 2004, whereas, by 2050, one in three Europeans will be aged over 65 years as a result of falling birth rates and increasing life expectancy (Economic Policy Committee, 2006; Grant et al., 2006) (Fig. 1).

This ageing population is of great concern because it may threaten future living standards and disrupt social cohesion between future generations (Eurostat, 2004; Commission of the European Communities, 2005). Economic growth rates are set to decline with the ageing of the European population, mainly owing to the reduction in the working-age population. Projections show that if current trends and policies remain unaltered, the average annual growth rate in gross domestic product (GDP) for EU-25 will fall from 2.4% between 2004 and 2010 to only 1.2% between 2030 and 2050 (Commission of the European Communities, 2006).
Communities, 2006). The CEC noted that their current policies do not address the expected decrease in the working-age population or the economic effects that this will have. They suggest that there is a 10-year window of opportunity to introduce reforms that will prepare Europe for the change in age demographics (Commission of the European Communities, 2006).

Although the EU initially focused on adapting to demographic change, it has moved towards proactively managing demographic change through an integrated policy response. The CEC has identified five key policy areas where Member States and the EU should develop a constructive response (Commission of the European Communities, 2006).

(i) Promotion of employment through more jobs and longer, better quality, working lives.
(ii) Increased productivity and more competition in Europe in order to withstand globalization.
(iii) Better preparation to receive and integrate immigrants.
(iv) Sustainable public finances that guarantee adequate social security and equity between the generations.
(v) Promotion of demographic renewal.

In all these key communications, however, the CEC has failed to address the relative contribution that ART may have in alleviating the decline in fertility rates. Therefore, advocating a ‘population policy mix’, involving increasing fertility, reform of welfare provision and management of migration, constructively responds to the complexity of the challenges presented by changing demographics. Although small, the relative impact of ART on economic and demographic factors is important. By incorporating ART into a population policy mix, the impact on mitigating current trends could be improved (Grant et al., 2006).

This has also been acknowledged recently by the European Parliament who, in a resolution adopted by the parliament on 21 February 2008, states that it ‘calls on the Member States, therefore, to ensure the right of couples to universal access to infertility treatment’ (European Parliament, 2008).

### Demographic and economic impact of ART

Widening the availability of ART represents a viable option for governments in promoting demographic renewal through addressing declining fertility rates (Grant et al., 2006). Using 2002 data from Denmark and the UK, Grant et al. developed a model incorporating fertility, costs, population age structure and behavioural components (Grat et al., 2006; Hoorens et al., 2007). The number of live ART births (not including intrauterine insemination) in Denmark in 2002 was 4.2% of total live births, whereas in the UK for the same year it was 1.4%. Using the model, it was determined that if ART was not available in the UK, the TFR would drop from 1.64 to 1.62. Alternatively, by increasing the number of ART cycles in the UK to a level similar to that in Denmark (which has the highest availability of ART in Europe), the TFR would increase to 1.68.

This rise was found to be equivalent to other policy interventions, such as welfare state reform, which are thought to increase fertility (Grant et al., 2006; Hoorens et al., 2007). Whereas a 25% increase in child benefits would raise the TFR by 0.07, with a cost of between £50,000 and £100,000 per additional birth (Gauthier and Hatzius, 1997), the average cost per additional ART birth was estimated at only £15,000—£25,000 (Grant et al., 2006; Hoorens et al., 2007). The authors concluded that including ART in a population policy mix is a cost-effective option and may complement pronatalist social intervention policies (Grant et al., 2006; Hoorens et al., 2007). However, it should be noted that while modelling is a useful predictive tool, results need confirmation in real-world situations.

As previously mentioned, one of the contributors to declining fertility rates is that women are delaying having children until later in life (Commission of the European Communities, 2005, 2006). Women’s natural fertility declines with increasing age and older women find it harder to conceive either naturally or with the help of ART (Pal and Santoro, 2003; Baird et al., 2005). Policies that make ART more widely available and affordable could have the adverse effect of further encouraging people to delay having children, because they falsely assume that ART will overcome any fertility problems they may have (Maheshwari et al., 2007). Thus the positive effect that ART might be expected to have on fertility rates could be partly offset by the reduced chances of success in older women. For this reason, ART should not be considered a panacea for improving fertility rates but be viewed as part of a population policy mix (Grant et al., 2006).

Lack of medical reimbursement can act as a barrier to people using ART, which in turn can potentially affect the TFR. For example, as part of the German healthcare modernization law implemented in 2004, infertile people now face a 50% co-payment of the total ART treatment, where previously the cost was fully reimbursed by the government. This has led to a drastic reduction in ART treatment cycles per year, particularly in economically disadvantaged areas (Griesinger et al., 2007a) (Fig. 2).

### Assisted reproductive technology and the law

ART legislation varies considerably across Europe (Table I). For example, Denmark allows three free embryo transfers in the public sector with additional transfers available privately. This service is also free in other Scandinavian countries and France, but it is only available in the private sector in Germany. Research
different laws and use this to improve current legislation for a unified strategy addressing infertility in Europe. These laws should aim to ensure that ART is safe, efficient, fully reimbursed or, at least, subsidised and that there is equity of access, while taking into account the varying cultural and religious values held throughout Europe. This could be facilitated through the organization of a pan-European ‘think-tank’ to compare current legislation between countries.

### Variability in ART availability

The term ‘availability of ART’ includes IVF, intracytoplasmic sperm injection (ICSI), frozen embryo transfer and oocyte donation but does not include other procedures, which may be considered within the definition of ART in other countries, such as embryo donation and surrogacy. It was introduced by the European Society for Human Reproduction and Embryology (ESHRE) European IVF Monitoring Committee (EIM), which published its first collaborative European report on ART in 2001 for treatments initiated in 1997 (Nygren and Andersen, 2001a). The availability of ART was quantified by recording the number of ART treatments per million inhabitants. The most recent data published by the EIM for ART cycles in 2004 showed huge differences in availability between European countries, ranging from 80 to 2128 ART cycles per million (Andersen et al., 2008).

Within Europe, the availability of ART services remains highest in Denmark with 2128 cycles per million inhabitants and also high in Belgium (1847) and France (1154) but lower in the UK (663). The proportion of children born as a result of ART treatment in 2004 was also high in the five Scandinavian countries (2.0–4.2%), Slovenia (3.4%) and Belgium (2.4%) whereas it was 1.7% in France and 1.6% in the UK (Andersen et al., 2008). Interestingly, the EIM report highlighted a significant decline in ART cycles in Germany from 1243 cycles per million in 2003, to 755 cycles per million in 2004 with a concomitant reduction in the proportion of children born from 2.6% to 1.6% (Andersen et al., 2007, 2008). This decline coincided with the introduction of a more restrictive reimbursement policy implemented in January 2004 and, according to the authors of the EIM report, provides evidence that reimbursement policies can have significant impact on the accessibility and use of ART treatments (Andersen et al., 2008).

When considering IVF services alone, the global need has been estimated to be at least 1500 cycles per million population per year (Collins, 2002). However, it has been demonstrated that the only countries in the world that approach this optimal IVF utilization are Israel and the smaller Scandinavian countries. These countries allocate a high proportion of public spending on health and subsidise healthcare expenses. In contrast, the USA and Japan, although being wealthy, provide <15% of the suggested IVF utilization. This is likely due to a lack of availability and the high cost of treatment (Nachrigall, 2006). Differences in the number of ART cycles per million between countries in Europe, states in the USA and selected countries worldwide are shown for 2003 in Fig. 3 (Adamson et al., 2006, 2007; Wright et al., 2006).

Worldwide, the availability of ART is influenced by a complex combination of public and private health policies, as well as economic, political and social/cultural forces (Nachrigall, 2006). A decade ago, the population of Europe made up <15% of the world’s total population but was home to ~60% of the world’s

### Table 1. Summary of results from a legislative survey of 14 European countries.

<table>
<thead>
<tr>
<th>Procedure</th>
<th>Allowed</th>
<th>Forbidden</th>
</tr>
</thead>
<tbody>
<tr>
<td>IVF/ICSI</td>
<td>14</td>
<td>0</td>
</tr>
<tr>
<td>Epididymal sperm</td>
<td>14</td>
<td>0</td>
</tr>
<tr>
<td>Testicular sperm</td>
<td>13</td>
<td>1</td>
</tr>
<tr>
<td>Oocyte donation</td>
<td>11</td>
<td>3</td>
</tr>
<tr>
<td>Sperm donation</td>
<td>13</td>
<td>1</td>
</tr>
<tr>
<td>PGD</td>
<td>11</td>
<td>3</td>
</tr>
<tr>
<td>PGS</td>
<td>7</td>
<td>7</td>
</tr>
<tr>
<td>Cryopreservation of human oocytes</td>
<td>14</td>
<td>0</td>
</tr>
<tr>
<td>Cryopreservation of human zygotes</td>
<td>13</td>
<td>1</td>
</tr>
<tr>
<td>Cryopreservation of human embryos</td>
<td>12</td>
<td>2</td>
</tr>
<tr>
<td>Embryo research</td>
<td>11</td>
<td>3</td>
</tr>
<tr>
<td>Oocyte sharing</td>
<td>7</td>
<td>7</td>
</tr>
<tr>
<td>hLA typing</td>
<td>8</td>
<td>6</td>
</tr>
<tr>
<td>Sex selection for medical reasons</td>
<td>12</td>
<td>2</td>
</tr>
<tr>
<td>Sex selection for non-medical reason</td>
<td>0</td>
<td>14</td>
</tr>
<tr>
<td>Insemination of lesbian</td>
<td>7</td>
<td>7</td>
</tr>
<tr>
<td>Insemination of single women</td>
<td>7</td>
<td>7</td>
</tr>
</tbody>
</table>

hLA, human leukocyte antigen; IVF, in vitro fertilization; ICSI, intracytoplasmic sperm injection; PGD, preimplantation genetic diagnosis; PGS, preimplantation genetic screening.

shows that a greater number of treatments are carried out in those countries with readily available, free access to ART (Nyboe Andersen and Erb, 2006). Reasons for the variability in legislation in Europe include cultural and religious differences. For example, in many countries in Western Europe, the utilization of gametes is restricted and access to infertility treatment and services by lesbians, single or post-menopausal women may be denied (Nachrigall, 2006).

Inconsistencies between ART legislation and other legislation can also exist within a country. For example, preimplantation genetic diagnosis (PGD) is not allowed in Germany since analysis of the human embryo is viewed as a ‘selection process’, yet women can terminate a pregnancy up to 20 weeks of gestation (Krones et al., 2005). In some cases, there are negative consequences associated with the diversity in European ART legislation. Civil disobedience may occur when ART professionals do whatever they feel is necessary in the best interests of their patients’ welfare, despite this contradicting the laws and regulations governing their country. This may include recommending local patients to foreign medical facilities (Heng, 2006, 2007b).

Cross-border reproductive care has developed in Europe whereby couples or individuals go to other countries to receive treatment that they cannot get at home (Heng 2006, 2007b; Nachrigall, 2006). The 1999 Belgian register of assisted reproduction indicated that 30% of patients receiving in vitro fertilization (IVF) were foreign (Pennings, 2004). When oocyte donation was considered separately, 60% of all recipients came from abroad to receive treatment. Social injustices may occur; for example, infertile people without the money to pay for ART may be denied treatment totally or have limited or no choice in the procedure undertaken, whereas more affluent patients can afford to pay for treatment at home or travel abroad for a choice of treatments. This may add to the perceived social stigma that is associated with infertility (Nachrigall, 2006).

The highly variable ART legislation throughout Europe has created an urgent need to identify common ground between
ART centres (Schenker, 1997). The number of units per head of population varied between countries, for example, 2–3 ART units per million in Scandinavian countries, 1–1.5 ART units per million in Western European countries, and only one ART unit per 10–30 million in the former Soviet Union. The explanation for these differences in the availability of ART services were related to differences in the standard of living (as expressed by GDP), especially between Western and Eastern European countries and between Northern and Southern Europe (Schenker, 1997).

The relationship between GDP and ART cycles in selected European countries is shown in Fig. 4. However, it should be noted that a recent World Health Organization analysis found that IVF availability and utilization is better correlated with a country’s infant mortality rate than with GDP or overall health spending (World Health Organization, 2000).

In addition to financial aspects, cultural, religious, legislative and demographic factors are important considerations when determining the availability of ART. Variations in the infrastructure and logistics of clinics and treatment regimens may also influence the extent to which infertile people use ART (Nachtigall, 2006). It could be speculated that countries with high access to ART within the National Health System might be risking treating too many people, too early and with inappropriate techniques. This could lead to potentially unnecessary ART treatments, which are a burden to couples and are associated with unnecessary financial costs to the healthcare system. For example, a randomized clinical trial by Steures et al. raised concerns that ART treatment (in this study, intrauterine insemination with ovarian stimulation) provided no real benefit compared with expectant management in subfertile women in The Netherlands (Steures et al., 2006).

However, a recent 5-year Danish cohort study of infertile women undergoing ART treatment demonstrated that, in the country with the highest availability of ART in Europe, the number of spontaneous conceptions before the first cycle of treatment was only 3.1% (Pinborg et al., 2007). In contrast, 69.4% of women who underwent ART treatment gave birth to a mean of 1.6 children within 5 years (Pinborg et al., 2007). Together, this suggests that the risk of overusing ART is small compared with the high delivery rate after treatment (Pinborg et al., 2007).

Importantly, the acceptance of ART by the public affects demand for ART. This includes perception of risk to benefit ratios for factors such as implantation failure, multiple births, prematurity and its associated issues and malformations (Adamson et al., 2006; Diedrich et al., 2007). Factors associated with greater ART acceptance and use include low-dose protocols, low cost of treatment and availability on the National Health Service. Improved technologies allowing for single embryo...
transfer (SET) also increase acceptance, but should be accompanied by increased access to further cycles in the event of a failed conception. Technologies reducing the risk of prematurity, as well as patient discomfort and psychological distress, also positively affect the acceptance of ART.

**SWOT analysis of ART in a society context**

A summary of ART strengths, weaknesses, opportunities and threats is provided in Table II.

**Strengths**

ART provides an opportunity to help prevent the ongoing decline in TFR and, therefore, help address the problems of an ageing European population. For example, in Denmark, the use of ART has increased the TFR from 1.65 to 1.72, whereas most countries in Europe still show a negative trend in TFR (Grant et al., 2006; Hoorens et al., 2007).

Since the first IVF birth in 1978, advances in ART technology have been improving outcomes and increasing birth rates worldwide (Steptoe and Edwards, 1978; Nygren and Andersen, 2001a,b, 2002; Nyboe Andersen et al., 2004; Andersen et al., 2005, 2006, 2007, 2008; Center for Disease Control and Prevention, 2006). Improved culturing and cryopreservation techniques, combined with improved embryo selection, allows for the increased use of SET in clinics. This has the benefit of reducing multiple births. For example, the introduction of a new law in Belgium increased SET from 14% to 49% of IVF/ICSI cycles, providing a significant decrease in the twin pregnancy rate without affecting the overall pregnancy rate (Gordts et al., 2005).

Meanwhile, developments in cryopreservation techniques and more frequent use of frozen IVF cycles ensure that patients do not needlessly undergo further ovarian stimulation should a pregnancy not occur during a fresh cycle (Griesinger et al., 2007b). Advances in ART procedures directed at reducing infection risk for HIV serodiscordant people have also reduced the current risk of infection by 1–2% (Zutlevics, 2006; Savasi et al., 2007).

There is an ongoing debate in society as to the need for regulations, jurisdiction and public control of the practice of ART. Developments in ART continue to provide major breakthroughs in the treatment of infertile couples at a rapid pace. Although this means that major breakthroughs in ART treatment are more likely to benefit patients in clinical practice more quickly, the rapid rate of progress in ART will inevitably mean that parliamentary legislation fails to keep up with these scientific advances. In contrast, attempts to hasten legislation through parliament may lead to excess bureaucracy and licensing policies that may prevent development in the ART field (Schenker, 1997; Soini et al., 2006).

Instead, national and international societies in ART have implemented a series of self-regulatory measures, which include the development of guidelines that evolve to keep abreast of the latest innovations in ART. Additionally, the establishment of registries that maintain detailed records (such as the number of

**Weaknesses**

- Commercial pressure (patients as customers)
- We do not know how to define successful IVF (we do not ask the right questions)
- We ignore problems associated with IVF (multiples, patient discomfort/drop-outs)
- Global differences in access to IVF (IVF is too complex and costly)
- IVF as false hope (backup for postponing childbearing)

**Threats**

- Social
  - Lifestyle
  - Immigration
  - Religion
  - Social perception
- Political
  - Policies in support of early maternity
  - Altered laws of adoption
  - Regulations that reduce the working capacity of ART clinics, protectionist laws that restrict the movement of professionals between countries
  - Lack of medical professionals in some countries
- Scientific
  - Inappropriate use of technology
- Medical
  - Insufficient supply (numbers of donated oocytes)
  - Inadequate funding

**Table II. Summary of key points from SWOT analysis.**

- **Strengths**
  - The founding of a family is a basic human right; ART aims to improve the likelihood of this occurring and is considered as an extension to this notion
  - The rapid advancement in ART techniques (e.g. cryopreservation) has improved birth rates and led to the increased acceptance and use of SET
  - PGD is now possible for >50 monogenic disorders (reciprocal and Robertsonian translocations), which can have an emotional, social and economical impact in affected families
  - Sperm washing and IUI and ICSI can help minimize infection of the seronegative parent and reduces vertical transmission of HIV to the baby
  - National and international registers mean that detailed information is accumulating on all aspects of ART (e.g. cycle numbers, complications and pregnancy rates)
  - Long-term follow-up studies in children born after ART mean that we have a better idea about the long-term effects of medication
  - The demographic issue in Europe and other developed countries mean that all options, including ART, should be considered and adopted

- **Opportunities**
  - Automation and robotics
  - Design of automated systems using microfluidics
  - Improved micromanipulation procedures
  - Better identification of good quality oocytes and embryos
    - Morphological and biochemical markers of development
    - Use of microarray technology
  - Low-cost IVF
  - Ultrasound-guided oocyte retrieval
  - Patient-specific embryonic stem cells

- **Weaknesses**
  - Commercial pressure (patients as customers)
  - We do not know how to define successful IVF (we do not ask the right questions)
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- **Threats**
  - Social
    - Lifestyle
    - Immigration
    - Religion
    - Social perception
  - Political
    - Policies in support of early maternity
    - Altered laws of adoption
    - Regulations that reduce the working capacity of ART clinics, protectionist laws that restrict the movement of professionals between countries
    - Lack of medical professionals in some countries
  - Scientific
    - Inappropriate use of technology
  - Medical
    - Insufficient supply (numbers of donated oocytes)
    - Inadequate funding

ART, assisted reproductive technology; HIV, human immunodeficiency virus; ICSI, intracytoplasmic sperm injection; IUI, intrauterine insemination; IVF, in vitro fertilization; PGD, preimplantation genetic diagnosis; SET, single embryo transfer.
cycles performed, complications and multiple pregnancy rates) provide transparent evidence regarding outcomes and risks following ART and should be considered as the best available source for monitoring the long-term efficacy and safety of various ART interventions.

Weaknesses

Multiple births are a major problem associated with ART and are risky for both the mother and the fetus. Risks to the mother include pre-eclampsia, inter alia hypertensive disorders, thromboembolism, anaemia, urinary tract infection and vaginal–uterine haemorrhage and fluid overload in association with inhibition of uterine contractions (parental tocolysis). Risk of stillbirth and early post-natal deaths are also increased. Long-term consequences of multiple births for the health of ART children are significant, and result mostly from premature birth and low birthweight. These include an increased risk of cerebral palsy, which increases with the number of fetuses (Soini et al., 2006; Sutcliffe and Ludvig, 2007).

In addition to the psychological impact of a diagnosis of infertility, ART treatments are an emotionally challenging experience. The uncontrollable and unpredictable process of a cycle itself is stressful, particularly after one or more unsuccessful attempts. Furthermore, the presence of a genetic defect may first be detected unexpectedly during the treatment process. Subsequently, psychological support may be needed during this time (Soini et al., 2006).

Commercial interest in IVF is often responsible for slowing down the advancement of treatment through insufficient focus on well-designed clinical trials (Heng, 2007a). Because there is no agreed definition of ‘successful IVF’, this can lead to manipulation of statistics to overstate the likelihood of success and promote further patronage of ART services (Peters et al., 2007). The high cost and complexity of treatment have presented barriers to access to ART in many countries worldwide (Nachtigall, 2006). Given the evidence to support the greater use of ART in society in the future (Grant et al., 2006; Hoorens et al., 2007), our focus should be on attempting to improve ART success rates at a lower cost and with less patient discomfort. However, it should be noted that more widely available and affordable ART could further encourage people to delay starting a family, because they might assume that ART will overcome any fertility problems they may encounter (Maheshwari et al., 2007). Clear communication between ART professionals and the public is required to help overcome these issues.

Opportunities

There are important opportunities available for re-examining the basic design of ART methodologies to determine if safe, low-cost IVF can be made available to patients in developing countries or in developed countries where cost is a major obstacle (Hovatta and Cooke, 2006). Although these low-cost IVF methods may limit success rates per treatment cycle and may not enable the treatment of more complicated cases, such as severe male infertility by ICSI or PGD, the opportunity to provide treatment of female infertility may be of sufficient social benefit to support such measures.

There are also substantial opportunities for greater involvement of ART clinics in embryonic stem cell (ESC) research (Cortés et al., 2006). This includes the production of disease-specific stem cells from discarded PGD embryos and potentially by nuclear transfer, utilizing cells from patients with cancers and other complex diseases (Thomson et al., 1998; Mitalipova et al., 2003; Trounson, 2006). It has now been shown that ESCs can be formed from parthenogenetic activation of human oocytes (Revazova et al., 2007). These cells are patient-specific for the woman donor. Similarly, the possible production of patient-specific ESCs by nuclear transfer may be important for cell therapeutic applications of human ESC derivatives (Trounson, 2006).

There are also opportunities for strategic recovery of sterility and infertility through the derivation of germ cell and gamete progenitors that may be used for germ cell or gamete repopulation of gonads in patients with complete sterility or dominant genetic diseases. This would involve the use of nuclear transfer to form patient-specific ESCs with targeted gene correction if required, as well as the differentiation of the ESCs into germ cells suitable for grafting into the gonads of the patient (Lacham-Kaplan et al., 2006; Trounson, 2006; Revazova et al., 2007).

Threats

Threats to ART exist not only within the scientific and medical communities but also within a broader social and political context. The greatest threats include malpractice by clinicians, inappropriate use of new techniques and the provision and subsequent use of low-quality oocytes/embryos because of insufficient numbers of donor oocytes to meet current demand. Ethical practice by clinicians is essential to safeguard the health of the mother, the embryos and the public perception of ART. Adverse and often sensationalist media coverage of high-profile incidents and malpractice has a negative impact of the perception of ART among the general population. In order to tackle these threats to ART, a robust regulatory framework is warranted with which to instil in the public trust and confidence.

Societal factors increasingly result in people delaying starting families. As a result, the number of older women using ART is increasing. Because older women find it harder to conceive both naturally and with the help of ART, this may lead to perceptions of low success rates (Grant et al., 2006). Political threats to ART include legal restrictions on techniques allowed, high costs not being viewed as justifiable, reluctance of governments to fund ART research, a lack of medical and embryological expertise in some countries and protectionist laws restricting movement of professionals. Governments (and health insurers) are often reluctant to provide funds for ART as they may not perceive it as a ‘serious’ healthcare issue, and it may not fit into their ideological definition of family.

Increasing migration is one method for combating an ageing population. However, the numbers of immigrants that would be required to compensate for population ageing would be politically debatable and, as governments continue to allow migration into Europe, these immigrants will eventually reach retirement age and contribute further to the overall problem of an ageing population and is, thus, a short-term solution at best (Hoorens et al., 2007).

The way forward: the importance of communicating the impact of ART on society

Communicating the scientific achievements of ART is crucial in creating a political and social environment that allows patients
to receive optimal care and supports advances in the field. There are a number of key messages that ART professionals should consistently communicate to politicians, the media and society in general in order to achieve these goals.

Epidemiological data suggest that ~80 million people worldwide are infertile. In developed countries, late marriage, postponed childbearing and primary infertility are the major factors affecting declining fertility rates. In the developing world, a high prevalence of sexually transmitted infections and other infections leads to increased rates of secondary infertility (Nachitagall, 2006). ART professionals need to communicate that infertility represents a serious global healthcare issue and should be treated accordingly.

Infertility treatment is a health need for both the individual and society as a whole. While on a personal level ART procedures provide people with infertility the chance to start their own family, there are also positive benefits for society in general. Birth rates in many European countries have decreased to dramatically low levels (Commission of the European Communities, 2005, 2006), with the resulting ageing population threatening future living standards. A TFR of ~2.1 children per woman is needed for a population to maintain its size (in the absence of migration) (Commission of the European Communities 2005, 2006); however, the average TFR in Europe is currently only 1.5 (Commission of the European Communities, 2005, 2006). ART professionals need to communicate that ART has an important role to play in addressing urgent population issues as part of a population policy mix.

Combining improvement in the understanding of embryonic development with advances in in vitro culture techniques, the ability to identify the developmental stage at which an embryo can be transferred has become more advanced, in turn allowing the evolution of embryo selection criteria. ART professionals need to communicate that this has allowed for an increasing trend towards the use of SET, which reduces the cost of ART and the risk of multiple births (Diedrich et al., 2007). In Europe, SET increased from 12.0% in 2001 to 13.7% in 2002 and to 15.7% in 2003 (Andersen et al., 2005, 2006, 2007). In countries such as Belgium and Finland, SET is now performed in ~50% of all treatments, whereas in Sweden this figure is even higher (closer to 70%) (Andersen et al., 2008).

There is also a need for widespread misconceptions about ART to be actively addressed through consistent communication by ART professionals to politicians, the media and society in general. The successful sequencing of the human genome has received widespread media attention and, with it, claims that we will soon know the genetic basis for most diseases and even potentially understand the genetic basis for complex intellectual functions. In the field of fertility, these genetic tools can be used for preimplantation genetic screening of embryos. It has been claimed that soon it will be possible to characterize the genetic make-up of an embryo to prospectively select for those with desired characteristics. Not surprisingly, this has led to widespread belief among the general public that this will allow us to produce ‘designer babies’ with specific and desirable physical traits, such as eye and hair colour, and mental attributes. This kind of media attention has a negative impact of the perception of ART in the general population. It is, therefore, important for ART professionals to communicate that the concept of producing ‘designer babies’ is purely fictitious. Besides the ethical considerations, the fact is that women are physiologically incapable of producing the sheer quantity of oocytes, and thus fertilized embryos, needed to screen and select for even a fraction of the genes that could potentially make up a ‘designer baby’.

Accurate, clear and consistent communication by ART professionals with the general public, based on sound clinical evidence, is crucial in ensuring community support for ART. This should include targeting readily understandable communications to relevant audiences such as those considering ART, politicians with influence in this area and the media. Collaboration between interested groups, including patients, fertility societies and campaigners, healthcare providers and policy-makers, in Europe is also crucial. In turn, this will help ensure a political and social environment that allows for future advances in the field that consistently benefits not only individuals with infertility, but also society as a whole.

Conclusions

Europe is facing serious demographic changes brought about by declining birth rates and increases in longevity, which may have long-term economic and social impacts (Commission of the European Communities, 2005, 2006). Introducing and/or revising current population policy initiatives with which to encourage more natural births and increasing the availability and use of medical interventions (such as ART techniques) are several approaches that have been proposed to close the gap between desired and observed fertility in Europe (Commission of the European Communities, 2005, 2006; Grant et al., 2006; Hoorens et al., 2007). It is clear that ART is able to play an important role in increasing fertility rates of European countries (Grant et al., 2006; Hoorens et al., 2007). The fact that this is now acknowledged by the European Parliament in its resolution of 21 February 2008 is a significant step in the right direction (European Parliament, 2008).

Moreover, health issues and the so-called ‘life choices’ of the population mean that the use of ART treatments is only set to increase. Although ART has come a long way since the birth of Louise Brown (Steptoe and Edwards, 1978), with considerable advances in the techniques and protocols used, there still remains much room for improvement to increase the success rate of ART treatments while reducing the risk of potentially life-threatening side effects and multiple pregnancy births.

The barrier to accessibility to infertility treatment must be addressed by governments. In Europe, this not only means providing financial assistance to couples undergoing ART treatment but also the clarification and possible convergence of the laws regulating infertility treatment in different countries. Evaluation of constructive legislation for individual ART procedures, based on rational scientific debate, and unification of reimbursement policies in Europe can but only improve access to infertility treatment and help reduce the emotional and psychological burden suffered by infertile couples. Ultimately, the increased use of ART should be seen as part of a population policy mix in Europe. However, this must involve better communication between ART professionals with politicians and the general public.

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Appendix

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