Anticipating the use of life extension technologies

Possible pointers from the adoption of assisted reproductive technologies

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If the claims of life extension advocates have any merit, it will soon be possible to slow down ageing and increase average human life expectancy to 100 years and beyond (Hall, 2003). Indeed, there have been reports that the first life extension drug could be available within 5–7 years (Wade, 2009). A reasonable initial increase in life expectancy for today’s generations would be an extra 7 years on average, although others are optimistic that slowing ageing could result in substantial improvements in ‘health-span’ and maximum lifespan (Olshansky et al, 2009; Miller, 2009). The development of effective life extension technologies (LETs)—the potential range of techniques, treatments, products and pharmaceuticals that might slow ageing—would have a significant impact on individuals, society, the medical profession, governments and legislators (Olshansky et al, 2009).

It is impossible to predict the exact types of LET that will eventually be developed and used but there are a number of promising avenues under investigation (Sierra et al, 2009). These include pharmaceuticals that act directly on genes involved in ageing processes, modify biological processes involved in cellular ageing, or mimic the life-extending effects of caloric restriction. There could be therapies based on a better understanding of epigenetic factors, the genetics of age-related diseases, or developments in stem-cell technology, neuroscience and regenerative medicine.

Anti-ageing therapies could also emerge from ‘off-label’ use of drugs developed for the prevention or treatment of health problems related to obesity or cognitive decline. Along with the popular ideology of ‘healthy ageing’, there is already a lucrative and expanding market for products that purport to maintain the appearance of youth (Horani & Morley, 2004). Although there is no proven therapy that slows the biological processes of ageing in humans, several companies are involved in developing treatments to extend longevity (Miller, 2009).

In this paper we consider the possible future development and uptake of LET in the light of the history of assisted reproductive technology (ART). ART represents a recent medical development that was initially considered radical and controversial and has been hotly disputed. Eventually, it evolved into a legitimate and lucrative clinical service that is funded by public and private health insurance in many countries. To what extent might LET follow a similar developmental path?

ART includes treatments or procedures that involve the in vitro handling of human oocytes and sperm or embryos in order to establish fertilization and subsequent pregnancy. Around 1% of babies in the USA and 3% of babies in Australia are now born as a result of ART treatment, and the number of procedures performed has increased by more than 10% per year for the past five years (Burry, 2007; Wang et al, 2009). Infertility affects around one in six couples in the USA and has been reported by 17% of Australian women who have tried to conceive (Burry, 2007; Herbert et al, 2009a).

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The first successful human in vitro fertilization (IVF) was performed as early as 1944, but the first live birth was not until 1978. Since, developments in reproductive biology have outrun societal discussions of their implications, as demonstrated by recent advances towards the development of an artificial womb allowing ectogenesis, or the growth of a fetus outside a human body (Burry, 2007; Simonstein, 2009). Developments in genetic engineering, stem-cell biology and therapeutic cloning might also generate new techniques for assisted reproduction (Burry, 2007).

Reproduction is a basic right and a primitive, biological desire, but many cultures also put a very high value on children (Burry, 2007). Infertility is consequently considered undesirable and there is a strong view in many cultures that women who do not have children live an unfulfilled life—even in some Western liberal cultures where women enjoy a measure of equality (Simonstein, 2009). As ART helps many infertile couples to conceive, basic research and the development of even more sophisticated clinical ART services have been justified as a means to...
meet both a basic human desire to reproduce and the societal and cultural value of having children.

Although there is variability in the extent to which different cultures value a long life, there is a general view in most Western cultures that ageing and death are undesirable states. The fear of death, age-related disabilities and the process of dying might strengthen a commonly held view that living longer is inherently good (Turner, 2004). The value of youth as the standard for beauty and the healthy ageing movement have been important factors for garnering public support for research into the biology of ageing and for fuelling an expanding market for products that claim to maintain the appearance of youthfulness and prevent age-related decline (Horani & Morley, 2004). Advocates of LET argue that they are simply seeking the means to realize a widespread and ‘normal’ desire to live longer (de Grey, 2005).

Objections to technologies that aim to enhance human functioning have been raised for both ART and LET. These include concerns about the violation of ‘natural order’ or ‘divine laws’; concerns about safety and efficacy; the potential for coercion and social pressure to use these technologies; doubts about whether it is possible for people to give truly informed consent; unequal access to the technology; the misuse of scarce social resources to develop these technologies; and how such technologies will affect our individual and collective human identities (Parenis, 1998). When Patrick Steptoe and Robert Edwards applied to obtain funding for their work on IVF from the UK Medical Research Council, they were rejected owing to serious doubts about the ethics of IVF. Ultimately, however, these ethical objections were not sufficient to halt research into human reproductive biology, the development of ART procedures, or their increasing adoption in fertility clinics.

Some ethicists have objected to the pursuit of human life extension in principle. For example, the American bioethicist Leon Kass—an early critic of ART—has argued that the more we use technology to change human form and function, the more we compromise our dignity, identity and human rights. He argues that there is an incompatibility between the desire for longevity and the desire to reproduce and has suggested that the desire to prolong youthfulness is a childish and narcissistic wish (Kass, 2001). Not all ethicists share his point of view. Some even argue that life-extending therapies are, in fact, life-saving therapies that we have a moral imperative to pursue (Harris, 2004). Others have concluded that the ethical objections are not sufficient to prevent the development and use of enhancement technologies but important ethical issues remain nonetheless (Baylis & Scott Robert, 2004; Partridge et al, 2009a).

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The key ethical issues of beneficence and non-maleficence, autonomy and justice that have been identified as particularly relevant to ART are similarly pertinent to LET (Chervenak et al, 2003; Partridge et al, 2009a). One important ethical debate about LET revolves around whether limited societal resources should be spent to fulfil the selfish desire of relatively affluent people to live to the age of 150, while millions of poor people die before the age of 50 (Mackey, 2003). Other critics argue that age-old global inequities will be further exacerbated...
by LET as the technology will increase the contrast between healthy, long-living, rich people and unhealthy, ageing, poor people.

Innovative health technologies are nearly all expensive when first implemented and effective LETs are unlikely to be different. Their availability will, at least initially, be limited to those willing and able to pay, which will therefore deny access to poorer people. Developed and developing countries already differ in life expectancy. If only the rich and powerful are able to afford LET, then, critics argue, not only will they enjoy the health benefits unattainable by the rest of society, but they will have more opportunity to consolidate wealth and power (Kass, 2001).

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Indeed, LETs are likely to mirror the advent of ART in initially offering an elite service—expensive, difficult to access for those in developing countries, and with significant barriers to the less affluent in developed countries. The use of ART has also been described as indulging the selfish desire of relatively affluent infertile people to achieve pregnancy, while thousands of poor, infertile people remain childless (Peterson, 2005). Despite efforts to address equality of access, only a small part of the world population benefits from reproductive technologies (Pennings et al., 2008; Ombelet & Campo, 2007). Most countries limit public funding for infertility treatment (Holm, 2009) and there are large differences in access to ART between developed and developing countries (Ombelet & Campo, 2007). The high cultural value attached to childbearing in some developing countries means that infertile women in these countries might suffer additional severe psychological, social and economic consequences. There is continuing debate about whether ART should be publicly funded and, if so, to what extent and under what circumstances. There have also been calls to develop low-cost options for ART in developing countries (Ombelet & Campo, 2007).

Ethical concerns about life extension are not confined to ethicists or social critics. A recent empirical study showed that many members of the public identified a diverse range of ethical issues related to LET that reflect those in the bioethical literature (Partridge et al., 2009a). The main concerns related to the potentially adverse impact of these technologies on the wider community, especially environmental and economic impacts and the unfairness of differential access. The most commonly identified ethical concerns were that life extension was unnatural (36%), it would have a negative impact on society (18%) and access to it would be unequal (14%; Partridge et al., 2009b).

It is essential for scientists and legislators in liberal democracies to listen to public concern because public opinion might have a greater influence on the direction and application of biomedical research than scientific evidence. While the initial public reaction to any new, ethically sensitive area of biomedicine is often unease, public discussion helps people to become more informed and comfortable with the new technology (Hall, 2003). This has been demonstrated numerous times, for example in initial public rejection of technologies that we now take for granted, such as childhood vaccination or organ transplants.

Public acceptance of ART has increased to the extent that people now often overestimate its success rate. Four phases of public attitudes to ART have been identified (Frame, 2008): first, from 1978 to 1984 attitudes were characterized by initial anxiety and mounting opposition. Second, from 1984 to 1994 attitudes focused on more specific objections and problems with the safety and efficacy of the technology. Third, from 1994 to 2005 attitudes focused on the need for increased regulation of ART, often by special legislation. Finally, from 2005 to the present there has been increasing acceptance of ART as an established practice, while broader questions have been raised about access to ART and the implications of possible new developments, such as ectogenesis.

Partridge et al. (2009a) also showed that members of the public identify a diverse range of personal and societal benefits and drawbacks related to LET. Negative personal issues included the potential for a prolonged life in a poor state of health (34%), the financial cost involved (16%) and the potential to outlive family and friends (12%). Possible social negatives included overpopulation (40%) and an increased burden on health care, welfare and housing (23%) as well as on other resources (19%). People also identified many potential benefits, such as having more time with family (36%), the opportunity to do more with one’s life (31%) and better health and quality of life (21%). Social benefits identified included the potential for an increase in collective knowledge (26%), the opportunity for socially important and useful people to live longer (15%), and making a greater contribution to society (12%; Partridge et al., 2009b).

Some religious objections are common to both ART and LET, particularly those related to concerns that these technologies violate a ‘natural’ or divine order of life. The objections to ART differ between religions depending on how they perceive infertility and the specific procedures used in ART (Dutney, 2007). The most strongly held opposition comes from those who oppose research that involves the destruction of human embryos. Eastern and Western religious traditions often express similar concerns about ART, but individuals might have more widely varying attitudes towards the subject than the official view of the religion that they espouse (Dutney, 2007). The same is likely to be the case for attitudes towards LET.

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In general, it seems that current public opinion is less favourable towards LET than ART, but today’s attitudes towards LET resemble those towards ART when it was a new technology. It is reasonable to expect that public opinion about life extension might become more favourable if a safe and effective technology is developed and if public concerns about the broad implications for society are responded to appropriately. These public concerns are likely to be dynamic and often sophisticated. Thus, while attitudes might become more favourable towards some aspects of LET, concerns about other specific issues or applications might remain. In the case of ART for instance, the discussion has moved away from the use of IVF to treat infertility towards the potential for sex selection or pre-implantation genetic diagnosis. Similarly, if demonstrably effective LETs are developed, concerns about extended
The concept of ‘anti-ageing medicine’ is already gaining increasing acceptance, even in the absence of any proven technology

Concerns have been raised about the medicalization of ageing (Holm, 2009). Although some claim it is wrong to call ageing a disease because it is the norm, it has also been argued that ‘normality’ does not preclude treatment (Mackey, 2003). Mackey argues that ageing can be considered a health problem similar to obesity and back pain, and so still falls legitimately within the concern of medicine. Turner (2004) has argued that the pursuit of good health, and the prevention and better treatment of chronic diseases of middle and older age, will increase life expectancy in ways that challenge current beliefs about maximum human lifespan, even if life extension is not pursued as a goal in itself.

Similar concerns were raised that ART would medicalize infertility. Critics of ART argue that medicine should be concerned primarily with treating and preventing disease and that we should set ethical boundaries around what reproductive medicine attempts to do (Revel, 2009). There is also a common view that doctors should not perform medical procedures for social reasons, such as sex selective abortion. The challenge in implementing this view is that the procedures involved are the same regardless of the reason for using ART. Similar objections were raised in the mid-twentieth century to the inclusion of contraceptive services in medical practice, but contraception is now considered an important component of general medical practice.

ART has become a whole new medical specialty. LET might similarly become a medical specialty if specific and effective techniques are developed, and if it is in the interest of medical practitioners to capitalize on business opportunities. As with ART, in which general practitioners are involved in initial investigations and treatments for infertility, some aspects of LET might occur in a primary care setting. It is easy, for example, to imagine general practitioners being asked to prescribe ‘off-label’ drugs that have been approved for other medical purposes in order to increase lifespan. Guidelines have been introduced recently for doctors faced with requests by healthy people for prescriptions to enhance cognitive performance (Larriviere et al, 2009).

ART guidelines and regulations have been developed primarily by medical specialists. Some critics suggest that as ART specialists are seeking to expand their business, they might be unreliable as interpreters of community attitudes and unsuitable to develop regulations or ethical guidelines (Frame, 2008). Guidelines developed by providers, these critics argue, are likely to serve the interests of the profession rather than those of users or society (Holm, 2009). ART guidelines differ substantially across jurisdictions (Burry, 2007). Differences in policies between jurisdictions have led to predictions of reproductive tourism—that is, patients travelling to other countries to obtain services that they are unable to obtain in their own place of residence, such as egg donation, pre-implantation genetic diagnosis for non-medical reasons, insemination with sperm from a relative, or the search for a surrogate mother (Revel, 2009).

A significant challenge is that it will be much more difficult to assess the safety and efficacy of LET than of ART. Clinical trials with older people might be able to determine the impact on health or lifespan within a reasonably short timeframe. As with caloric restriction, it has been possible to conduct observational studies or short trials on factors that predict exceptional survival, and on age-related changes in physiological measures (Sierra et al, 2009). However, if the interventions are targeted at people in mid-life or earlier adulthood and require treatment for the remainder of life, then clinical trials would need to be conducted over decades. These trials would be very expensive to conduct, if they were feasible at all.

All too often, policies result from disconnected reactions rather than systematic decision-making. The success of the UK model for overseeing ART, which includes extensive public consultation, presents an attractive model for the regulation of emerging LET (Deech & Smajdor, 2007). It is important for any decision-making body to be sensitive to local cultural and religious concerns. Therefore national, rather than international, organizations should take up the task. The likelihood that LET will include a range of developing and potentially controversial biomedical interventions suggests that regulatory bodies will need to oversee a range of new biomedical technologies. Apart from the evaluation of new drugs, the regulation of new medical technologies is fragmented. As many of the ethical issues and regulatory bodies will need to oversee a range of new biomedical technologies. Apart from the evaluation of new drugs, the regulation of new medical technologies is fragmented. As many of the ethical issues and traditional medical guidelines if administered by a medical practitioner, or is a form of dietary supplementation and therefore largely unregulated (Juengst et al, 2003). The sale of ‘life extension’ tablets over the internet is subject to the same concerns as the sale of any unproven substance without medical supervision. Efforts have already been made to protect the public from potentially dangerous anti-ageing products (Olshansky et al, 2004) but these measures would become even more important if the public were required to discriminate between ‘real’ and unproven ‘anti-ageing’ products. Once LETs are developed, they will need to be regulated, presumably under whichever regulation framework is appropriate to their specific characteristics. Consideration must also be given to an appropriate regulatory framework in which to assess and monitor safety and efficacy.
The changing nature of public opinion about ART suggests that public attitudes towards LET might become more positive as the field develops.

It is impossible to predict how LET might be developed and used, but the history of the development and uptake of ART gives some hints. As with ART, there are strong cultural values facilitating support for basic research in ageing as well as its clinical application. Ethical concerns about the future access for disadvantaged groups to LET are similar to ethical concerns raised about ART, which have not prevented its development and clinical application. The changing nature of public opinion about ART suggests that public attitudes towards LET might become more positive as the field develops. This comparison of ART and future LET has highlighted the lack of a coherent framework for managing new technological developments in biomedicine. The increasing likelihood that some forms of LET will be developed in the next few decades gives urgency to the task of better managing public deliberation about ethical concerns by means of coordinated public consultation, and development of guidelines for use of these technologies.

CONFLICT OF INTEREST
The authors declare that they have no conflict of interest.

REFERENCES
Burry KA (2007) Reproductive medicine: where we have been, where are we going? An ethical perspective. Am J Obstet Gynecol 196: 578–580

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