Anticipating the anti-ageing pill

Lessons from the history of the oral contraceptive pill and hormone replacement therapy

Jayne C. Lucke, Phillippa C. Diedrichs, Bradley Partridge & Wayne D. Hall

Throughout history, the prospect of extending the human lifespan—with the ultimate aim of living forever—has been an attractive fantasy. Now, some researchers argue that it will soon be possible to increase our average life expectancy to at least 100 years, if not more, by slowing down the processes of ageing (Guarente & Kenyon, 2000). There are several potential methods for life extension interventions (Lucke & Hall, 2006), but perhaps the most likely is an anti-ageing pill, possibly one that mimics the well-described, life-extending effects of caloric restriction (Everitt & Le Couteur, 2007; Michalow, 2008). Let us assume, for the purpose of argument, that a pill could be developed in the next couple of decades that extended the average human lifespan to around 150 years.

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The development and distribution of an effective anti-ageing pill would have significant societal impacts that could easily catch many parties unawares, including governments, medical practitioners and legislators. A useful way to anticipate what these impacts might be is to look at the history of two other innovations that profoundly changed society: the oral contraceptive pill (OCP; Asbell, 1995; Marks, 2001; Tone, 2001; Watkins, 1998) and hormone replacement therapy (HRT; Watkins, 2007). Such analogies are a useful tool for the bioethical analysis of new technologies (Hofmann et al, 2006) and therefore we propose to address the issue of human life extension by applying this approach.

Since its creation more than 50 years ago, the OCP has been heralded as one of the “greatest miracle drugs” (Goldin & Katz, 2002), a “medical milestone” (Djerassi, 2007) and the first “lifestyle and designer drug” (Junod & Marks, 2002). It was the first virtually fail-safe contraceptive method that women could use independently, and was controversial as it was the first drug to be taken by millions of otherwise healthy people with claims that it had both risks and benefits to health. Its impact on sexual attitudes, women’s liberation, the medical and pharmaceutical professions, and birth control policy and funding have also been profound. Almost 200 million women have used the OCP since it was introduced in 1957 (Marks, 2001) and it is now used by over 100 million women worldwide.

HRT emerged from the scientific and commercial development of pharmaceutical oestrogen in the 1930s. By the end of the twentieth century it had become the most popular drug in the USA and was used by around 40% of postmenopausal women. Although physicians initially prescribed HRT to temporarily relieve the symptoms of the menopause, it quickly found widespread use to forestall the diseases of ageing and to maintain youthfulness. It has been hailed both as an “elixir of life” and “one of medicine’s most revolutionary breakthroughs”, as well as being condemned as “the greatest experiment ever performed on women” (Watkins, 2007).

Scientific research into modifying human ageing might well lead to the twenty-first century equivalent of these two revolutionary pills; in this case, one that effectively slows down ageing and increases lifespan. It is impossible to predict the exact method of action of an anti-ageing pill, but it could act by reducing various risk factors for chronic disease and/or improving the performance of vital systems, thereby keeping the body healthier for longer. Indeed, the actual number of years—particularly healthy years—likely to be added to the current average European life expectancy of 75–80 years is similarly uncertain, but a reasonable aim for current generations would be a modest deceleration in the rate of ageing to delay the onset of ageing-related diseases and disorders by an average of seven years (Olshansky et al, 2006).

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Even if life-extension research were not funded publicly, it would still attract considerable finance from the private sector; many pharmaceutical products that were originally developed to treat serious conditions have found widespread ‘off-label’ use for enhancement purposes, which markedly increases their profitability. Future anti-ageing interventions could be “developed under the aegis of legitimate medical endeavours to treat and prevent traditionally defined disease, disability, and suffering in the sick” (Juengst et al, 2003a). For example, the use of oestrogen over the past decades has been significantly expanded from its original use—to temporarily relieve the symptoms of menopause—to being used to prevent heart disease and osteoporosis (Hanna, 2003). Similarly, after the OCP was approved to treat menstrual and gynaecological disorders in 1957, the USA saw a “curious epidemic” of women...
complaining of irregular menstrual cycles (Barrett-Connor, 2002); consumers often find ways to get access to a product even if it has not been approved for their use. A similar phenomenon could occur if, for example, a drug approved for lowering cholesterol, managing weight or preventing dementia and cognitive decline was shown, or plausibly believed, to extend human life.

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The debates in the literature are usually framed by ethical concerns about the likely consequences of extended human lifespan (Mackey, 2003; Post, 2004; Turner, 2003), but little attention has been paid to the question of whether society would embrace an anti-ageing pill in the first place. One lesson from the development of the OCP and HRT is that such advances and their popularity often emerge as the result of a complex combination of various conditions. Indeed, there are several factors that might facilitate the development of an anti-ageing pill, many of which are similar to those that led to the development and widespread adoption of the OCP and HRT.

Cultural values have an important influence on the acceptability of innovations; as Karin Knorr Cetina, Professor of Sociology at the University of Konstanz, Germany, wrote: “the Enlightenment ideals of human reason and the perfectibility of society have been replaced with the idea of the perfectibility of life through life enhancement, life extension and the anti-ageing possibilities on the individual level” (Knorr Cetina, 2005).

This focus on the perfectibility of life is consistent with a view expressed by some ethicists that there is a moral obligation to enhance ourselves through new technologies, including those that attempt to slow the ageing process (Harris, 2007; Savulescu, 2007). Similarly, Gregory Stock, Director of the Program on Medicine, Technology and Society at the University of California, Los Angeles, USA, in a debate with Dan Callahan, co-founder of The Hastings Center (Garrison, NY, USA) argued that if anti-ageing medicines are of value to individuals, then they will, on average, also be of value to society (Stock & Callahan, 2004). Although this view is hotly debated, it shows that certain current cultural values might support research efforts to develop an anti-ageing pill.

One such value is the culture of youth as a standard of beauty. One reason for the popularity of HRT was the prolongation of a youthful appearance, and this idea is evident in the expanding market for products (Horani & Morley, 2004), such as cosmetics, vitamins and HRT, that promise to maintain youth and have created a fertile social climate in which to develop an anti-ageing pill. Another sympathetic value, which is increasingly prevalent at the other end of the spectrum, is the ideal of ageing healthily. This movement is, in part, a response to concerns about the societal burden of an ageing population and an increasing number of incapacitated elderly people (Horani & Morley, 2004; Rinaldi, 2004).

The healthy ageing movement also played a crucial role in the development of HRT, which was intended to prevent problems in old age by using the body’s natural processes (Rinaldi, 2004). Much that has been written about HRT has been cautionary but, as with life extension, there are many examples in both the scientific and popular press that hail hormone treatment as an “elixir of life” (Watkins, 2007). HRT thus provides an important example of how the ideology of healthy ageing facilitated the promotion of a new treatment.

Life-extension technologies that would allow people to stay healthier for longer would also mesh well with this ideal, even if the societal burden was postponed rather than avoided. Advocates of research on life extension argue that slowing the ageing process “would greatly reduce the incidence of cardiovascular disease, cancer and dementia” (Gems, 2003). This is “compressed morbidity”; people have longer lives, free of chronic disease, and die quickly when they reach the limits of the human lifespan (Juenst et al, 2003a). This approach to life extension is in line with current thinking about ‘good’ or ‘healthy ageing’.

Another factor supporting the development of life-extension interventions is the enthusiasm for the application of technological advances to solve health and social problems. This has increased public approval of interventions that were initially considered too ‘radical’ to be acceptable. Examples include assisted reproductive technologies and, more recently, gene and stem-cell therapies. Their popularity suggests that most of the population will progressively accept an anti-ageing pill in the same way that they accepted the OCP and fertility treatment.

The OCP also demonstrates the importance of advocacy in developing new medical interventions. Margaret Sanger (1879–1966), founder of the American Birth Control League (New York, NY, USA), campaigned for a form of birth control that was safe, inexpensive, easy to use and controlled by women (Watkins, 1998). Katharine McCormick (1875–1967), a biologist and wealthy philanthropist, provided the financial backing and, together with Sanger, funded the investigation that led to the development of the OCP (Garcia, 2004). Once the research had advanced to the point where it was clear that it would be possible to develop it into a contraceptive, public support was enlisted to bring the OCP to market.

If it were not for passionate advocates such as Sanger and McCormick, it is unlikely that the OCP would have been developed at all, or at least that it would have taken much longer. There are also passionate advocates of an anti-ageing pill, who might push development forward by securing philanthropic and private funding, and by recruiting other supporters to the cause (Bostrom, 2005; de Grey, 2005; Stock & Callahan, 2004).

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Another issue to address when considering an anti-ageing pill is the increasing medicalization of the processes of the human body, including ageing, which allows interventions to move more quickly into medical practice. Reframing ageing as a disease or an unnatural process might facilitate this process (Caplan & Elliott, 2004) but, just as the critics of HRT argued that the menopause was ‘natural’ and that HRT was simply another method of medicalizing women’s bodies (Houck, 2003), similar
concerns have been raised about defining ageing as a target for medical intervention (Juengst, 2002).

In addition to a wide range of ethical concerns, there are more material social doubts about the cost of human life extension in terms of the use of natural resources (Rinaldi, 2004) and the planet’s ability to support its current population, let alone more elderly people in wealthy countries (Davis, 2005; Louria, 2005; Olshansky et al, 2007; Stock & Callahan, 2004). These debates have some resonance with the history of the OCP, which some advocates supported because it promised to limit population growth (Accampo, 2003). An anti-ageing pill would certainly increase population growth unless a pre-condition for its use were an agreement not to reproduce (Miller, 2002). One reason people give for accepting a hypothetical opportunity for life extension is to see their children and grandchildren grow up (Lucke et al, 2006), therefore, this is unlikely to be an effective policy. Thus, there are potentially strong arguments against life extension from a Neo-Malthusian view and concerns about natural resources.

Another important factor in determining the fate of an anti-ageing pill is the possible risks and benefits to health. Again, HRT is a good predictor as it is similar in the sense that it is not a life-saving medication, but is primarily used to treat short-term menopausal symptoms and, secondarily, to prevent long-term disease outcomes caused by oestrogen deficiency in asymptomatic women. An anti-ageing pill is likely to be used in much the same way: the most important goal for people who are potentially interested in life extension is to increase the quality and not just the quantity of their lives (Lucke et al, 2006). For example, current development work based on sirtuin enzymes aims to increase the healthy lifespan by establishing new treatment approaches to a range of age-related conditions, including dementia, cardiovascular disease and cancer (Lavu et al, 2008).

There are likely both positive and negative effects on personal health, and it will be important to compare and balance the relative risks of each. The risks of taking a pill that would extend the human lifespan beyond 100 years are likely to be favourable compared with the risk of dying earlier. Even a small decrease in the risk of death might therefore be considered an improvement, at least for those who already enjoy a high life expectancy. Similar arguments were marshalled in support of the OCP, which many argued was either less risky or at least no more risky to women’s health than were pregnancy and childbirth (Marks, 2001). Moreover, the OCP has remained popular among women despite widely publicized health risks — many women are willing to accept these in order to achieve peace of mind from using a highly effective method of contraception (Tone, 2001).

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Similarly, HRT has both benefits and risks that depend on how it is used and by whom. Early commentators acknowledged that women who were first to try HRT were taking risks, but the benefits were seen to outweigh the risks, and it was argued that women should make up their own minds after seeking advice from doctors and friends (Houck, 2003). This type of risk-taking is also likely to occur with regard to an anti-ageing pill. Those who are eager to extend their lives might be willing to accept negative side effects as long as their overall quality of life is not heavily compromised (Lucke et al, 2006).

If an anti-ageing pill becomes widely available, there will also be a broader impact on the healthcare system. The role of life extension in medicine is debated at present, but the concept of ‘anti-ageing medicine’ is gaining increasing acceptance (Caplan, 2005; Elliott, 2003). Some suggest that the effect of population ageing on health expenditure is likely to be small and manageable (Coory, 2004); but the debate is not yet settled (Shoven, 2004); again, it is useful to analyse the impact of the OCP on the healthcare systems in Western countries.

The OCP transformed the medical and pharmaceutical professions and the way in which women interacted with the healthcare system (Tone, 2001). The rapid uptake of the prescription-only OCP forced physicians to give advice about contraceptives, and early concerns about the safety of the OCP led to changes in the regulation of drugs and the information provided to the users. After the OCP-related thromboembolism health scare in the 1960s, the US Food and Drug Administration (FDA; Bethesda, MD, USA) made its requirements for drug approval more stringent. In addition, feminists lobbied for package inserts to detail the side effects of the OCP—a practice that was later extended to all types of drugs (Watkins, 2007).

Initial support for an anti-ageing pill will probably come from the supporters of life extension and those who stand to benefit from its manufacture and sale—such as pharmaceutical companies and medical professionals. There might also be an economic incentive for governments to support an anti-ageing pill if it enables people to remain healthier and work for longer, and so pay for their own care and retirement (Rinaldi, 2004).

There are similarities here to the identity of the advocates of the OCP and HRT. Supporters of the OCP included passionate advocates of birth control who were concerned with controlling population growth, as well as eugenicists who wanted to use the OCP for social engineering purposes. In the case of HRT, its supporters included individual women who wanted to slow their own ageing, drug-makers promoting their products and doctors who believed HRT would benefit women suffering from an “oestrogen deficiency disorder”. The support of research scientists, government regulators and the popular media eventually created a vast market for oestrogen products (Watkins, 2007); the role of the media was important in promoting both the OCP and HRT. There are already general discussions of the anti-ageing potential of hormone research (Watkins, 2007), and it is easy to envisage an anti-ageing pill gathering media attention and support in the same manner that the OCP and HRT were supported.

An anti-ageing pill is likely to be used initially by the same early adopters of other new technologies; people who can afford them—often middle to upper class, well-educated people in the developed world. For example, most of the women who were first to take the OCP and HRT were white, middle to upper class women who had time to seek medical counsel and had the money to purchase discretionary medical treatment (Watkins, 2007). There were also many poorer women keen to use the…
OCP, who offered themselves as guinea pigs for clinical trials (Marks, 2001). Strong consumer demand for effective contraception eventually paved the way for public acceptance and rapid uptake after the OCP was approved for clinical use. Consumer demand was also an important factor in the rise of HRT; as awareness of the availability of HRT increased, more and more women demanded hormones from their doctors and were prepared to seek out doctors who would prescribe them (Houck, 2003). The modern obsession with reducing the appearance of ageing suggests that any effective anti-ageing therapies would find a large market (de Grey, 2004). The use of anti-ageing products increased markedly during the 1990s (US General Accounting Office, 2001), and some people already go to great lengths to attempt to extend their lives through cryogenics or caloric restriction, even without any evidence of success. With the increasing demand for products to extend or enhance youthful appearance, the time might now be ripe for the introduction of life-extension technologies; an anti-ageing pill is likely to be lucrative for any pharmaceutical companies involved in its manufacture and distribution. The original developers, consumers and regulators of the OCP could not have foreseen the wide social consequences of its development. There is little evidence that the OCP reduced poverty, despite predictions to that effect by population control advocates. However, effective contraception and increased investment in family planning have probably made a significant contribution to reducing fertility rates, delaying marriage and increasing female participation in the labour market; although there is debate about whether it was a causal or supportive factor (Cook, 2005; Critchlow, 1999). The availability of the OCP also supported moves towards increasing sexual freedom for women and changed the nature of marriage and sexual relationships. Some argue that the OCP largely contributed to the sexual revolution of the 1960s, whilst others suggest that it was one of several factors that facilitated this social change (Marks, 2001).

A n anti-ageing pill might have other intended and unintended legal, political, economic and societal consequences, which, Eric Juengst—Professor of Bioethics at Case Western Reserve University (Cleveland, OH, USA)—and colleagues argued, should be more widely debated (Juengst et al, 2003b). The likely consequences of life extension continue to generate calls for dialogue by biogerontologists, their scientific organizations, ethicists, philosophers and society at large (Pijnenburg & Leget, 2007). The history of the OCP and HRT might nonetheless provide some pointers to what these consequences might be. The original developers, consumers and regulators of the OCP could not have foreseen the wide social consequences of its development. There is little evidence that the OCP reduced poverty, despite predictions to that effect by population control advocates. However, effective contraception and increased investment in family planning have probably made a significant contribution to reducing fertility rates, delaying marriage and increasing female participation in the labour market; although there is debate about whether it was a causal or supportive factor (Cook, 2005; Critchlow, 1999). The availability of the OCP also supported moves towards increasing sexual freedom for women and changed the nature of marriage and sexual relationships. Some argue that the OCP largely contributed to the sexual revolution of the 1960s, whilst others suggest that it was one of several factors that facilitated this social change (Marks, 2001).

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The social and cultural stigmatization of ageing was a crucial factor in the development of HRT, as menopause became a medical condition rather than a natural phase of life (Watkins, 2007). Some would say that HRT assists women in the fight against ageing in a culture that values youth (Houck, 2003); yet, this fight would be taken to a new level if an anti-ageing pill became available.
The history of the public acceptance of HRT and the OCP therefore provides some clues about how an anti-ageing pill might find acceptance. Public demand for HRT has fluctuated considerably with emerging evidence of the health risks and benefits (Kennedy et al., 1985), although the path to acceptance for the OCP has not been as rocky despite starting from a less favourable position. Yet, acceptance has not been universal (Belfield, 2001): the Roman Catholic Church has never had a favourable view of artificial methods of contraception (Critchlow, 1999) and remains opposed to the OCP. It would also be likely to oppose an anti-ageing pill for similar reasons, and with possibly similar results; for example, rejection or concealed use among members of the Church.

The OCP also changed government policy, as well as the law, because it was the first drug to be used primarily for social rather than medical reasons (Tone, 2001). Although contraception was widely accepted and used in most developed countries by the 1950s, it was not until the late 1960s, when population control became a pertinent political issue, that most governments became actively involved in funding reproductive research and birth control programmes (Critchlow, 1999). When the OCP was introduced, there were still restrictions on the distribution and advertisement of contraceptives in many countries (Watkins, 1998); however, by 1980, many countries were subsidizing some, if not all, of the costs of OCP prescriptions and supply (Marks, 2001). The political and legal changes in birth control policy, and law and funding that occurred after the introduction of the OCP provide further evidence of its dramatic social, cultural, political and economic effects.

The anti-ageing industry has already raised questions about the best way to regulate its products and activities. One potential result of an effective anti-ageing pill is likely to be more and better regulation of the research and its applications. Such regulation could well be supportive if there are significant health benefits and savings on health spending from such a pill. The regulatory challenge could be considerable if an anti-ageing pill were first developed for other purposes and then used off-label. In the USA this would bring it under existing FDA regulations (Hanna, 2003). There are already difficulties in regulating purported anti-ageing treatments because the Dietary Supplement Health and Education Act of 1994 allows some products to be marketed as ‘dietary supplements’ without proof of safety or efficacy (Juenest et al., 2003a).

As the adage goes, it is difficult to make predictions, especially about the future. It is thus impossible to predict how an anti-ageing pill might be developed and widely used, but the history of similarly radical innovations provides some indications. There is already a great deal of public interest in scientific research into ageing, which might lead to greater support for the engineering of an anti-ageing intervention. We might become more sceptical about supposed ‘magic bullets’ in the light of the experiences with HRT and the OCP, but recent developments in genetics, nanotechnology and biomedical science suggest that we would be naive to believe that the development of an anti-ageing pill is an unattainable goal. If such a pill were to be created, it would almost certainly be heavily promoted and widely adopted. Thus, as others have argued, thinking about the potential implications and impacts now is a wise and timely thing to do.

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