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Sixty years of the Pill 76

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An employee of a family planning NGO distributes contraception to students in the Philippines, as part of World Population Day in July

The Pill: no heir apparent

Carl Djerassi, who helped develop the first oral contraceptive, sees a future in which sex becomes entirely divorced from reproduction

How many people—other than those trying to hide their age—celebrate the same birthday in successive years? And why should that happen to a drug? In 2001, people celebrated the 50th birthday of the contraceptive Pill; nine years later, a media frenzy exploded with another 50th anniversary. Now, in 2011, we are doing it again by commemorating the date, 50 years ago, when the Pill was authorized in Britain. All this

would seem to indicate that the Pill is thriving. And in a way it is, especially in light of two overwhelming facts of the last half century—the global population explosion and the rise of women's rights—without which oral contraceptives would have been just another medical advance and not an invention with enormous societal consequences. Yet, in my view, the Pill survives only because there are no fundamentally new

methods of birth control on the horizon.

Over the years, I have been interviewed, filmed, and encouraged to pontificate on the occasion of the Pill's various birthdays, perhaps because one of its ironies is that its own conception has been so hard to pin down. It all depends (as any obstetrician will tell you) on who is counting. In 1997, I spoke at a congress in Vienna commemorating the 35th anniversary of the Pill in Austria, while in May 2010, I was bombarded by requests from many American print, radio, and TV reporters to comment on the "50th birthday" of the Pill, as the media were dating the Pill's debut to its approval by the Food and Drug Administration (FDA). As far as I am concerned

(and I was concerned), the real birth date of the Pill was 15th October 1951. That was the day my colleagues and I at the pharmaceutical company Syntex, in Mexico City, completed the first synthesis of a steroid destined to be used for oral contraception. A few days later, the first few precious milligrams of “norethindrone”—the generic designation of the formally named 17α -ethynyl-19-nortestosterone—was already in the mail to Dr Elva G Shipley at Endocrine Laboratories in Madison, Wisconsin, with the request that the substance be tested for oral progestational activity. (When Syntex established its subsidiary in Britain in the mid-1960s, its first managing director, the late David Moreau, chose Maidenhead as its location purely because of his English sense of humour).

But do we need new methods of contraception and if so, who is “we”? The answer is clear, once we accept that demographically, instead of dividing the world into developed and developing nations, we need to make the division between “geriatric” and “pediatric” countries.

“In 1989, I listed six fundamentally new methods that would vastly expand the choice for human fertility control. Twenty-two years later, only one has been realised”

As seen in Table 1, all of the top pediatric countries are African with the exception of Afghanistan, while the most geriatric countries (Table 2) are found in Europe, with the exception of Japan. By examining Table 3, which lists the ten countries which are projected to have the largest populations by 2050, Pakistan, Nigeria, Bangladesh, Ethiopia and partly India will fall into the pediatric category.

Clearly, the contraceptive needs of the pediatric countries, which are of no commercial interest to international pharmaceutical firms, are not only urgent but also totally different from those of the geriatric countries. What most of Africa and parts of Asia and Latin America need are not newer methods, or “birth control hardware,” but rather improvements in “birth control software.” This means advances in education, public health and, foremost, changes in the status of women, because improving those will cause an explosion in the use of existing methods of family planning.

The only markets that could afford new methods of birth control are in the geriatric

Table 1: Countries with youngest populations (2010)

| Country | % ages < 15 |
|-------------------|-------------|
| Niger | 50.1 |
| Uganda | 48.7 |
| Burkina Faso | 46.4 |
| Congo, Dem Rep of | 46.4 |
| Zambia | 46.2 |
| Malawi | 45.9 |
| Afghanistan | 45.9 |
| Chad | 45.6 |
| Somalia | 44.9 |
| Tanzania | 44.7 |

Table 2: Countries with oldest populations (2010)

| Country | % ages 65+ |
|----------|------------|
| Japan | 22.6 |
| Germany | 20.5 |
| Italy | 20.4 |
| Sweden | 18.3 |
| Greece | 18.3 |
| Portugal | 17.9 |
| Bulgaria | 17.6 |
| Austria | 17.6 |
| Latvia | 17.4 |
| Belgium | 17.4 |

Table 3: Projection of most populous countries (2050)

| Country | Population (m) |
|-------------------|----------------|
| India | 1,748 |
| China | 1,437 |
| United States | 423 |
| Pakistan | 335 |
| Nigeria | 326 |
| Indonesia | 309 |
| Bangladesh | 222 |
| Brazil | 215 |
| Ethiopia | 174 |
| Congo, Dem Rep of | 166 |

SOURCE: 2010 WORLD POPULATION DATA SHEET, POPULATION REFERENCE BUREAU

countries, but those populations have already learned how to limit their families by existing methods. In the large majority of European countries, the average-sized family (1.5 children) is far below replacement level (2.1 children). For those countries, the leitmotif “contraception” in the field of reproductive medicine has been replaced by “conception,” whereas the reverse applies to the pediatric countries. But I do not want to imply that the geriatric countries would not be better off if there were a wider choice of contraceptives, including in those countries where birth control is already practised by a large portion of the population. So what new ones might make sense in Europe or Japan?

In 1989, I listed six fundamentally new methods (Table 4)—not piddling improvements in existing ones—that, if implemented, would vastly expand the choice for human fertility control for all constituencies: poor and affluent, pro-choice and anti-abortion, female and male. The methods would also be more convenient, cheaper and possibly safer. Note that improved efficacy is hardly an issue any more.

Twenty-two years later, only one of the items on this list, ovulation prediction, has been realised. But in terms of usage, it is employed much more widely for purposes of conception rather than contraception. Work on the first item, an antiviral spermicide, is still progressing—primarily because of its applicability to the Aids pandemic rather than for reasons of improved contraception—but so far with little success.

Table 4: A priority list of new contraceptive methods [C. Djerassi, *Science* 1989; 245: 356].

1. Spermicide with antiviral properties (effective during normal coitus)
2. Once-a-month pill effective as menses inducer
3. Reliable ovulation predictor (“red” & “green” light)
4. Easily reversible and reliable male sterilisation
5. Male contraceptive pill
6. Antifertility vaccine

The fourth item, easily reversible and reliable male sterilisation, would be of great advantage in both pediatric and geriatric countries, since vasectomy is practiced widely—notably in China and the US—but mostly by men who are already fathers and do not want any more children. If reversibility were guaranteed—a very expensive proposition, requiring large numbers of volunteers and years of observation—then vasectomy, since it is simple as well as safe, might well be practiced by young men before they had ever fathered a child. For drug companies, however, this approach would be of zero financial interest.

This leaves three options—a once-a-month pill, a male contraceptive pill, and an antifertility vaccine—which would represent fundamental advances that would also fill enormous lacunae in our contraceptive arsenal. But the costs for developing such agents would be enormous (each easily exceeding \$1bn), time-consuming and likely prone to litigation. Only the largest pharmaceutical companies would have the scientific and financial resources for such an endeavour. Given their focus on the diseases of ageing and deterioration that afflict the ever-increasing geriatric populations of these rich countries, it is not surprising that not one of the 20 largest pharmaceutical companies is conducting research and development work on a male contraceptive or a fertility vaccine.

Because of the huge cost of developing even minor chemical variants of existing female Pills, considerable effort was also directed by these companies as well as non-profit organisations such as the Population Council towards introducing new delivery vehicles, such as injectables, implants, vaginal rings, skin patches and the like. In my opinion, such research is justified in extending the use of these steroid contraceptives to a wider population. But what about creating new oral contraceptives? Aside from marketing considerations, is there a societal need and would the money expended on such an endeavour not be better justified if it addressed the develop- ▶

ment of fundamentally new methods, since the existing ones already work so well?

Again, from a societal standpoint, the answer must be a resounding yes. But in terms of the financial considerations of pharmaceutical companies, the answer must be no. None of the major pharmaceutical companies is spending money on new areas for the obvious reason that in the geriatric countries, birth control cannot and possibly even should not have a high priority. Few will argue that spending a billion pounds on a new contraceptive would be more societally or commercially useful than a drug preventing Alzheimer's.

It remains the case, however, that the only entities with the financial and scientific resources to create new chemically-based contraceptives are the large pharmaceutical companies. A focus on improvements in postcoital agents—the “morning after pills”—might well be more useful for consumers, but hardly to these companies. They are focusing on the problems of an increasingly geriatric population where the illusory “totally safe” criterion does not apply, nor does the potential of liability suits. A cancer patient is unlikely to sue as a result of side effects that a user of contraceptives or vaccines would consider unacceptable. Pharmaceutical companies are not philanthropic organisations, which can afford to ignore the bottom line. But there is a second reason why I believe that major new work on contraceptives will not occur as the emphasis in Europe and other geriatric countries shifts from “contraception” to “conception.”

As I argued in both a book and two plays, what we must face—at least in the western geriatric countries—is a de facto divorce of sex from reproduction. When people have sex hundreds of times during their lifetime, is it not time to consider the option of purposefully planned infertility (ie sterilisation) and resorting to planned conception for the couple of times that fertilisation is desired? One way of achieving this is to cryopreserve one's young gametes, followed by early sterilisation, and planned conception by resorting to in vitro fertilisation with one's thawed gametes. According to WHO estimates, 50 per cent of current conceptions worldwide are unplanned with half of those unwanted, resulting in well over 50m abortions annually, many of them illegal and unsafe. Couples resorting to the approach I just outlined would never have to face the question of abortion.

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The Met Office headquarters in Exeter: are blue skies ahead for the organisation?

The month ahead

Anjana Ahuja on non-communicable diseases, weather forecasting and the unfair beauty bias



The UN General Assembly has called a high-level meeting on a health issue, for only the second time in its history. In 2001 it was HIV-Aids; this time it will be non-communicable diseases (NCD). Developing countries now suffer more premature deaths from NCDs (primarily heart disease, stroke, cancer, diabetes and chronic respiratory disease) than developed countries, thanks in part to tobacco, alcohol and inactivity. The historic New York summit on 19th and 20th September—President Obama may attend—is recognition that a “co-ordinated global response” is required to stop fledgling healthcare systems from collapsing under the strain.

The British Science Festival, one of the biggest in Europe, bursts into Bradford on 10th September. As well as famous faces giving the lowdown on highfalutin' ideas, check out the up-and-coming Cambridge astronomer Andrew Pontzen riffing on dark matter. Family events include the Science of the Circus and the *Dr Who* Science Show; teenage detectives can case out CSI Bradford, which is about DNA fingerprinting (www.britishscienceassociation.org/web/BritishScienceFestival)

An imminent period of high pressure is predicted for the Met Office as a parliamentary inquiry into its science remit gets under way. The public weather forecasting service, formerly part of the Ministry

of Defence, has suffered a blizzard of criticism from climate change sceptics and owners of wet barbecues. Its computer models have attracted frosty scepticism, and the question of privatisation hangs in the air. Submit pun-free evidence by 14th September via www.parliament.uk.

Should ugly people get government aid? That's one question contained in the new book *Beauty Pays* (Princeton University Press), a no-warts-and-all exposé of how attractive people earn more, marry better and enjoy a wealth of positive discrimination. Economist Daniel Hamermesh's theory accords with psychological research suggesting that beauty is not in the eye of the beholder but can be measured objectively. **P**

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*“De ni aut incto officatur
conse vel magniet”*