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Tomorrow's contraceptives—yesterday's problem?

In 1970 research into contraception seemed full of promise. New areas were being explored, and with the perils of overpopulation becoming widely recognised funds for this research were readily available. At the end of the decade the picture has changed. In many developed countries population growth has slowed. In the developing world, though there has been some decline in fertility, the main problem with population control is now seen to be making the contraceptives we have both available and culturally acceptable—not developing new methods. Furthermore, in most industrialised nations the amount of government spending on contraceptive research has levelled out or declined since 1974, and of today's budget the proportion contributed by institutions and pharmaceutical companies is about half of what it was 10 years ago. Finally, worthwhile results from this research have proved elusive: for example, the development of a vaccine against pregnancy has run into many problems, and the "male pill" seems as far away as ever.

Referring to some of these difficulties in his introduction to the *British Medical Bulletin's* issue on reproduction,[1] Professor R V Short reminds us that our current preoccupation with recession and the energy crisis should not obscure the pressing problem of world overpopulation. The decline in the British birth rate now seems to have halted, and women are becoming disenchanted with the limitations of oral contraceptives[2] and intrauterine devices. As more side effects are discovered public confidence in existing methods of contraception will be eroded further. A World Health Organisation research programme, applying existing knowledge, has failed to produce new contraceptives of widespread applicability. We need more basic research, and the *British Medical Bulletin's* wide-ranging series of reviews suggests several approaches.[3]

Immunology provides promising possibilities: vaccination against pregnancy can be carried out by immunising women against pregnancy-specific proteins. Primates[4] and indeed human beings[5] have been immunised against the β-subunit of chorionic gonadotrophin with the aim of making pregnancy fail as soon as the gonadotrophin is produced. Unfortunately a form of tolerance develops, so that miscarriages occur later and later in pregnancy. Perhaps this problem could be avoided by immunisation against spermatozoa, or against the complex proteins of the zona pellucida of the ovum—or by immunological attack against other transmitters[6] which the conceptus produces before implantation to signal its existence to the mother. Implantation is made possible by the persistence of the corpus luteum, which is itself vulnerable to luteolytic agents (such as prostaglandins or diethylstilboestrol): luteolysis could also be achieved by inhibition of luteotrophic hormones, using analogues of chorionic gonadotrophin or agents which interfere with binding at luteinising-hormone receptors.

Developing a male pill requires suppression of spermatogenesis without loss of libido. This can be produced by gestogens in combination with testosterone implants, or by cyproterone acetate—which, although it causes oligospermia and decreased sperm motility, seems a poor contraceptive. Oligospermia might be achieved with normal plasma testosterone concentrations by developing a synthetic analogue of "inhibin," a testicular hormone which acts on the pituitary (independently of testosterone) to decrease the production of follicle-stimulating hormone. Nevertheless, inhibin has proved extremely difficult to isolate and would probably be equally difficult to synthesise and administer.

Other possibilities include antiprogestins to prevent the action of progesterone on the endometrium, or analogues of gonadotrophin-releasing hormone to exhaust the pituitary supply of gonadotrophins. But perhaps the most attractive idea is the mimicking of "nature's contraceptive"—the infertility associated with lactation.[7] Anovulation during lactation appears to be caused by high concentrations of prolactin acting on the hypothalamus to inhibit the production of gonadotrophin-releasing hormone. Clarification of this mechanism might lead to a more physiological method of contraception.

In all these possibilities the gap between theory and application is still wide, and inevitably some possibilities will be ruled out by unwanted side effects. Even so, as Professor Short points out, not all side effects are unwanted, and our goal should be "healthy infertility"—contraception which promotes good health rather than compromising it.

[1] Short, R V, *British Medical Bulletin*, 1979, **35,** 97. Obtainable from the British Council, 65 Davies Street, London W1Y 2AA, price £5.
[2] Nuttall, I D, *et al*, *British Medical Journal*, 1979, **2,** 641.
[3] Aitken, R J, *British Medical Bulletin*, 1979, **35,** 199.
[4] Hearn, J P, in *Maternal Recognition of Pregnancy: CIBA Foundation Symposium No 64*. Amsterdam, Excerpta Medica, 1979.
[5] Talwar, G P, *et al*, *Proceedings of the National Academy of Sciences*, 1976, **73,** 218.
[6] Heap, R B, Flint, A P, and Gadsby, J E, *British Medical Bulletin*, 1979, **35,** 129.
[7] McNeilly, A S, *British Medical Bulletin*, 1979, **35,** 151.