degree of fibroid regression is dependent on the degree of oestrogen suppression, many prefer to give the drugs as a subcutaneous depot.^{5,6} Biodegradable implants given every month usually result in complete amenorrhoea,⁸ which is advantageous in women with heavy menstrual loss.

Despite encouraging results treatment with luteinising hormone releasing hormone analogues is not yet an alternative to an operation for most women. Complete regression is unusual, and once treatment is stopped the fibroids rapidly grow back to their original size.^{5,6} So far the treatment has been tried for only a few months, and it is not known whether long term treatment would produce permanent regression. There are, however, considerable anxieties about the theoretical adverse effects of a prolonged hypo-oestrogenic state on the mineral content of the bones.⁹ In addition, the immediate side effect of hot flushes may limit the acceptability of the treatment to young women, although this has not reduced compliance in the studies reported.

At present treatment of fibroids with luteinising hormone releasing hormone analogues should be limited to women approaching the natural menopause and those with medical contraindications to surgery. They may be valuable as a preoperative adjunct to surgery. In a controlled pilot study blood loss was significantly reduced at hysterectomy in a group of women pretreated for three months with goserelin.¹⁰ The cost of such treatment must be balanced against the potential reduction in operation time, the avoidance of blood transfusion, and the shorter stay in hospital that may result from preoperative shrinkage of the fibroids. But these benefits must be confirmed by randomised prospective study.

There is a considerable demand for medical treatment of fibroids from young women who wish to preserve the uterus. This is particularly important within some ethnic groups who have high prevalences of fibroids.¹¹ High doses of medrogestone have been reported to induce degenerative changes in fibroids,¹² and more recently a significant reduction in fibroid volume was reported after treatment with gestrinone.¹³ Treatment with a combined luteinising hormone releasing hormone agonist and a non-oestrogenic progestogen such as medroxyprogesterone acetate is under investigation; the progestogen may protect against bone loss.¹⁴ Ross *et al* have recently suggested that the combined contraceptive pill, particularly one with a high progestogen content, may protect against the development of fibroids.¹⁵

It is not clear how luteinising hormone releasing hormone agonists induce fibroid regression. Shrinkage is most rapid during the first treatment cycle with little further decrease in size after three months,⁵ suggesting that reduction in blood flow may be important (W H Matta *et al*, Blair Bell Research Society, 1988). But there may also be a reduction in the concentration of receptors for oestradiol and progesterone (M A Lumsden *et al*, annual conference, Society for the Study of Fertility, 1987). Cell proliferation is under the control of growth factors, and epidermal growth factor binds to uterine muscle.¹⁶ The binding of epidermal growth factor to myometrium and fibroid tissue was significantly reduced in women treated with goserelin before surgery compared with untreated controls,¹⁷ suggesting that epidermal growth factor may mediate the effect of oestrogen on the growth of fibroids.

Future developments in the medical management of fibroids will be aided by greater understanding of their cause and nature, a research subject that has been neglected. At present treatment with agonists of luteinising hormone

releasing hormone is a limited, although effective, alternative to an operation in some circumstances.

DAVID T BAIRD

MRC Clinical Research Professor of Reproductive Endocrinology

CHRISTINE P WEST

Senior Lecturer

Department of Obstetrics and Gynaecology,
University of Edinburgh,
Centre for Reproductive Biology,
Edinburgh EH3 9EW

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Release of genetically altered viruses into the environment

An organism's phenotype may be varied by changing its genome—for example, by altering, deleting, or adding genes. Over the past decade procedures have been developed to engineer such changes deliberately. The selection of natural variants and breeding for particular traits have become commonplace in agriculture, forestry, aquaculture, and animal husbandry. Modern genetic engineering now offers the additional opportunity to obtain change by specifically modifying (adding, replacing, or deleting) a particular sequence of genetic information, by introducing a synthetic gene, or by introducing genes from a source that would not otherwise be interactive with that organism.

Ethical and moral issues are raised by these technologies, particularly as they begin to be applied to higher organisms such as mammals. Most of the genetic information in such complex organisms is unknown and unexplored. Because of this (and some technical difficulties) there are few, if any, opportunities to make precise genetic changes in the genomes of higher organisms and to obtain riskless, predictive results. This will change with time: nascent programmes of research

will undoubtedly illuminate the mammalian genome and allow predictive genetic engineering and genome alterations. Eventually society will have to settle the moral and ethical issues.

In the simplest genetic systems, exemplified by viruses, the basic information is already at hand to undertake predictive genetic engineering. Such information includes knowledge of how to introduce precise changes into specific sites, the complete nucleotide sequences of genes and their regulatory elements, complete genome sequences, the regulation of expression of viral gene products, and in some cases the three dimensional structures of viruses. The molecular biology of viruses has been studied for decades, and a great body of information is at hand, particularly for certain plant, insect, and mammalian viruses—for example, poliovirus.¹ Much practical experience has been gathered with live virus vaccines—for example, vaccinia²—and since the turn of the century naturally occurring baculovirus insecticides have been used to control insect pests of crops, with environmentally acceptable results.³

The genetic engineering of viruses to cause a specific change in their phenotype is a commonplace technology. Alterations can be introduced to test theories of structure and function and determinants of virulence. Many such studies have been already conducted, and as experience grows so do the accuracy and predictability of the results. Consequently scientists are now turning to tackling practical problems by releasing genetically engineered viruses into the environment. These are new generations of live virus vaccines and of viral insecticides.

Because of their replication cycles some viruses are released from the person vaccinated to infect others—for example, poliovirus, which is spread by the faecal oral route.¹ The use of live poliovirus vaccines, which are engineered to be safer than the current vaccines, will raise questions of what, if any, will be the environmental consequences.⁴ Detailed risk-benefit analyses will be needed before such viruses will be licensed for use in medical practice, which should stimulate international discussions, agreements, and regulations.

Another virus that is the subject of intensive genetic engineering is vaccinia virus—to be used, for instance, as a vector of foreign genes to which an immunological response is required. Foreign genes can be engineered into vaccinia and expressed in the patient vaccinated.⁵ Vaccinia has many advantages as a vector, particularly with inducing both humoral and cell mediated immunities.⁵ There are also opportunities to reduce the potential pathogenicity of the parent virus.^{6,7} Currently under trial are vaccinia recombinants designed to induce protection in man to human immunodeficiency virus⁵ and to protect wild life from rabies.⁸ A deliberate release of live vaccinia virus containing the requisite rabies virus genes to infect (and protect) wild life from the disease was started in 1987.

Limited field trials using genetically altered baculoviruses as viral insecticides have been undertaken in Britain since 1986 with government approval and with publicity in the media.⁹ The studies are part of a cautious programme of research into the improvement of natural biological insecticides. The eventual objectives are to produce fast acting insecticides against which the pest species cannot acquire or develop resistance. An example of how this might be achieved would be to incorporate an insect hormone gene into the genetic make up of the virus so that early during a caterpillar infection the pest becomes physiologically

deregulated, causing it to stop eating. Baculoviruses are good subjects for genetic engineering as they are restricted in their host ranges to particular insect species and do not infect, or otherwise affect, other insects, let alone other invertebrates, plants, or vertebrates. These viral insecticides do not pose a threat to man and are environmentally and ecologically preferable to chemical insecticides. A programme of risk assessment into their use has already led to self destructive, pest specific, baculovirus insecticides that can infect a target caterpillar but which afterwards are swiftly degraded. Further studies with the release of genetically engineered virus insecticides with new phenotypes are planned for 1988 and subsequent years.

D H L BISHOP

Professor of Virology and Director,
Natural Environment Research Council Institute of Virology,
Oxford OX1 3SR

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“Dr Kildare let me down”

Soon women will make up half the medical workforce in Britain. Yet they are still rare at the top of the profession. None of the current college presidents are women (although Dr Eileen Adams is dean of the faculty of anaesthetists) and only 2% of consultant surgeons are women—and there is a widespread feeling that life is difficult for women in medicine. Some suggest that “women doctors will be the overseas doctors of the 1990s.” Now a large study of doctors’ careers funded by the Department of Health and Social Security and published last week has produced the chilling finding that not only are many women doctors deeply unhappy about their chosen profession but so also are many men doctors.¹ One told researcher Isobel Allen that “medicine is no longer a desirable profession to be in, and I wouldn’t recommend anyone to go into it.”

A questionnaire was completed by 314 men and 326 women randomly selected from graduates in 1966, 1976, and 1981. The doctors were asked why they had chosen a medical career, and most had done so because they were good at science subjects. Women were more likely than men to have wanted to help people, and they were also more likely to have succumbed to parental pressure—surprisingly from their mothers. Careers advice at school was non-existent or useless—one doctor had been told to take Latin at ‘O’ level and had studied this instead of biology only to discover later that biology ‘A’ level was essential. Schools painted a romantic picture of life as a doctor: “If I’d known more about the hours . . . I don’t think I’d have gone into it. . . . Dr Kildare let me down. . . .” Careers advice at medical school was little better. Of the 1966 cohort, 99% had received no advice, and by 1981, 80% were still getting no careers information from their medical schools. Most of the doctors