

negative result (say, at day 31 of a conceptual cycle) would also reliably induce menstruation. Moreover, RU 486 inhibits ovulation when administered at midcycle before the appearance of the luteinising hormone surge, indicating a further contraceptive possibility for the antiprogestones (R L Collins *et al*, G Schaison *et al*, papers delivered at seventh international congress of endocrinology, Quebec City, 1984). Though these actions chart quite new territory in the regulation of fertility, several problems lie ahead. Regular administration of an antiprogestone as a monthly contraceptive has potential difficulties; if it was given on day 31 of a conceptual cycle chorionic gonadotrophin secreted from the early (and aborting) embryo might remain in the maternal circulation for several days because of its long plasma half life. That might in turn sustain the corpus luteum and the secretion of progesterone for long enough to delay the return of normal ovarian folliculogenesis. The patient would be unlikely to ovulate 14 days after the start of her menses—and could, therefore, take the antiprogestone steroid at an inappropriate, preovulatory time in her next cycle.

Antiprogestone drugs may have a further use in the induction of labour in late pregnancy, because they appear to release prostaglandins from human endometrium.¹⁰ We do not know, however, whether antiprogestones cross the placenta and whether they can affect the fetus directly. Placental progesterone seems an important substrate for the fetal synthesis of cortisol as the fetal adrenal lacks the 3β hydroxysteroid dehydrogenase enzyme necessary for biosynthesis of cortisol from pregnenolone. An antiprogestone might, therefore, reduce fetal secretion of cortisol and interfere with glucocorticoid dependent processes such as the production of surfactant in the fetal lung, quite apart from any concomitant antagonist action on glucocorticoid receptors.

These drugs might also offer a new medical treatment for Cushing's syndrome. In keeping with its binding to the glucocorticoid receptor RU 486 raises concentrations of adrenocorticotrophic hormone and cortisol in monkeys and in man.^{11,12} This antiglucocorticoid action occurs at a substantially higher dose than the antiprogestone effect, suggesting a margin of safety in pregnant patients who might later require curettage to complete emptying of their uterus. The induction of anaesthesia in such women does not alter their cortisol secretory response to this stress and does not interfere clinically with their anaesthetic.^{8,9}

All these developments represent a real breakthrough in the regulation of fertility. Several pharmaceutical companies have given priority to the development of antiprogestones, aiming at developing drugs which specifically antagonise through the progesterone receptor without binding to the glucocorticoid receptor.^{5,13} If their efficacy is proved the progesterone receptor antagonists will herald a new contra-gestational approach to fertility control and raise several critical medical, moral, and legal questions (E E Baulieu *et al*, paper delivered at CIBA Foundation symposium No 115, November 1984). Firstly, what are the risks to the fetus in early pregnancy if the patient takes an incomplete course of antiprogestone treatment? Secondly, will prescription of such drugs be confined to hospitals or allowed on the NHS by general practitioners? Thirdly, how should the demands of women for their right to choose in this new aspect of gynaecology be addressed? Should antiprogestones be available without prescription? And, finally, is it indeed legal to prescribe these medicines in Britain? In England and Wales abortion is taken to include

all procedures performed from the time of implantation.¹⁴ Giving an antiprogestone drug to a woman whose period is delayed by two or three days may therefore be an offence under the 1967 Abortion Act. By contrast, Scots Common Law takes abortion to mean those procedures performed from the time that the woman can be shown to be "with child" by reasonably available methods, which is usually accepted as six to eight weeks of pregnancy. Similar laws requiring proof of pregnancy are widespread throughout the Commonwealth and would allow antiprogestones to be used in those countries without legal liability for abortion.

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Who should have an intraocular lens?

Should we advise our patients to have a lens implant after removal of their cataracts?

Replacement of a cataractous lens by an equivalent implant of plastic has many advantages over the traditional pebble spectacles. These limit clear vision to a central field, are initially very distorting and clumsy, and prevent the use of the eyes in unison unless the fellow eye is also aphakic. Contact lenses may minimise these disadvantages, but they bring problems of their own—particularly for the elderly, who along with poor sight often have shaky or arthritic hands and so find them hard to manipulate. So the appeal of the implant is enormous, most patients have heard about them, and many are disappointed if their eye surgeon declines to provide this undoubted benefit.

It is now 35 years since that first lenticulus was inserted at St Thomas's Hospital, initiating a controversy that has swollen journals, provoked the ingenuity of technologists and the polemics of their advocates, and resulted in over 20 national intraocular lens societies and a flood of congresses (including a three day international intraocular lens congress at Harrogate in September 1984), in which the indications, techniques, and minuscule alterations in design were disputed as warmly as ever. The overall legitimacy of implants is fully accepted, but in most other aspects consensus still seems far away.

Well over 100 patterns of implant have already been marketed; and though the essential requirements are now fairly well accepted refinements continue unabated. These are issues of concern only to the specialist, however, and until there is established evidence of priority the individual surgeon may reasonably continue to use the type and procedure with which he feels most at ease. Apparently most implants in Britain are now almost equally divided between the pupil supported lenses after intracapsular extraction and the (increasingly popular) posterior chamber lenses within the lens capsule after extracapsular extraction; the various types of anterior chamber lenses take third place.¹

The real problem is the risk of complications. The most common and most damaging is injury to the corneal endothelium, leading to gross loss of vision from intractable corneal oedema, which corneal grafting cannot always rectify. These endothelial cells have negligible powers of regeneration, and their population diminishes throughout life; should it fall below a critical level aqueous can no longer be excluded from the cornea, which then becomes opalescent. So damage to the endothelium when the implant is being introduced may not only cause an immediate (and disastrous) oedema but even if insufficient to reduce the cell population below a critical level at once it may well bring nearer the day when the population does become too sparse, and oedema (bullous keratopathy) ensues. Thus the failure rate of implant surgery may well increase as the years pass, and for this reason most surgeons normally reserve the use of implants for the elderly with a short life expectancy. In a recent follow up at Oxford two eyes had corneal oedema three years after surgery, but five years later nine patients (12% of the 77 survivors) were affected,² and this has been paralleled by figures from other long term follow ups.^{3,4} As a grim reminder we find in Britain⁵ as in the United States (R Lindstrom, personal communication) that bullous keratopathy due to implants has now become the most common indication for corneal grafting.

The incidence of bullous keratopathy—as of other direct complications (including dislocation of the implant and persistent uveitis)—has steadily declined, however, as a result of improvement in techniques, instrumentations, and medication, along with the gradual elimination of the less satisfactory types of implant and better selection of patients. So this increasing risk of corneal damage as the postoperative years pass may soon become less formidable.

On the other hand, the gratifyingly low rate of complications in most published series does not reflect the frequency of disasters in the world at large, nor indeed do such reports always provide really adequate documentation and follow up. And the integrity of the results is further impeached when we discover that some eye doctors have a direct (but concealed) financial interest in promoting certain types of lens.⁶

Unhappily, the adoption of this major clinical advance of such wide and unquestioned benefit has been darkened by

alien commercial pressures and immoderate publicity—reflected in the contrasting popularity of implants among Western countries: from about 70% of cataract operations in the United States to 46% in Britain,¹ and probably nearer 20% elsewhere in western Europe.⁷ Furthermore, the absence of any real consensus on the indications for implant surgery leaves the field wide open, with a few enthusiasts inserting lenses into the eyes of children or already damaged eyes while at the other end of the spectrum many surgeons still decline to use them at all. It could be added that the market price of such lenses is rarely less than £100 (at nearly £10 000 a month at Moorfields their cost is greater even than the budget for contact lenses and a quarter of the total drug bill). This cost may conceivably be justified in terms of fewer outpatient visits afterwards and an improvement in the quality of vision, but this has already forced some British hospitals to curtail their use of lenses.¹

Thus the accepted indication for an implant is an otherwise sound eye with an advanced cataract, especially if the fellow eye is not only healthy but retains good vision, in an elderly patient (over 60) who is unlikely to cope with spectacles or contact lenses. Younger adults deserve implants if they have especial need for binocular vision (the other eye having good vision) and cannot tolerate contact lenses because of sensitivity and so on.

In still younger age groups implants are recommended only when the circumstances are very exceptional, when the surgeon himself is an expert, when follow up will be scrupulous (the lens may also need to be replaced, with doubled risks, in the case of a growing child), and when the patients are fully aware of the pros and cons.¹ Indeed, all patients should be informed of the added morbidity—about a 5-10% risk overall—and this applies with greater force when the eye is already damaged or when the fellow eye is imperfect. Simpler forms of implants are well within the compass of any experienced eye surgeon, as long as he knows the special risks and will provide scrupulous postoperative care, which often entails protracted use of topical steroids and of pilocarpine when the lens is held by the pupillary sphincter.

Implants are less often justified in patients with a long-standing myopia, especially when this is over about 5 dioptres, for the removal of an opaque lens may largely neutralise their myopia (and the implant also carries a slightly increased risk).

These reservations have already been sadly stretched by surgeons who are most vulnerable to commercial and social pressures and whose technical confidence shrouds the manifest need for longer term follow ups. One fine day implantation may become almost routine, especially if we can show that the new materials and methods have lived up to their promise. But not yet.

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