BRITISH MEDICAL JOURNAL

LONDON, SATURDAY 5 JUNE 1976

# Mid-trimester termination

Two factors are tending to increase the demand for an efficient, safe method of midtrimester abortion. There are, firstly, recent advances in prenatal diagnosis of fetal malformation, and, secondly, late attendance by some patients requesting termination of pregnancy. An ideal method should combine ease of induction, freedom from side effects and dangers, minimal requirement for surgical intervention, and, finally, a short induction-abortion interval. How do our techniques match up to these needs?

Since prostaglandins were introduced for clinical use many earlier methods have been discarded in favour of these potent, pharmacologically active agents. Intra-amniotic injection of hypertonic saline continues to be used in some units, but, though generally effective, it may lead to the potentially lethal condition of hypernatraemia, especially if technical difficulties are encountered.[1] Changes in coagulation factors also occur and may progress to a consumption coagulopathy.[2] Comparisons of the efficacy and safety of intra-amniotic saline and of prostaglandin administration by the same route have hitherto been ill-defined, so that the article at p 1373 is welcome in providing objective data.

The prostaglandin preparations continue to have disadvantages related to the route of administration and to high dosage regimens. Oral, vaginal, and intravenous routes may all be complicated by a high incidence of unpleasant side effects —especially diarrhoea, vomiting, and (in the case of intravenous therapy) a progressive painful phlebitis. The induction-abortion interval is more unpredictable than with alternative methods, and coupled with the high incidence of side effects renders these routes generally unacceptable.

These problems have been largely overcome by the use of intrauterine routes, when a smaller total dose of prostaglandin may be given with an improved abortifacient effect. Successful termination of pregnancy using an extraovular technique was described by Wiqvist and Bygdeman in 1970.[3] Intermittent extraovular instillation results in abortion within 36 hours[4] and this induction-abortion interval can be further reduced by adding an intravenous infusion of oxytocin.[5] The disadvantages of intermittent instillation may be overcome either by a continuous infusion system[6] or by intra-amniotic injection. The incidence of postabortal uterine infection is low; nevertheless, the extraovular route is contraindicated when gonococcal infection of the genital tract is present, emphasising the need for bacteriological examination before inducing abortion.

Intra-amniotic injection has the disadvantage of requiring transabdominal puncture, which may be complicated by occasional bloody taps and by a more prolonged induction-abortion interval, probably owing to the dilutional effect of the amniotic fluid. A combination of intra-amniotic prostaglandin with urea resulted in a reduction of the time to abortion to about one-third,[7] but MacKenzie *et al*[8] showed that it also led to an increase in blood concentrations of fibrin degradation products and a fall in fibrinogen and platelets, with the risk of developing intravascular coagulation. These changes were not observed when patients were treated with prostaglandin alone.

Instillation-abortion intervals show a wide variation with intrauterine routes. Csapo *et al*[9] and Tyack *et al*[10] showed that a short induction-abortion interval was related to a rapid decrease in peripheral plasma progesterone levels. Moreover, since progesterone is produced by the placenta this decrease may reflect placental damage as a result of the initial uterine contraction after the prostaglandin injection—the so-called "prostaglandin impact." Conversely Jouppila *et al*[11] failed to show any significant relationship between the induction-abortion interval and the primary hormonal response of the placenta or the interval between induction and fetal death. The rise in maternal serum alphafetoprotein which preceded fetal death was also unrelated to the time to abortion, a finding confirmed by Ward *et al*.[12] These factors suggest that the abortifacient effect of prostaglandin is not due to an effect on the fetus or placental function.

Recognising that some patients showed a lack of subsequent cyclical uterine contraction after instillation of prostaglandin, Csapo[13] suggested the double-impact technique, in which the initial effect is amplified through the direct and rapid contact between the drug and uterus at two extraovular points. He showed that termination of pregnancy occurred in virtually all patients with a mean induction-abortion interval of 16½ hours. This method compares well with the intra-amniotic route: it is less invasive and does not require the frequent attention to equipment that may become necessary with constant-rate infusion techniques.

The use of powerful uterine stimulants is not without risk of uterine rupture, which has taken the form of posterior cervical laceration[14] in most reported cases. Patients in whom this complication occurs are mainly young primigravidae with a cervix resistant to dilatation, a well-recognised problem preceding suction termination. All patients should have a vaginal examination after abortion. The practice of priming

the cervix with prostaglandin before vacuum aspiration may perhaps be extended to include patients for mid-trimester abortion with the aim of reducing cervical trauma.

Methods for mid-trimester termination will continue to improve. Nevertheless, inevitably their efficiency depends on understanding the role of prostaglandin in stimulating uterine muscle activity and that of progesterone and 17β oestradiol in the maintenance of pregnancy.


[1] Kerenyi, T D, Mendelman, N, and Sherman, D, *American Journal of Obstetrics and Gynecology*, 1973, **116**, 593.
[2] Cohen, E, and Ballard, C A, *Obstetrics and Gynecology*, 1974, **43**, 300.
[3] Wiqvist, N, and Bygdeman, M, *Lancet*, 1970, **2**, 716.
[4] Embrey, M P, Hillier, K, and Mahendran, P, *British Medical Journal*, 1972, **3**, 146.
[5] Morewood, G A, *Journal of Obstetrics and Gynaecology of the British Commonwealth*, 1973, **80**, 473.
[6] Midwinter, A, Bowen, M, and Shepherd, A, *Journal of Obstetrics and Gynaecology of the British Commonwealth*, 1972, **79**, 807.
[7] Craft, I, *Lancet*, 1973, **1**, 1344.
[8] MacKenzie, I Z, *et al*, *Lancet*, 1975, **2**, 1066.
[9] Csapo, A I, Kivikoski, A, and Wiest, W G, *Prostaglandins*, 1972, **1**, 305.
[10] Tyack, A J, *et al*, *Journal of Obstetrics and Gynaecology of the British Commonwealth*, 1974, **81**, 52.
[11] Jouppila, P, *et al*, *British Journal of Obstetrics and Gynaecology*, 1976, **83**, 303.
[12] Ward, R H T, *et al*, *British Journal of Obstetrics and Gynaecology*, 1976, **83**, 299.
[13] Csapo, A I, *et al*, *American Journal of Obstetrics and Gynecology*, 1976, **124**, 1.
[14] Wentz, A C, Thompson, B H, and King, T M, *American Journal of Obstetrics and Gynecology*, 1973, **115**, 1107.


# Diploma in Pharmaceutical Medicine

The number of doctors in the British pharmaceutical industry has increased steadily over recent years. The responsibilities of these medical advisers (or pharmaceutical physicians as they are now frequently known) have grown with the demand for more extensive, elaborate, and controlled testing of new medicines for safety and efficacy. There is also an increasing need for closer monitoring of medicines when they are marketed and become freely available to the prescribing doctor. Add to this the detailed knowledge of the mushroom growth in medicines legislation in recent years, and the result is a challenging job-specification.

The recommendations of the Royal Commission on Medical Education led to the formation of groups to consider higher medical education and training, and these were given added urgency when Britain joined the European Community and so entered its discussions on specialist registration. In consequence the Association of Medical Advisers in the Pharmaceutical Industry (AMAPI) began to look for ways by which physicians in the industry could secure their own special professional status. These moves, which began in 1969, led to the formation in 1973 of a small working party of doctors, later to become formalised as the Joint Advisory Committee on Pharmaceutical Medicine, drawn from the AMAPI and the medical committee of the Association of the British Pharmaceutical Industry (ABPI). This group met with the Council for Postgraduate Education in England and Wales, the Joint Committee on Higher Medical Training, and the Royal Colleges of Physicians, among others, to determine how the professional status of the doctor in industry might be secured through specialist registration and to explore the possibility of the foundation of a specialist medical diploma. The group is also planning to maintain the standards of medical entrants to the industry by providing for their training and further education—and, indeed, the AMAPI organised a successful training course during 1974.

The Royal Colleges of Physicians have now invited applications from candidates intending to sit the first examination for the Diploma in Pharmaceutical Medicine. The Joint Advisory Committee has recently completed the organisation of a two-year training course in pharmaceutical medicine, and the first course will begin in November. It will meet part of the requirements demanded of candidates wishing to sit the examination for the diploma. Regulations also require that the candidate should have undergone certain periods of general medical training and experience in the pharmaceutical industry. While many established and experienced doctors in the industry and physicians in the medicines division of the DHSS should be eligible to sit the examination without meeting these specific requirements, the training course should not only attract new entrants to the industry but also serve as a refresher course.

The Joint Committee on Higher Medical Training has also agreed that time spent in certain approved posts in clinical pharmacology in the pharmaceutical industry will count towards the period of higher medical training leading to accreditation in clinical pharmacology. Meanwhile, discussions about specialist registration continue throughout and on behalf of the whole medical profession. Doctors in industry hope that, by securing their professional status and by maintaining their current high standards through the diploma and training programmes, they may ensure that pharmaceutical medicine will become a recognised specialty.

# Treatment of retinitis pigmentosa

Retinitis pigmentosa is the term used to describe a heterogeneous group of heritable disorders, each with a different prognosis and probably a different basic aetiology. It is a common cause of hereditary blindness, with a prevalence possibly as high as 0·5% of the world population.[1] A few of these disorders produce blindness in childhood and adolescence; others result in blindness in the third and fourth decades of life; while an appreciable proportion of patients with retinitis pigmentosa retain useful central vision into old age.

During the past few months, largely as a result of publicity in the national press, increasing interest has been shown in a method of treatment for retinitis pigmentosa which is being carried out in one hospital in Moscow and possibly in a few other centres throughout the world. As a direct result of this interest some patients with retinitis pigmentosa have travelled to the USSR to undertake treatment (their trips being financed privately or sponsored by charitable organisations or other bodies). Many others have been inquiring about the value of this treatment.

Ever since retinitis pigmentosa was first adequately described over a century ago a steady stream of methods have been advocated for its treatment—vasodilators, tissue therapy, anticoagulants, vitamins, corticosteroids, hormonal extracts, miotics, mydriatics and enzymes, as well as galvanism, *x* rays, ultrasound, and surgical methods intended to improve the circulation of the eye. Few, if any, had a good scientific basis for their use; and none have stood the test of time. Only one