Prostaglandins in obstetrics and gynaecology

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THE first reports of the use of the natural prostaglandins in the field of obstetrics and gynaecology appeared in 1968, initially for the induction of term labour in patients with fetal death and subsequently for patients with a live fetus. Since then numerous clinical reports have described the efficacy of using prostaglandins for this purpose administered by a variety of different routes and also for other indications particularly the induction of pre-term labour and for termination of pregnancy.

In physiological terms, the role of prostaglandins in the functions that this speciality covers, e.g. fallopian tube and spermatozoal motility, ovulation, conception, corpus luteal development, and myometrial contractility, remains inconclusive since there appear to be important differences between members of various animal species and the human female. Earlier problems with assaying the natural prostaglandins led to differences of opinion as to whether, for example, circulating prostaglandins increased during pregnancy and labour, and whether their release was possibly associated with the initiation and maintenance of the latter process. Peripheral blood sampling has failed to confirm any such definite association but that does not imply that subtle and possibly transient changes do not occur in the foeto-placental unit, since it has been suggested that the more stable prostaglandin metabolites increase in liquor during late pregnancy and indeed during labour, and that prostaglandin levels are higher in the foeto-placental unit than in the mother. Results of tests in circulating natural prostaglandin levels performed in the Institute of Obstetrics and Gynaecology do not indicate a surge immediately preceding the onset of labour as has been described in the sheep, but rather a peak occurring at about 36 weeks with a subsequent fall. With regard to corpus luteal function there is evidence in some animals that prostaglandins are luteolytic. However, prostaglandins do not appear to be luteolytic in the human female with doses that are clinically tolerable. The

implications for fertility control would be profound if this were so.

The current situation so far as the clinical use of prostaglandins are concerned in obstetrics and gynaecology indicates that their introduction has revolutionized certain aspects of management. With one particular application we have established that fetal death *in utero* can be actively managed with a minimum of disturbance to the patient by injecting prostaglandin E_2 suspended in a base of methyl ethyl cellulose (Tylose) extra-amniotically via a simple catheter inserted through the cervix and outside the gestation sac, with subsequent removal of the catheter. The dose used will depend upon the favourability of the cervix and the gestational length but it is unusual to require more than 2.5 mg prostaglandin E_2 . The results to date have been very encouraging and associated with very few side effects. Whilst we have previously established that intra-amniotic prostaglandin $F_{2\alpha}$ (50 mg) or prostaglandin E_2 (20 mg) may also be effective following a single injection, the hazards of performing a trans-abdominal intra-amniotic injection in this situation are far greater.

The use of a smaller dose of prostaglandins E_2 (300 μ g) administered in the same manner as previously described has also been found to be particularly applicable for improving the state of the unfavourable cervix in patients in whom induction is planned. In an initial pilot study comparing the effects of injecting prostaglandins in Tylose, with Tylose alone in unfavourable patients, eight out of fifteen patients receiving the prostaglandin preparation went into spontaneous labour as opposed to only one receiving the Tylose alone. In addition, in the remainder of patients, the state of the cervix improved sufficiently to make induction technically more feasible the following day, whilst no change was noted in the other group. Further studies have confirmed that the use of prostaglandins administered in this manner to unfavourable patients has resulted in a lowered Caesarean section rate. The use of the same agent has also been applied as a method of inducing

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labour in patients with more favourable induction features and has a high patient acceptability since labour commences in an apparent spontaneous manner when compared with alternative techniques such as amniotomy and intravenous oxytocin stimulation.

Whilst prostaglandins administered in this fashion may have obvious indications and advantages, it is still possible to achieve these objectives by other routes of administration; however, the time to achieve mid-trimester abortion or delivery may be longer and the incidence of side effects more frequent with systemic as opposed to local administration. Oral prostaglandin (PGE_2) is also effective for inducing labour particularly in multiparous patients with a relatively favourable cervix when given in doses of 0.5–2 mg every 1–2 hr but larger doses may be necessary to induce effective uterine activity in patients with less favourable conditions and consequently gastro-intestinal side effects are more likely to result. Similarly, the augmentation and potentiation effects reported with oxytocin have led some to consider that, with intravenous usage, the two agents should be administered together rather than sequentially, since quantitatively less of

each drug is required than if either were used alone and hence side effects of prostaglandins are likely to be reduced. However, there still remains a certain hesitancy in using prostaglandins in routine therapy for many obstetric patients either for augmentation or induction of labour since oxytocin administered intravenously usually is effective and most obstetricians have already become familiar with this agent. In some situations where water retention due to oxytocin is a potential problem, for example pre-eclampsia, prostaglandins may have a particular role.

The place of prostaglandins in the management of first trimester abortion is really undecided. Some have advocated using pessaries as a pre-operative measure to induce some degree of uterine activity and thereby minimize the amount of cervical trauma needed to dilate the cervical canal at surgical evacuation of the uterus. Most institutions in the U.K. still favour surgical evacuation rather than the alternative of using an impact dose of prostaglandin $\text{F}_{2\alpha}$ 50 mg as has been advised by others. Prostaglandins suspended in Tylose have been found to be efficacious particularly in those patients in whom the cervix is rigid and especially in those difficult situations between 12 and 16 weeks' gestation.