Opening Remarks

E.Saling

Our great international community of obstetricians and perinatologists is holding its family get-together in Berlin again. Berlin is in the true sense of the word a meeting place full of nostalgia - the greek word nostos means "home-coming" and algos means "pains", so "homesick for the good old days".

It was here in Berlin 15 years ago that the 1st International Meeting of the then active perinatologists took place from 28th to 30th March 1968 within the framework of the 1st European Congress of Perinatal Medicine. From the number of participants - 1,287 took part - it is clear to see how much interest already existed at that time.

But we should not look at the Berlin meetings only in a nostalgic way; during the course of the first congress mentioned above, the European Association of Perinatal Medicine was founded and has met every other year since 1968 - eight times in all - in various European cities under the presidency of outstanding colleagues. Independent of these, 10 German congresses dealing with this important and new field of medicine have taken place here in Berlin. These congresses - 18 in all - held in Europe and Berlin have offered the most highly concentrated impulses for continuing research and have conveyed medical and clinical knowledge from all over the world. These facts are highly encouraging and stimulating both for you as participants and for us, the organizers.

It is not our wish that the International Berlin Meeting - affiliated to the German Congress for four years - should become a big event. Its purpose is rather to give all foreign colleagues sympathizing with the scientific activities going on in Berlin, the opportunity of visiting the meantime classical old home of perinatal medicine, and so to renew old memories and also at the same time to hear about the latest scientific findings first hand from the abundant contributions to the great 11th German Congress taking place here now, and also from the contributions of guests invited from overseas.

With this in mind I wish every success to the 3rd International Berlin Meeting and a pleasant and informative stay in Berlin to all the participants.

CLINICAL ROLE OF PROSTAGLANDINS IN MODERN OBSTETRICS

Moderator: Fritz Fuchs, M.D., Cornell University Medical College, New York, New York

Panelists: Andrew A. Calder, M.D., University Department of Obstetrics and Gynaecology, Royal Infirmary, Glasgow, Scotland

Klaus Goeschen, M.D., Arbeitsgruppe Perinatale Medizin, Freie Universität Berlin

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F. Fuchs: Physiological Role of Prostaglandins in Human Parturition.

The ability of prostaglandins (PG) E_1, E_2, and $F_{2\alpha}$ to stimulate the uterus to contract at any time of gestation suggest a role in the physiological activation of the uterus in parturition. This hypothesis is supported by the fact that prostaglandin synthetase inhibitors can inhibit preterm labor and delay parturition, by the marked rise in the amniotic fluid levels of PGE_2 and $PGF_{2\alpha}$ during term labor, and by the rise in the circulating levels of the $PGF_{2\alpha}$ metabolite 13,14-dihydro-15-keto-$PGF_{2\alpha}$ (PGFM) during advanced labor.

All uterine tissues have the capacity to synthetize PGs, although the spectrum varies from tissue to tissue, and no marked changes occur at the onset of labor. It seems clear that the capacity to produce PGs from endogenous substrates exists long before labor begins and substrate availability is not a limiting factor. We must assume that under in vivo conditions, prostanoid synthesis is kept at bay by inhibitory factors which are withdrawn during parturition, or that stimulatory factors increase the rate of production of PGs during labor. We have found that oxytocin is a potent stimulator of prostaglandin synthesis. It is an attractive hypothesis that a fetal signal initiates labor, a belief held already by Hippocrates. We propose that fetal oxytocin provides such a signal by stimulation of the prostanoid production in uterine tissues which then enhances the contractions elicited by oxytocin. Besides PGE_2 and $PGF_{2\alpha}$, prostacyclin and to a lesser degree thromboxane and PGD_2 are formed within the human uterus. The decidua may be an important site of PG synthesis and its proximity to the myometrium suggests that oxytocic PGs from this tissue could play an important role in myometrial activation. Both myometrium and decidua contain oxytocin receptors, with the highest concentrations in early labor.

Prostaglandins, together with relaxin, estrogens and progesterone participate in the control of cervical ripening which is necessary for successful parturition.

The evidence suggests that oxytocin initiates labor and that the prostaglandins interact in the maintenance of labor, expulsion of fetus and placenta, and the post partum hemostasis.

A.A. Calder: Comparison of Various Methods of Induction of Cervical Ripening and Labour, Including Prostaglandins, Oxytocin, Oestradiol and Mechanical Means.

Human parturition is not the rather sudden phenomenon it may sometimes appear, but a gradual evolution of uterine contractility and cervical ripening, occurring in concert over several weeks at the end of pregnancy. When induction of labour becomes necessary for the safe delivery of the infant, attention must be paid to the status of the cervix; methods to accelerate ripening of the cervix will greatly increase the success of induction of labour and reduce the need of surgical intervention. There is no better indicator of the likely response to induction of labour than the condition of the cervix, the dilatation, effacement and compliance of the cervix. If the cervix is not ripe then induction of labour without first taking steps to ripen the cervix may lead the mother, the fetus and the obstetrician into trouble.

(1) Mechanical methods, often of bizarre character have been proposed but are mostly of historical interest with the exception of intracervical balloons and laminaria which result in release of prostaglandins as do amniotomy and even sweeping of the membranes.

(2) Oxytocin, the most commonly used agent for induction, does have some effect on cervical ripening, but its effect is greatly enhanced by amniotomy. The primigravida with an unripe cervix will respond poorly to oxytocin infusion, if amniotomy cannot be done.

(3) Prostaglandins have largely compensated for the deficiencies of oxytocin. The method of choice is direct application of PGs toward the cervix (extra-amniotically, endocervically, or vaginally) in a gel or pessary. When the cervix is ripe, amniotomy and/or oxytocin infusion can be used to enhance uterine contractions.

(4) Other hormones, such as oestrogens and relaxin have been used for cervical ripening. They may be less effective but do not seem to cause uterine contractions, allowing ripening and induction to be accomplished separately.

K. Goeschen: Comparison of Various Applications of Prostaglandin E_2 for Cervical Ripening.

It is important to determine the best form of application, the optimal doses, the best frequency of application, and the best way to avoid or treat excessive uterine activity. PGE_2 can be given as infusion, as endocervical injection dissolved in a gel, as application in a cervical cap or as injection through a cervical balloon catheter. Our studies have shown that the simplest and most practical application is 400 µg PGE_2 dissolved in gel endocervically every 8 hours. The best results were found in the catheter group but the difference was small and the ease of injection of a gel with a blunt cannula made this form of application the preferred method. In more than half of the cases, a single application was sufficient. If more than one application was required, an interval of 8 hours was found to be best. Doubling the dose to 800 µg did not improve the results but led to a higher incidence of undesirable uterine activity.

Simultaneous administration of a betamimetics did not reduce the ripening effect of the PGE_2 application. This supports the hypothesis that PGE_2 applied endocervically exerts its effect locally and not by enhancement of the uterine activity.

The recommended procedure for cervical ripening is:
(1) Endocervical injection of 400 µg PGE_2 in gel.
(2) If ripening has progressed by 8 points in score, induction of labor by oxytocin and/or amniotomy.
(3) If the score is less than 8, a 2nd inj. of 400 µg PGE_2 gel.
(4) If a third application is necessary, place a 15 ml balloon catheter in the cervix for injection of 400 µg PGE_2 gel.
(5) If uterine contractions are undesirable, use tocolytic agents simultaneously.

M.J.N.C. Keirse: Comparison of Various Prostaglandins for Induction of Abortion, Missed Labour and for Treatment of Post-Partum Atony.

In the first trimester, none of the known PG regimens can match the convenience and acceptability of vacuum aspiration for termination of pregnancy. Moreover, the use of PGs do not eliminate the need for aspiration since the incidence of incomplete abortion is considerable, though depending on method and gestation age. Selective use of PGs to lower the cervical resistance in women with a rigid cervix is an advantage, though there is disagreement about the choice of PG and the dosage. Vaninal suppositories of 0.5-1.0 mg of 16,16-dimenthyl PGE_2 analogues, intramuscular injection of 250-500 µg sulprostone or intracervical injection of 25 µg sulprostone has been recommended.

In second trimester termination a number of applications have been studied. Systemic application of natural PGs is obsolete. Extraamniotic instillation of 200 µg PGE_2 or 750 µg $PGF_{2\alpha}$ every 2 hours or by continuous infusion has a high success rate and low incidence of side effects but oxytocin may be needed as adjuvant treatment. Many analogues have been tested; at the moment sulprostone appears to be the best choice; 0.5 mg i.m. every 4 hrs, 1.5 mg i.v. over 6 hrs or 1.0 mg i.v. over 10 hrs seem to be useful schedules.

For the management of antepartum fetal death the natural PGs have more disadvantages than some of the newer analogues. Intramuscular administration of 250 µg of 15-methyl-$PGF_{2\alpha}$ every 2 hours or 500 µg sulprostone every 4-6 hours is very effective; reducing the dose to half may yield almost as good results.

Post partum atony is a dreaded complication where the use of PGs may be life-saving. The reported experience is limited, but the available data suggest that intramyometrial injection of 250 µg sulprostone, 125 µg 15-methyl-$PGF_{2\alpha}$ or 1.0 mg $PGF_{2\alpha}$ may control severe postpartum bleeding due to inability of the uterus to contract spontaneously or respond to oxytocin or ergot preparations.

The subsequent discussion dealt with the problems raised by the panelists.