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Clinical Use of Prostaglandins

There is little doubt that in the prostaglandins we have a group of new and powerful oxytocic hormones with a wide clinical application. A recent conference in New York[1] showed the remarkable advances made in this field. In particular, speakers discussed termination of pregnancy, induction of labour, and, possibly most important of all, chemical synthesis of the compound.[2-4]

Three groups, led by S. M. M. Karim at Makerere in Uganda, M. P. Embrey at Oxford, and M. Bygdeman and M. Wiqvist at Stockholm, have carried out clinical studies with prostaglandins to induce abortion.[5-9] These hormones have also been used to evacuate the uterus in cases of missed abortion and hydatidiform mole.[10 11] Karim's and Embrey's results show that both the E series of prostaglandins (prostaglandin E_1 or E_2) and the F series (prostaglandin $F_{2\alpha}$), given as an intravenous infusion, will stimulate spontaneous abortion in more than 90% of women with pregnancies between 9 and 28 weeks of gestation. Prostaglandin E_2 has some advantages over $F_{2\alpha}$, for it is about ten times more potent and rather less apt to cause the unpleasant vomiting and diarrhoea that accompany intravenous prostaglandins in high concentration. The Swedish workers[8 9] have not been so successful with inducing abortions in the second trimester with either intravenous or intrauterine prostaglandins, the reason for which is not clear. At the New York Conference Karim[1] reported on the administration of 20 mg. of prostaglandin E_2 or 50 mg. of $F_{2\alpha}$ to 45 patients in the form of a pessary inserted into the vagina every 2½ hours. Abortion was successful within 15 hours in every case. This remarkable result carries the implication that if prostaglandins became readily available, abortion on demand and at any time in pregnancy will become a practical possibility. The social ethical, and clinical consequences of putting them to such use will need careful evaluation.

Prostaglandins have also been used to induce labour in the last trimester of pregnancy.[10 11 13-16] The sensitivity of the myometrium to these substances varies at different stages of pregnancy,[17] but published studies, which now include reports on 174 women, indicate that prostaglandins are efficient oxytocics. Successful induction of labour, as judged by the presence of regular uterine contractions and progressive dilatation of the cervix, was achieved in all but five women. It thus seems possible that prostaglandins are more effectual than oxytocin. This does not mean that they are necessarily preferable in clinical practice, and here it is worth recalling an observation from a leading article[18] in these columns two years ago: "It would be difficult for any drug to supersede intravenously administered oxytocin for the induction of labour unless it caused neither uterine hypertonus when infused in excessive amounts nor an antidiuresis."

A recent study[19] with prostaglandin $F_{2\alpha}$ at a therapeutic dosage showed it to be free of the antidiuretic effect of oxytocin given at a comparable oxytocic dose. However, uterine hypertonus in response to prostaglandin

still remains a possibility. Transient hypertonus of the uterus at term has been reported when a high dose of prostaglandin E_2 was used,[14 15] but since this is likely to occur with any oxytocic in excessive dosage the observation is of limited clinical significance. Of greater importance is the possibility that occasionally prostaglandins in therapeutic dosage may, like oxytocin, increase the resting tone of the uterus. Karim[13] considers that this can be avoided by always using constant low-dose infusion. However, other workers[14] have thought that, because of the wide variation in myometrial sensitivity to prostaglandins, a variable dose tailored to suit each patient is necessary. Such an approach, unless uterine pressure is carefully monitored, would be more likely to increase the possibility of hypertonus. Perhaps the double blind trials with oxytocin and prostaglandin E_2, recently completed at Makerere and Queen Charlotte's Hospital, London, will resolve this question.

Speculation is now active on whether prostaglandins or a prostaglandin-antagonist may prove to be effective in the control of fertility. This could take the form of early abortion by the insertion of a pessary of prostaglandin into the vagina as soon as the first period has been missed.[2] But prostaglandins also have other interesting properties, recently well reviewed by L. Speroff and P. W. Ramwell,[20] in that they may act at an even earlier stage of conception by delaying nidation or interfering with the function of the corpus luteum. B. Pharriss has found that they terminate the production of steroid by the corpus luteum in several species, including the monkey.[21] Prostaglandins are also known to alter tubal motility in women,[22] and that could impede the passage of the ovum down the tube. Alternatively a prostaglandin inhibitor may prove to have contraceptive properties in either sex, and the recent report[23] of the successful use in animals of such a compound, polyphloretin phosphate, is of considerable interest.

Now that prostaglandins can be chemically synthesized there should be sufficient for all at reasonable cost. They will not be regularly available for clinical use until the completion of the trials at present in progress.

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Seebohm Sequel

Some doctors have been astonished at the scale of salaries now being offered in the spate of advertisements for directors of social service departments in local authorities. Over £8,000 per annum is not uncommon. But those doctors who have closely followed the unfolding of the Seebohm scenario—whatever else they may feel—will not be very surprised.

The social workers, having won their battle for separate departments within the local authority, can argue logically that the heads of these departments as chief officers should receive rewards comparable with their fellow chief officers, including of course the medical officer of health. The question which immediately comes to mind is whether there will be enough candidates of suitable qualifications and experience to fill these posts. With difficulties already arising over the division of responsibilities between the old health and the new social services departments and with unhappiness among some local authority doctors about the nature of their role as advisers to these new departments, the situation calls for departmental heads of considerable experience and ability if inter-departmental friction is to be avoided.

In broad terms the objective of the Seebohm Report's proposals[1] and the subsequent Act[2] was to improve the co-ordination of the welfare services and to ensure the concentration of social-work skills for the greatest benefit of the family. It was a commendable objective, but public health doctors, strongly supported by the B.M.A., thought all along that the reorganization proposed could well have the opposite effect. Their opinion was shared by the Central Health Services Council, which in its 1969 annual report[3] made some severe criticisms of the report, saying that the "proposed separation of medical and social work would not only be administratively disastrous but would be to the great disadvantage of the patient." The Central Health Services Council also foresaw that there would be "insufficient trained social workers available to enable social service departments to be set up within the time limit proposed by the Report."

Nevertheless, the political pressure was such that there was a headlong rush to enact the legislation, and the relevant bill was one of the last to be hastened through Parliament in the dying days of the last administration. Whether politicians on both sides of the House saw the creation of separate social work departments as a potential *quid pro quo* for the removal of health responsibilities from local authorities in the reorganization of the Health Service is a matter for conjecture. On the administrative side there was no doubt some attraction in having the hitherto overlapping health and social services neatly compartmented. But it seems as though the interests of the patients were rather lost in the political and administrative jockeying. Certainly some of those with long experience of both fields of work—and there were many successful combined health and welfare departments in the country—considered that the new pattern would make functional co-operation more rather than less difficult.

There is, of course, a shortage of social workers as there is of doctors and nurses. The standards of qualification in nursing and medicine are well defined, long established, and recognized by a public which has the protection of the General Nursing and General Medical Councils. Social workers are still establishing their discipline, and there might have been less oppo-

1 The Committee on Local Authority and Allied Personal Social Services 1965-8, *Report*, Cmnd 3703. London, H.M.S.O., 1968.
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