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INDUCTION OF ABORTION AND LABOUR BY MEANS OF OESTRIN

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As a result of the experimental work of many investigators it has been established that progestin and oestrin have a contrary effect upon the uterus, and that while the one inhibits, the other stimulates, the spontaneous activity and the responsive sensitivity of the uterine muscle. On these grounds it is believed that during pregnancy expulsive contractions remain in abeyance so long as a state of equilibrium is maintained between these antagonistic hormones, and that the onset of labour (or abortion) is preceded by a failure of equilibrium whereby the stimulating factor gains ascendancy and leads to the spontaneous evacuation of the products of conception.

Following upon the introduction of this idea of the hormonal control of pregnancy, many attempts were made to induce labour by means of ovarian extracts, and it was expected that the exhibition of oestrin, if given in large enough doses, would override the inhibitory effect of the corpus luteum, and so afford a method of inducing abortion or the premature onset of labour. Such experiments have been almost uniformly successful when applied to animals such as the rodents, but they have been a complete failure in the human subject. We believe that one or more of the following reasons may account for this lack of success.

1. Any conception of the hormonal balance as a simple equation existing between progestin and oestrin is misleading; it is quite certain that in rodents the corpus luteum is the chief inhibitory hormone, but this is not true for the human subject, because the result of many operations has proved that the removal of the corpus luteum has no effect upon the human pregnant uterus so long as the operation is carried out after the sixth week of gestation. Reynolds¹ has shown, and we ourselves have confirmed his work,² that the inhibition of the human uterus is also due to the direct action of the anterior pituitary hormone, prolactin.

2. Many workers have assumed that oestrin must perforce overcome progestin if given in sufficient quantity, whereas animal experiments³ have shown that it is not always possible to overcome the action of small doses of progestin by very large amounts of oestrin.

3. Other sources of failure have been the impurity of the preparations used for experimental purposes and the

marked variations that such preparations have shown in their hormonal content.

4. Sometimes the method of administration has been at fault, and the hormone has been injected with a view to a direct excitation of the uterine muscle comparable to that obtained by the action of the pituitary. But, as we were among the first to point out,^{2,4} oestrin is not directly oxytocic; it has no effect whatever upon the isolated uterus, and its influence is only to be seen when it is administered parenterally to the animal organism; and then some time must elapse before its action can become manifest.

Before describing the results of the present research we propose to restate our own views concerning the action of the follicular hormone, and to indicate the principles upon which we have based our experiments. We believe that oestrin produces its effect in at least three different ways, and of these the second is by far the most important: (1) by causing hypertrophy of the muscle fibres and general hyperaemia of the uterus; (2) by sensitizing the muscle and nerve elements of the uterus; (3) by stimulating the production of infundibulin in the body.

The preparation of oestrin in a pure and concentrated form has provided us with an opportunity for putting these views to an experimental and clinical test. The results we have obtained are in some respects surprising, but we believe that they throw fresh light upon the hormonal control of uterine activity during pregnancy and labour, and demonstrate that the state of activity of the uterus is essentially dependent upon the relative quantity and quality of oestrin, progestin, and prolactin in the blood stream.

Oestrin Preparations Used

The oestrin preparations used were "oestroform" (10,000 international units per c.cm. in the earlier, and 100,000 international units per c.cm. in the later experiments), and we are indebted to the British Drug Houses for a liberal supply of this preparation at a greatly reduced cost. Latterly "dimenformone" (10,000 and 100,000 international units per c.cm.) has also been used, and we are grateful to Dr. Alison Macbeth, scientific investigator to Organon Laboratories, for free supplies of this special preparation.

Animal Experiments

Parkes⁵ and other workers have shown that the administration of oestrin rarely fails to produce abortion at any period of gestation in the smaller rodents. Parkes has also demonstrated that the follicular hormone sensitizes the mouse uterus to the action of pituitrin, and that an interval of time must elapse between the administration of the hormone and the onset of expulsive contractions. This known abortifacient action upon the rodent uterus may be employed as a means of testing the activity of any preparation containing oestrin, and with this purpose in view we carried out a series of preliminary experiments in which we injected the preparation of hormone into a number of pregnant rabbits. For the most part we used oestroform containing 10,000 international units per c.cm., and the results are shown in Table I.

TABLE I.—*Induction of Abortion in Rabbits*

Case No.	Duration of Pregnancy	Total Amount of Oestroform 10,000 units per c.cm.	No. of Injections	Interval of Time between Injections	Results. Period of Time is Expressed in Hours after First Injection
1	22 days	1.35 c.cm.	5	8 hours	Abortion in 120 hours
2	22 "	1.68 "	6	8 "	" 36 "
3	22 "	1.93 "	7	8 "	" 144 "
4	17 "	1.10 "	4	12 "	" 86 "
5	8 "	0.75 "	3	12 "	" 90 "
6	14 "	0.78 "	3	12 "	" 90 "
10	13 "	0.10 "	1	—	Abortion at some time between 90 and 180 hours
11	12 "	0.10 "	1	—	Abortion in 36 hours
12	14 "	0.05 "	1	—	Abortion at some time between 48 and 144 hours
13	11 "	0.05 "	1	—	Abortion in 144 hours
14	9 "	0.05 "	1	—	" 163 "
15	9-10 "	0.05 "	1	—	Failure to produce abortion; normal delivery at term
16	14 "	0.05 "	1	0.5 c.cm. pituitrin given 12 hours after oestrin	Abortion in 96 hours
17	9 "	0.05 "	1	—	Abortion at some time between 43 and 100 hours
25	15 "	0.10 "	1	—	Abortion in 120 hours
26	14 "	0.10 "	1	—	" 120 "
27	14 "	0.05 "	1	—	" 110 "

Seventeen experiments were performed, and one or more injections of the oestroform were given subcutaneously in each case. The diagnosis of pregnancy was made by palpation and by correlating the physical signs with the time of copulation. The occurrence of abortion was determined by palpation, and confirmed on four occasions by killing the animal immediately after the uterus had emptied itself. It was not always easy to decide the exact time at which abortion had occurred, but, over the whole series, the average time taken to produce abortion was 109 hours as calculated from the time of the first injection, the shortest period being thirty-six hours in Case 2 and the longest interval 180 hours in Case 10. In sixteen cases abortion was successfully induced, and in one case only did the pregnancy continue to term. In this instance it should be noted that the pregnancy was advanced nine days only, and that a very small amount of oestrin (500 international units) was given.

Since oestroform is a preparation of ovarian hormone in castor oil, we felt it necessary to control these experiments by the administration of castor oil alone. Four pregnant rabbits were given 5 c.cm. of castor oil by

repeated subcutaneous injections, and in each case the pregnancy was unaffected, although the amount of oil given was much greater than that injected as a vehicle for the oestroform. Having made certain that our preparation was actively abortifacient to rabbits, we then proceeded to test its effects upon the human subject.

Scope of Investigation in the Human Subject

At the outset we determined to base our method of administration upon the known biological properties of the hormone. We argued that if oestrin produces its effects by sensitizing the uterine muscle, then it ought to be given in repeated doses, and the peak of sensitivity should not be reached until at least 100 hours had elapsed since the administration of the first dose. We hoped that the uterus might become so sensitized by the injection of oestrin that any further stimulation would be unnecessary, but we decided that if labour or abortion did not commence when the uterus reached this peak of sensitivity then we ought to try the effect of an oxytocic agent such as quinine or pituitrin.

We realized that the giving of this substance would affect the issue to some extent, but we did not think it would materially affect our observations on the action of oestrin, because it is well known that neither pituitrin nor quinine has much, if any, effect upon the uterus until the patient is near or at full term.

Based upon these principles an attempt was made to induce abortion and premature labour in a series of forty cases. For descriptive purposes we have divided the results of these experiments into four groups: (1) induction of therapeutic abortion; (2) induction of premature labour in normal pregnancy; (3) induction of labour in abnormal pregnancy; and (4) induction of labour in cases of missed abortion or intrauterine death of the foetus.

The Induction of Abortion

This method was used with the object of inducing therapeutic abortion on twelve occasions (Table II). In each case the medical indication for the termination of pregnancy was a general one and the local condition was apparently normal; the duration of pregnancy varied from seven to fourteen weeks. In no case was abortion induced, although in three instances uterine haemorrhage and definite intermittent painful uterine contractions occurred at the expected time. In a fourth case the patient experienced a sensation of an impending menstrual period.

Although these results are in one way disappointing they nevertheless add something to our knowledge of the action of oestrin, for whatever the reason of failure may be it can hardly be lack of adequate dosage. Our results strongly support the view that the normal balance which exists during pregnancy between the sensitizing and the inhibitory hormone is not directly a quantitative one.

The Induction of Premature Labour

Normal Pregnancy of more than Twenty-eight Weeks' Duration

Attempts to induce premature labour were made ten times (Table III). In five cases labour resulted from this treatment, although in one of them we were left in some doubt as to whether we could fairly attribute the successful result to the influence of the hormone because the pains came on so quickly after the first injection had been given. In one other case uterine contractions appeared but passed off again without bringing the patient into labour. In the remaining four cases the injections had no discernible effect upon the uterine muscle. It must be remembered that with two exceptions, of which one only was successful, all these patients were given quinine and

TABLE II.—*Induction of Abortion (Normal Pregnancy of less than Twenty-eight Weeks' Duration)*

No.	Duration of Pregnancy	Preparation Used	Total Dose in International Units	No. of Injections	Interval between Injections	Additional Substances given 100 hours (approx.) after First Injection	Results
7	10 weeks	Oestroform	100,000	5	12 hours	Pituitrin 0.5 c.cm. × 4; Quinine 10 grains	Patient commenced to bleed at 120 hours after first injection, but abortion did not proceed
8	12 "	"	50,000	5	12 "	None	No effect
9	13 "	"	60,000	6	Irregular for 6 days	Pituitrin 0.5 c.cm. × 4; Quinine 10 grains × 3	"
14	10 "	"	120,000	6	12 hours	Quinine 10 grains × 3	Painful uterine contractions and slight bleeding 72 hours after first injection. Patient had a mental impression of impending menstruation
16	12 "	"	120,000	6	12 "	Quinine 10 grains × 3	No effect
17	7 "	"	600,000	6	12 "	Quinine 10 grains × 3	Patient experienced a sense of impending menstruation about 100 hours after first injection
23	10 "	Oestroform and Dimenformone	3,200,000	32	8 "	Quinine 10 grains × 3; Pituitrin 0.5 c.cm. × 4	Patient commenced to bleed and had painful uterine contractions at 160 hours after first injection. (At that time she had received 1,900,000 units.) Bleeding continued for four days, but abortion did not proceed
26	14 "	"	6,800,000	34	8 "	Quinine 10 grains × 3; Pituitrin 0.5 c.cm. × 3	No effect
27	10 "	Oestroform	1,800,000	18	4 "	Quinine 10 grains; Pituitrin 0.5 c.cm. × 3	"
28	12 "	"	4,200,000	42	4 "	Quinine 10 grains; Pituitrin 0.5 c.cm. × 3	"
32	10 "	"	3,000,000	30	4 "	Pituitrin 0.5 c.cm.	"
33	14 "	"	2,500,000	21	4 "	Pituitrin 0.5 c.cm. × 4	"

TABLE III.—*Induction of Labour (Normal Pregnancy of more than Twenty-eight Weeks' Duration)*

No.	Duration of Pregnancy	Preparation Used	Total Dose in International Units	No. of Injections	Interval between Injections	Additional Substances given 100 hours after First Injection	Results	Comments
4	30 weeks	Oestroform	70,000	5	12 hours	Pituitrin 0.5 c.cm. × 4	Failed	No effect.
5	37 "	"	50,000	5	12 "	Pituitrin 0.5 c.cm. × 4	"	Intermittent painful contractions occurred at 100 hours after first injection, but passed away after a few hours.
11	38 "	"	100,000	5	12 "	Quinine 10 grains × 3	Successful	Patient had had pain and uterine haemorrhage and the cervix had reached two fingers dilatation before the quinine was administered; labour commenced 80 hours after the first injection.
12	38 "	"	80,000	4	12 "	—	"	Labour commenced 48 hours after the first injection. This early effect leaves one to doubt whether the onset of labour was due to oestrin.
13	37½ "	"	120,000	6	12 "	Quinine 10 grains × 3; pituitrin 0.5 c.cm. × 4	Failed	No effect.
21	38 "	Dimenformone	1,200,000	6	12 "	Quinine 10 grains × 3; pituitrin 0.5 c.cm. × 4	Successful	Onset of labour at 100 hours after first injection. Duration of labour was only three hours, although patient had a contracted pelvis and a breech with extended legs.
22	33 "	"	1,200,000	6	12 "	Quinine 10 grains × 3	"	Onset of labour at 44 hours after first injection. It is to be noted that by the time labour ensued this patient was on term.
24	36 "	Oestroform	370,000	11	8 "	Pituitrin 0.5 c.cm. 12-hourly	Failed	No effect.
25	40 "	Dimenformone	1,600,000	16	8 "	Quinine 10 grains × 3	Successful	Onset of labour at 100 hours after first injection. Quinine induction prior to oestrin failed to induce labour.
37	? 40 "	Oestroform	2,000,000	10	8 "	—	Doubtful	No result in 100 hours after first injection. At that time the pregnancy was terminated by other means.

pituitrin in addition to oestrin, and that most of them were near full term when the treatment was begun. In such circumstances we recognize that labour may be induced by drugs alone, and hence we are unable to bring forward the present results as examples of the induction of labour by oestrin.

Nevertheless, we desire to emphasize the undeniable fact that in all the successful cases uterine contractions were unusually good and the labours were noticeably short. We have no doubt in our own minds that the lively condition of the uterine muscle was directly due to the sensitizing effect of the previously injected hormone. We must also record that we have never noticed any ill effects* either to mother or child following the administration of this hormone, although this experience is contrary to that of other observers.⁶

* In a more recent case (not included in this paper) a patient exhibited pyrexia and collapsed a short time after the administration of 20,000 international units of dimenformone. However, this was a case of retained placenta associated with obstetric shock, and we do not feel justified in regarding the symptoms as being due to the hormone preparation administered.

The Induction of Labour in Abnormal Pregnancy

These two cases are classified separately because in both instances there were local factors that may have been responsible for the onset of labour, and we therefore hesitate again to ascribe the onset of expulsive contractions to the effects of oestrin.

It will be noticed that in Case 3, a pre-eclamptic patient, convulsions occurred during labour that set in thirty-three hours after the injection of the hormone. The explanation of the onset of these fits is difficult. If it be true that one function of oestrin is to liberate secretion from the posterior lobe of the pituitary body, then it is theoretically possible that the oestroform injections may have played some part in the production of the convulsions. On the other hand it is a common clinical experience that the onset of labour itself (or merely the onset of individual uterine contractions during labour) is liable to initiate convulsions in any patient who is suffering from pre-eclampsia, and this explanation may well be the correct one in the present instance. Whatever the explanation, we do not consider that such a

TABLE IV.—*Induction of Labour in Abnormal Pregnancy*

No.	Abnormality	Duration of Pregnancy	Preparation Used	Total Dose in International Units	No. of Injections	Interval between Injections	Results
1	Twins with hydramnios	35 weeks	Oestroform	50,000	5	12 hours	Onset of labour 90 hours after first injection. In spite of hydramnios, the uterus contracted well and labour lasted only 9½ hours
3	Anencephalus pre-eclampsia	35 "	"	20,000	2	12 "	Onset of labour 33 hours after first injection. Soon after pains commenced, patient commenced with eclamptic fits. Labour was complete after 23 hours

remote contingency as the development of fits should constitute a contraindication to the therapeutic use of oestroform.

Induction of Abortion or Labour in Cases of Intrauterine Death of the Foetus

It is to this group that we wish to draw special attention. Normally the death of the foetus is soon followed by the onset of labour (and the evacuation of the contents of the uterus), but in cases of missed abortion the foetus is retained *in utero* and the onset of labour does not supervene for a considerable and sometimes a long period. This interesting condition may be explained in two ways: it may be due to the persistence of those factors which normally inhibit uterine activity; or it may be due to the absence of those stimulating factors that normally bring about the onset of expulsive contractions.

who are suffering from missed abortion, and we are convinced that in all our successful cases the hormone alone was the primary and essential cause of the evacuation of the uterus.

Case 15 was most instructive. For many weeks this patient had been suffering from an attack of malaria, which had killed the foetus, but, in spite of the exhibition of massive doses of quinine, there had been no evidence whatever of uterine contractions or discharge. The uterus was clearly resistant to the effects of quinine, and yet, after a course of oestrin, quinine and pituitrin produced a painless labour lasting only three and a half hours.

With reference to these results, it is of great interest to note that Spielman, Goldberger, and Frank⁷ in 1933 demonstrated that the retention of a dead foetus is characterized by the absence of a demonstrable amount of oestrin in the blood. This condition is in marked contrast to that

TABLE V.—*Intrauterine Death, including Missed Abortion*

No.	Duration of Pregnancy		Preparations Used	Total Dose in International Units	No. of Injections	Interval between Injections	Additional Substances given 100 Hours after First Injection	Result	Time of Abortion after First Injection	Remarks
	Dates	Physical Signs								
2	31 weeks	34 weeks	Oestroform	40,000	4	12 hours	Castor oil	Successful	150 hours	Bleeding and pain commenced before administration of castor oil. Macerated twins expelled
6	32 "	16 "	"	100,000	5	12 "		"	200 "	
10	26 "	16 "	"	100,000	5	12 "		"	80 "	Prior to administration of oestrin no dilatation of the cervix. Injections of quinine and pituitrin had failed to stimulate uterine contractions
15	28 "	22 "	"	120,000	6	12 "	Quinine 10 grains × 3; Pituitrin 0.5 c.cm. × 4	"	90 "	This patient had had malaria and this caused foetal death. She had massive doses of quinine as treatment of the malaria, but no pain or haemorrhage had occurred prior to the administration of oestrin
18	25 "	18 "	Progynon oleosum	1,100,000	7	12 "	Quinine 10 grains × 3; Pituitrin 0.5 c.cm. × 4	Failed		This patient commenced to bleed at 100 hours after first injection, but evacuation of the uterus did not proceed. She had had no previous bleeding
29	33 "	28 "	Oestroform	100,000	1			Successful	3 "	No pain or uterine haemorrhage before injection of oestrin
30	33 "	25 "	"	1,400,000	10	8 "		"	80 "	
31	36 "	30 "	"	2,000,000	10	8 "	Pituitrin 0.5 c.cm. × 4; Ol. Ric.	"	96 "	
34	26 "	10 "	"	2,430,000	15	8 "	Quin. sulph. 10 grains × 3; Pituitrin 0.5 c.cm. × 4	"	200 "	
35	28 "	20 "	"	3,200,000	16	8 "	Pituitrin 0.5 c.cm. × 6; Quin. sulph. 10 grains × 3	Failed		Uterine haemorrhage and definite painful uterine contractions commenced 120 hours after first injection. These passed away after a few hours
39	34 "	25 "	"	1,600,000	8	8 "		Successful	66 "	No pain or discharge prior to administration of oestrin
40	24 "	20 "	"	1,000,000	5	8 "		"	36 "	

We believe that the results recorded in Table V put the issue beyond all doubt by demonstrating that the latter explanation is the correct one. In 83 per cent. of cases (ten out of twelve) evacuation of the uterus, weeks and even months after foetal death had occurred, was induced without mechanical interference by the injection of oestroform (? the missing factor). In the remaining two cases bleeding (previously absent) and painful uterine contractions were set up at the expected time, but the contractions were not sufficiently powerful (or sustained) to effect the expulsion of the products of conception.

In seven of the successful cases nothing but oestrin was used for the induction of labour, but in the remainder quinine and pituitrin were also administered. It is, of course, a well-known clinical fact that quinine and pituitrin alone have practically no effect upon women

which obtains in normal pregnancy, and it was therefore put forward by these observers as a means of determining the occurrence of intrauterine death. This work has been recently confirmed by Dr. J. Polonsky, working in this department, and to him we are indebted for carrying out the test in six of our cases and demonstrating the absence of oestrin in the blood prior to the attempts at induction. We conclude that the reason why the foetus is retained *in utero* in cases of missed abortion is the absence of the normal sensitizing factor—oestrin—and that if this is supplied by the correct technique the uterus will empty spontaneously in most cases.

It is hardly necessary to emphasize the advantages accruing from the employment of a non-operative method of treating such cases, because it is well recognized that any mechanical interference is accompanied by a serious

risk of injury and sepsis to any patient who is suffering from missed abortion. The absence of bleeding and pyrexia was noteworthy in all our cases, and we are confident that the use of oestrin will prove to be of great value in the treatment of this condition.

It should be clearly understood that "missed" abortion is a definite clinical entity in which a dead ovum and placenta are retained *in utero* because the uterus has remained inactive, and, as it were, "missed" its chance of abortion. This condition of missed abortion is quite separate and distinct from incomplete abortion, which implies that abortion has taken place, but is incomplete because some of the products of conception are retained in the uterus. We wish to emphasize that while we claim that oestrin will empty the uterus in cases of missed abortion, we do not claim that the injection of this hormone will lead to the expulsion of pieces of retained placenta from the uterus of a patient suffering from incomplete abortion.

We have, more recently, attempted to induce abortion in a patient suffering from a mole which was partly carneous and partly vesicular in type. Nearly 2,000,000 international units of oestroform were administered. The attempt failed, and this result is to be expected on theoretical grounds. The excessive formation of prolan associated with hydatidiform mole makes it probable that the uterine musculature is inhibited even more than in normal pregnancy.

Administration of Oestrin for Uterine Inertia

These four cases stand by themselves, since it was impossible to devise any control experiments, but the results are of exceptional interest, and they are in complete agreement with our view of uterine inertia as expressed elsewhere. Moreover, they open up possibilities of a harmless and effective treatment for a condition which entails much difficulty for the obstetrician and great risk to both mother and child.

We wish to draw special attention to Case 36. At her first confinement this patient was in labour for some

Conclusions

1. We believe that the results brought forward support the view that oestrin is the main sensitizing factor of the human uterus.

2. We find that it is impossible to overcome the inhibitory phase of the normal pregnant uterus by the injection of very large quantities of the non-stimulating factors, and we confirm our belief that the hormone balance in normal pregnancy in the human being is not maintained simply by the relative quantities of progestin and oestrin. We confess to some feeling of relief in our inability to procure abortion by means of oestrin, because we are convinced that if this method were reliable it would indubitably lead to a great increase in the number of unnecessary inductions and criminal abortions.

3. Our clinical results have shown that when administered near term oestrin may or may not induce premature labour, but that it is not a reliable means of induction. It is an especially unsuitable method for cases in which it is necessary to bring on labour immediately because of the uncertain interval (up to seven or eight days) that intervenes between the commencement of treatment and the onset of expulsive contractions.

4. Our experience has demonstrated that oestrin is the best method of evacuating the uterus in cases of missed abortion or intrauterine death of the foetus. The method when correctly carried out is successful in at least 80 per cent. of cases, and it has the additional merit of being free from risk. The patient has the discomfort of several intramuscular injections, but she is immune from the danger of uterine trauma, infection, and haemorrhage.

5. Finally, we are led to hope that oestrin will prove to be of value in dealing with primary uterine inertia, for our results have shown that the response to oestrin therapy is dramatic and that it entails no risk to either mother or child. This treatment is at present expensive, but we have so far made no attempt to determine how little or how much of the hormone is required for therapeutic use, and it is quite possible that the amount we have been using may have been unnecessarily large.

TABLE VI.—Administration of Oestrin for Uterine Inertia

No.	Duration of Pregnancy	Conditions Present	Preparation Used	Total Dose	No. of Injections	Interval of Time between Injections	Results
19	40 weeks	L.O.P.; membranes ruptured. No contractions for four days	Dimenformone	20,000	2	6 hours	Onset of pain 8 hours from first injection. Low forceps for foetal distress. Rapid advance
20	37 "	V.D.H.; membranes ruptured for three days. No contractions	"	1,300,000	7	12 "	Pain and show after second injection. Definitely in labour 100 hours from first injection. Rapid delivery
36	38 "	Twins with hydramnios. Six days in labour. Cervix three fingers for four days in spite of quinine, etc., previous pregnancy Caesarean, for non-dilatation of cervix	Oestroform	800,000	4	2 "	Delivered in 7 hours from first injection. One foetus dead and one alive
38	40 "	Adipose multipara. R.O.P.; four days in labour. Weak and infrequent pains. No advance. Cervix not dilating	"	700,000	7	—	Improvement in pains soon after commencing treatment. Delivery completed within 12 hours of first injection. Low forceps

days, and although there was no evidence of mechanical disproportion Caesarean section was eventually performed on account of defective action of the uterus and failure of the cervix to dilate further than two fingers. In the present confinement she was found to have twins with hydramnios causing overdistension of the uterus. Before the administration of oestrin she had been in labour for six days, and during the last four the cervix had remained at two to three fingers dilatation. Uterine contractions were feeble and very infrequent, and the administration of quinine had failed to influence the contractions to any appreciable extent. Very soon after the administration of oestrin, regular and strong uterine contractions set in and delivery was completed within eight and a half hours from the first injection of the hormone.

We desire to express our gratitude to Dr. A. S. Parkes of University College, London, for his valuable help and advice, and also to thank our colleagues at the Maternity Hospital and the Royal Infirmary, Liverpool, for allowing us to carry out this form of treatment upon patients under their care and for permitting us to report the results incorporated in this paper.

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