A Critical Review of Current Methods for Induction of Parturition in the Mare

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SUMMARY
The efficacy and safety of oxytocin, dexamethasone and prostaglandin, used alone or in combination as inducing agents, are discussed. It is contended that insufficient evidence exists to support the routine application of any of these methods in practice. Oxytocin has been the most widely used and it is claimed by some to be free from side effects. However, the synthetic prostaglandin analogue, fluprostenol, seems to pose the least risk to the foetus and dexamethasone appears to be either ineffective, or too dangerous to use at all.

The main indications for induced foaling are managerial convenience or for research and teaching purposes. There are few clinical indications, although ventral rupture and cases of prolonged gestation have been mentioned by various workers. It is considered that foetal maturity is the pre-requisite before a decision to induce should be made in practice, and 3 criteria are essential: 1) a gestational length of >320 days, 2) substantial mammary development, 3) the presence of colostrum in the mammae.

INTRODUCTION
VARIOUS methods of inducing parturition in the mare have been reported. Most experience has been at full-term with single injections of oxytocin, alone or in combination with oestrogen (Britton, 1963, 1972; Purvis, 1972; Klug and von Lepel, 1974; Hillman, 1975; Rossdale and Jeffcott, 1975). More recently, fluprostenol a synthetic prostaglandin analogue, (Rossdale, Jeffcott and Allen, 1976) and natural prostaglandin Fα, in combination with flumethasone and oestrogen (van Niekerk and Morgenthal, 1976) have been successfully used to induce foaling at full-term.

The administration of corticosteroids during the latter part of pregnancy will induce parturition in ruminants (Drost and Holm, 1968; Adams and Wagner, 1970). Adams (1969) was able to induce 18 out of 22 cows (235-280 day gestation) within 48 hours of a single injection of 20 mg dexamethasone (DXMS). Although calving was apparently normal, the placenta was retained in 20 animals, all of which subsequently developed endometritis. A number of the calves showed signs of prematurity and 8 did not survive the first 2 weeks of life. Since Adams' initial report there has been an extensive amount of work published in this field and DXMS induced-birth is now used with much reduced calf losses and a lower incidence of retained placenta (Dawson, 1977). DXMS has also been used to induce parturition in the last 20 days in the sheep and goat and in the last 7 days of pregnancy in the rabbit (Jochle, 1973). Comparative higher dose rates than those used in ruminants are required in the sow (North, Hauser and First, 1973) and mare (Alm, Sullivan and First, 1974).

This paper is concerned with the indications for induced foaling, the prerequisites for safety and the methods available for choice.

THE INDICATIONS FOR INDUCED FOALING
Induction may be practised for managerial or clinical reasons, for teaching or research.

Managerial indications
There are economic advantages in causing mares to foal at specified hours during daylight or in the early evening. For example, the cost of having attendants watch mares all night ("sitting-up") is, in the U.K., currently about £8 per night and, therefore, the aggregate sum which may be incurred by an establishment where large numbers of mares are foaled, could be £1,200 for a season lasting 150 days.

Planned birth may also help reduce risks associated with parturition to both mare and foal in circumstances where management has reduced resources of manpower and experience, as for example where an owner has only 1 or 2 mares. In these circumstances it is often not possible to arrange a system of "sitting-up" and veterinarians or skilled personnel may not be easily available for urgent assistance.

Clinical indications
Conditions which have been suggested as warranting the use of induction include uterine atony (Britton, 1963),...
prolonged gestation, loss of colostrum, pre-parturient colic, pelvic or other injury of the mare, ventral rupture (fig. 1) and arthritic or other painful skeletal disease, which may become more severe as pregnancy nears fullterm. The objective of elective induction is to alleviate the maternal condition and enable delivery to occur when veterinary assistance is immediately available.

Teaching and research
An induced foaling enables veterinary and agricultural students to observe and assist at foalings with the minimal expenditure of time and teaching resources. These occasions may supplement, or be used concurrently in research on such aspects as the efficacy of various inducing agents; parturient and neonatal physiology; and maternal and foetal risks at parturition.

FULL-TERM INDUCTION
The assessment of foetal maturity is a fundamental requirement before induction should be contemplated for clinical or managerial purposes. The terminology of full-term delivery needs to be defined for clarity of discussion.

Full-term implies a gestational length sufficient for the foetus to achieve the maturity necessary for successful adaptation to the extra-uterine environment. The equine foetus has little or no chance of survival even under conditions of intensive care, if delivered before the 300th day of gestation (i.e. in the so-called pre-viable period). Full-term foaling lies in the range of 320 to 360 days gestation.

Prematurity. Thoroughbred foals born between the 300th and 320th day of gestation are smaller and have a reduced chance of survival compared with foals delivered after 320 days gestation; and are described as premature (Rosspdale, 1976).

Dysmaturity is a state of placental deprivation causing retardation in growth or premature-like signs (weakness, undersize and/or emaciation) in a foal delivered at a gestational age greater than 320 days (Rosspdale, 1976).

The criteria by which foetal maturity may be assessed before the clinician decides to induce foaling include the state of mammary development and its secretions, cervical relaxation, foetal position, posture and heart rate, and maternal endocrinology.

Mammary development
Although the actual size of the udder may be affected by variables such as parity, breed and nutritional status, a substantial increase in size should occur before foaling is induced. A scale based on subjective observations ranging from 0 to +++ is suggested (fig. 2). The presence of oedema of the udder and ventral body wall are additional indications of full-term.

Mammary secretions
The most important indication of full-term is the presence of colostrum in the mamme. Typically, mammary secretions pass from straw- or amber-colour to cloudy-straw in the weeks preceding parturition and then to yellow or yellowish-white and viscous, close to the natural termination of pregnancy. In most mares a bead of colostrum dries at the teat end as “wax” 1 to 4 days before foaling. Some individuals may “run milk” and lose variable quantities of milk-like secretions. In general, induction should not be practised unless there is a readily-available volume of colostrum or milk-like secretions present in the mamme.

Relaxation of the cervix and pelvic ligaments
The cervix has been described as becoming softer and relaxed shortly before full-term. Hillman (1975) advocates that two-finger sized dilation should be present before foaling is induced. In the authors' limited experience of natural birth they have found that the cervix may be widely dilated before the foetus moves into the birth canal. However, they have successfully induced several mares in which the cervix remained firmly closed and covered in tacky mucus until the end of first-stage labour. In the mare the relaxation of the pelvic ligaments (i.e. sacroiliac and sacrosciatic) is a much less obvious sign of impending parturition than it is in the cow. There is a degree of hollowing and softening of the quarters in some mares and this may be accompanied by relaxation and lengthening of the vulva.

Foetal position
The equine foetus lies in a ventral position and a flexed posture during the latter part of gestation (Roberts, 1971; Arthur, 1975). It turns into dorsal position and extended posture during first and early second-stage labour. Fraser, Hastie, Callicott and Brownlie (1975), employing doppler ultrasound have demonstrated frequent foetal limb movements from about the third month of gestation and peak foetal activity 3 days prior to parturition. Furthermore, we have observed from radiographic examination (fig. 3) and from manual palpation of the birth canal, that the foetus extends its forelimbs and head, apparently by active reflex movements, during early first-stage labour. The turning of the foetus from the ventral to the dorsal position is accomplished, in many cases, just before the onset of second-stage labour. The foetal appendages appear to play a significant role in dilating the cervix and causing rupture of the allantochorion in induced foaling. The forefeet forcibly protrude into the fornix of the vagina and eventually one of them enters the cervical canal, carrying with it the allantochorion, which ruptures as the foof protrudes into the vagina. However, rupture may
occur independent of the foetal appendages as demonstrated in those cases where dystocia occurs due to carpal flexion. This postural defect may be associated with reflex foetal inertia from reasons of dysmaturity, prematurity, or the action of inducing agents (Rossdale and Jeffcott, 1975). Fraser (1977) has noted a reduction in foetal kinesis when there is foetal malposture and dystocia.

Maternal endocrinology

Progestagen levels rise within about one week of natural parturition (Barnes, et al., 1975; Holtan, Nett and Estergreen, 1975) but results from serial samples are necessary to interpret the imminence of full-term delivery because considerable variation in levels occurs between individuals. The value of this assay depends in the present context on the availability of facilities and the quick reporting of results.

Foetal heart rate

Foetal electrocardiography is a quick, safe and simple technique to confirm the presence of a live foetus after 150 days gestation (Parkes and Colles, 1977). The foetal heart rate varies between 60-160 beats per min. The average rate is about 100 per min at 5 months and falls to about 60-80 per min at term. Foetal arrhythmias may be a sign of impending abortion and progressive bradycardia probably indicates foetal distress, but intermittent tachycardia is probably of no consequence (Colles, 1977).

Conclusions

In summary, the 3 criteria essential for full-term induction are a gestational length of >320 days, substantial mammary development and the presence of colostrum in the mammae with wax on the teats. Daily examinations are recommended since a changing situation is considered more significant than one that is static.

METHODS OF INDUCTION

The clinician must make a subjective preference of the method of induction in the absence of definitive studies. There are 3 techniques in current use (Table I), each based on the parenteral administration of hormones. In the course of an investigation of foetal blood pressure changes during and immediately after foaling we induced 20 pony and Thoroughbred mares by a variety of means (Table II).
TABLE I
SUMMARY OF CURRENT METHODS FOR THE INDUCTION OF PARTURITION IN MARES

<table>
<thead>
<tr>
<th>Induction Agent</th>
<th>Method of Administration</th>
<th>Route</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Oxytocin</td>
<td>0.04—0.26 iu/kg</td>
<td>i.m.</td>
<td>Britton (1972); Purvis (1972); Hillman (1975)</td>
</tr>
<tr>
<td>Oxytocin + Stilboestrol</td>
<td>0.04—0.26 iu/kg + 12—30 mg</td>
<td>i.m.</td>
<td>Britton (1972); Purvis (1972); Hillman (1975)</td>
</tr>
<tr>
<td>Dexamethasone</td>
<td>100 mg for 3—4 days</td>
<td>i.m.</td>
<td>Rossdale and Jeffcott (1975)</td>
</tr>
<tr>
<td>Prostaglandin F₂α + Stilboestrol + Flumethasone</td>
<td>10 mg + 10 mg + 7.5 mg + 30 mg</td>
<td>i.m.</td>
<td>Rossdale, Jeffcott and Allen (1976)</td>
</tr>
<tr>
<td>Prostaglandin (Fluprostanol)</td>
<td>250—1000 μg</td>
<td>i.m.</td>
<td>Rossdale, Jeffcott and Allen (1976)</td>
</tr>
<tr>
<td>Corticosteroids</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Campbell (1971) failed to induce birth in mares between 40 and 60 days gestation, with doses of 10-40 mg daily for 5 days; and Drost (1972) was unsuccessful when employing 20 mg DXMS i.m. on 5 ponies carrying mule foetuses during the last third of pregnancy. Therapeutic doses (10-80 mg/day) of DXMS from about 300 days gestation did not appear to induce parturition nor alter gestational length (Burns, 1973). But Alm, et al. (1974) showed that 100 mg daily given from day 321 to 324 induced premature parturition within 4 ± 1.6 days from the last injection. They reported that the induced foals were weaker at birth than control animals, but that they improved after 7-10 days and then grew normally.

TABLE II
METHODS OF INDUCTION USED IN 20 PONY AND THOROUGHBRED MARES

<table>
<thead>
<tr>
<th>Method of Induction</th>
<th>No. of Mares</th>
<th>Dosage and Route of Administration</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dexamethasone alone</td>
<td>2</td>
<td>100 mg Dexamethasone for 3-4 days</td>
</tr>
<tr>
<td>Dexamethasone + Oxytocin</td>
<td>1</td>
<td>100 mg Dexamethasone for 3 days + 37 iu Oxytocin i.v.</td>
</tr>
<tr>
<td>Oxytocin alone</td>
<td>5</td>
<td>45 iu (20-90 iu) Oxytocin i.v.</td>
</tr>
<tr>
<td>Fluprostanol alone</td>
<td>11</td>
<td>250-1000 μg Fluprostanol i.m.</td>
</tr>
<tr>
<td>Fluprostanol + Oxytocin</td>
<td>1</td>
<td>500 μg Fluprostanol i.m. + 12.5 iu Oxytocin i.v.</td>
</tr>
</tbody>
</table>

Mammary development in some of the mares was less than expected but milk let-down did occur at birth and they did not apparently retain their placentae.

We encountered serious complications and dystocia in 2 out of 3 pony mares (331-347 days gestation) after administering doses of 100 mg DXMS daily for 3 and 4 days. One mare, which had substantial mammary development with colostrum present in the glands, was given DXMS for 3 days from day 327. On day 331 oxytocin (37 iu) was administered i.v. and parturition occurred within one hour. No serious difficulties were encountered but the mare appeared rather more distressed than usual and sweated profusely. The placenta was retained for 36 hours. In the other 2 mares the DXMS (100 mg per day for 3-4 days) was started on days 344 and 347 when there was only moderate mammary development. In one mare the udder size reduced slightly following the initial dose of DXMS. Neither animal showed any indication of foaling and the onset of labour was not witnessed in either case. Both mares were found in second-stage with dystocia due to malposition of the foetus. The poll of the foal's head was presented at the pelvic inset and there was bilateral carpal flexion. Realignment of the foetal appendages was effected with difficulty and both foals were stillborn. The cause of dystocia was not ascertained but it was possible that second stage was initiated before the foetus had time to take up the normal foaling position in the birth canal so that it became impacted at the pelvic brim. In both cases the placentae were retained and removed manually at approximately 48 hours post partum.

Oxytocin

The administration of oxytocin has been the most widely used method of induction in the mare and reports (Table I) have appeared from the United States (Britton, 1972; Purvis, 1972; Hillman, 1975), Germany (Klug and von Lepel, 1974), the United Kingdom (Rossdale and Jeffcott, 1975) and New Zealand (O'Flaherty, 1975).
The administration of stilboestrol 12-30 mg a few hours prior to induction has been used to relax the cervix (Purvis, 1972; Hillman, 1975) but in the authors' limited experience this has not been necessary. The most frequently employed route of administration has been by a single i.m. injection at dose rates ranging from 0.04-0.26iu/kg body weight.

We gave the drug by i.v. infusion in a saline drip to 5 pony mares and smaller doses of oxytocin (mean 0.09iu/kg) seem to be required by this technique (Table III). Following i.m. injection of oxytocin foaling begins within 30 min with some discomfort and sweating which is more pronounced than in natural birth. First- and second-stage labour are usually uneventful but may appear more stressful than normal parturition. One mare foaled standing and in another there was malposition of the foetus due to lateral deviation of the head and bilateral carpal flexion. This was corrected without much difficulty and the foal appeared normal after birth. Four of the 5 foals were weaker than normal at birth although in only one case was this severe enough to warrant destruction. Foetal malposition is also mentioned by Klug and von Lepel (1974), and Hillman (1975) stressed the need to ascertain the correct posture and presentation of the foetus by rectal examination prior to a decision to induce foaling.

**Table III**

**RESULTS OF INDUCTION USING INTRAVENOUS INFUSION OF OXYTOCIN IN 5 PONY MARES**

<table>
<thead>
<tr>
<th>No.</th>
<th>Gestation length (days)</th>
<th>Dose rate (iu)</th>
<th>Delivery time (min)</th>
<th>Time for foal to stand (min)</th>
<th>Placenta expelled (min)</th>
<th>Remarks</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>335</td>
<td>48</td>
<td>45</td>
<td>100</td>
<td>1080</td>
<td>Foal very weak for 48 hours</td>
</tr>
<tr>
<td>2</td>
<td>326</td>
<td>20</td>
<td>15</td>
<td>120</td>
<td>70</td>
<td>Foal rather weak for 24-48 hours; had severe 'contracted tendons' at birth</td>
</tr>
<tr>
<td>3</td>
<td>335</td>
<td>41.5</td>
<td>80</td>
<td>60</td>
<td>74</td>
<td>Foal malpresented but normal after birth</td>
</tr>
<tr>
<td>4</td>
<td>325</td>
<td>25</td>
<td>25</td>
<td>170</td>
<td>37</td>
<td>Foal rather slow initially but progressed satisfactorily</td>
</tr>
<tr>
<td>5</td>
<td>—</td>
<td>90</td>
<td>47</td>
<td>—</td>
<td>193</td>
<td>Foal very weakly and dysmature; necessitated euthanasia at 48 hours</td>
</tr>
<tr>
<td>Mean</td>
<td>328</td>
<td>45</td>
<td>42.4</td>
<td>112</td>
<td>291</td>
<td></td>
</tr>
</tbody>
</table>

(— not recorded)
Hillman (1975) showed encouraging results in his series of mares induced at studs with 25 out of 26 foals surviving. However, 4 of 11 foals induced at a veterinary clinic died within 2 weeks from various infectious conditions. Retention of the placenta sometimes occurred and was thought to be dose-dependent.

**Prostaglandins**

The synthetic prostaglandin analogue, fluprostenol, has been found to be a potent birth-inducing agent when used in mares between 322-367 days gestation. Eleven mares (Table IV) received doses varying from 250-1000 µg by i.m. injection (8 mares were dosed once and 3 of them on two occasions), and signs of first-stage labour were noted within 30 min of the first injection. There was progressive dilation of the cervix, and the foetus moved into dorsal position and extended posture (fig. 3). All the mares produced living foals within 4 hours of the first injection, but 2 foals suffered from some degree of dysmaturity and another from fractured ribs sustained during foaling.

A mare with ventral rupture (fig. 1) was induced with 1,000 µg fluprostenol and once in second-stage a small i.v. dose of 12.5 iu oxytocin was given. Some assistance was required in the delivery but a live foal was produced. It was rather weak for the first few hours and was somewhat jaundiced, but soon improved and looked normal by 48 hours.

Natural prostaglandin F₂α, following preparatory injections of stilboestrol and flumetolone, has been used to induce foaling (van Niekerk and Morgenthal, 1976) but Alm, et al. (1975) found that natural PGF₂α used alone was ineffective in normal intact mares, and that foals born to ovariectomised mares treated between 321 and 324 days gestation suffered a high incidence of foetal and neonatal deaths. The exact mechanism involved in prostaglandin-induced foaling is unknown but the luteolytic properties of natural PGF₂α and fluprostenol are well known (Douglas and Ginther, 1972; Allen and Rowson, 1973; Oxender, Noden and Hafs, 1975) and the limited smooth muscle activity of fluprostenol has been well documented (Allen, et al., 1974; Dukes, Russell and Walpole, 1974).

**THE CASE FOR AND AGAINST INDUCED FOALING**

The subject of induction touches upon several disciplines. The physiologist is concerned with the manner in which the inducing agent triggers the mechanism of birth, and in how this action throws light on some of the still unsolved problems of the hormonal control of parturition. The process may also be compared with natural birth in terms of such events as the manner and timing of the dilated cervix, force and frequency of uterine contractions, speed of delivery and adaptive powers of the newly born.
The pathologist may study the effects of induction on placental uterine tissues or investigate its consequences on the newborn in terms of maturity, neonatal maladjustment or other conditions which may be related to the nature of the inducing drugs or the extrinsic effects of the birth process. The pharmacologist has to develop the optimal compound for the purpose and to advise on its dose rate and route of administration. Drug manufacturers have a duty to define the possible side-effects and contra-indications of the marketed product.

The manager of a breeding establishment may wish to control the day or time of foaling for convenience, or to ensure that attendants are present, thus reducing cost and administrative disturbance. Finally the clinician has responsibilities towards each and all of the foregoing interests as well as a prime duty to the well-being of his "patients" which, in this context, are the mare and her foal. He must judge the particular circumstances of each case before making a decision to influence an event which, in about 90 per cent of cases, is normal in all respects when allowed to proceed naturally.

In the absence of compelling reasons, the clinician should not resort to induction for routine purpose unless there is a wide margin of safety for both mare and foal. There have been few critical investigations into the deleterious effects of induction, but the use of oxytocin has been associated with foetal malposture (Klug and van Lepel, 1974), prolonged retention of the placenta (Hillman, 1975) and with foals that were weaker than normal (Rossdale and Jeffcott, 1975) or more prone to neonatal infection in certain circumstances (Hillman, 1975). Foetal malposture and neonatal deaths were the sequelae of treatment with dexamethasone (Rossdale and Jeffcott, 1975). Oedema of thechorion and damage to the choriocapillaris following induction by various methods have been reported by Samuel, Steven and Rossdale (1976).

Natural birth must be assumed as being more physiological than one that is induced and no controlled trials have been reported that compare the advantages and disadvantages of induction. Dystocia and weak or premature-like foals have been encountered in cases of induction, but there is a natural incidence of these conditions which reduces the authority of any comparison. Samuel, et al. (1976) found increased damage to the endometrium and placenta in induced, compared with natural, birth but it is not possible to determine the practical implications of these observations because of the small number of cases on which they are based. The clinician will therefore tend to judge the effects of induction in a gross sense, namely in that the mare and foal appear healthy during and subsequent to the event; the endocrinological and histopathological changes per se do not concern him.

CONCLUSIONS
It appears that DXMS poses the greatest, and fluprostenol the least, risk to the foetus, but oxytocin has been used more extensively and several authors claim that it is free from side-effects. However, it is our belief that methods to induce foaling require further study before they are routinely applied. In addition to overt and subclinical side-effects from the method itself, the clinician is faced with the possibility of coincidence because of the relatively high risk of untoward happenings associated with perinatal events, which owners may relate to induction, even if there is no known connection. It is important, therefore, for the clinician to identify the purpose of induction and to ensure that he has warned the client of coincidental risks, as well as the risk of the therapy itself. In particular, the clinician has a duty to ensure that the foetus is mature, and this diagnosis is, in the authors' opinion, the most difficult consideration and the one that requires objective investigation.

REFERENCES


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**RéSUMÉ**

L'efficacité et l'immocuité de l'ocytocine, du dexaméthasone et des prostaglandines utilisées soit seules soit en association pour induire la mise bas, sont discutées. Il apparaît qu'aucune base suffisante n'existe à ce jour, qui justifie l'emploi routinier de l'une de ces substances en pratique courante.

L'ocytocine a été la plus largement utilisée et d'aucuns prétendent qu'elle ne provoque aucun effet secondaire. Pourtant le fluprostenol analogue synthétique de la prostaglandine, paraît comporter les moindres risques pour le foetus. Quant au dexaméthasone il semble soit inefficace soit trop dangeureux pour être employé.

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Les indications majeures pour l'induction du part sont soit des raisons de convenance soit des motivations didactiques, recherche ou enseignement. Bien que des cas d'éventration et de gestation prolongée aient été invoqués par divers auteurs, il semble que les indications cliniques soient rares.

On considère que la maturité foetale est une condition nécessaire pour décider l'induction. En outre trois critères semblent essentiels:

1. une durée de la gestation supérieure à 320 jours,
2. un développement mammaire suffisant,
3. la présence de colostrum dans les mamelles.

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**ZUSAMMENFASSUNG**


Die hauptsächlichsten Indikationen für die Geburtseinleitung bestehen in der Bequemlichkeit für die Gestüte und in Lehrzwecken. Es scheinen nur wenige klinische Indikationen wirklich zu bestehen, obgleich Bauchbrüche und verlängerter Tragzeiten von verschiedenen Autoren ins Feld geführt werden. Der Foetus sollte ausgereift sein, bevor der Entschluss zur Geburtseinleitung in der Praxis gefasst werden darf; drei Kriterien sind dabei von besonderer Wichtigkeit:

1. Trächtigkeitsdauer >320 Tage
2. gute Euterentwicklung

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