Onset of Labour:

H.L. CHONG M.B.,B.S.

H.C. ONG M.B.,B.S.

L.T. ANG M.B.,B.S.

Department of Obstetrics and Gynaecology,
University Hospital,
Kuala Lumpur,
West Malaysia.

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University Hospital,
Kuala Lumpur,
West Malaysia.

Introduction

The onset of labour is a fascinating but complex subject and up till today, mechanisms involved in the spontaneous onset of labour are little understood. Control of uterine contractility in pregnancy and control of parturition itself has been the subject of a great deal of study and an even greater amount of speculation has arisen in recent years.

Bengtsson (1965) commented that all important mechanisms controlling the maintenance and termination of pregnancy are influenced and safe-guarded by a number of different factors, some, improving or activating and others, depressing uterine activity. Based on this concept, he suggested in equation form that:

$$\text{Uterine activity} \propto \frac{\text{oestrogen} + \text{oxytocin} + \text{volume} + \text{neural factors}}{\text{progesterone} + \text{oxytocinase} + \text{other neural factors}}$$

Factors like oestrogen and oxytocin, he refers to as "activating" factors, and progesterone and oxytocinase, as "depressing" factors.

In recent years, the possible role of prostaglandins has been brought into the picture (Karim, 1971).

Labour may therefore start, by either an increase in one or several of the activating factors, or by a decrease in one or several of the depressing factors. There is no doubt that multiple factors involving placenta, fetus and mother are responsible for the onset of labour in the human. (Gillard, 1973).

PART I: ROLE OF HORMONES

I. Hormonal Factors in the onset of labour

Endocrine mechanisms involved in the onset of labour are also essential for parturition as well as for lactogenesis and normal expression of maternal behaviour and nursing impulses (Catala and Deis, 1973).

Various hormones have been implicated in the onset of labour and these include:

i) Progesterone
ii) Oestrogen
iii) Oxytocin
iv) Oxytocinase
v) Human placental lactogen (HPL)
vi) Cortisol, and the role of the fetal adrenal gland

i) Progesterone

The role of progesterone is still very much debated. As early as 1949, Reynolds has shown in rabbits, that progesterone withdrawal leads to termination of pregnancy and progesterone replacement therapy maintained it.

Csapo (1960) proposed that progesterone is the key hormone in the "defence mechanism" of human gestation and in 1961, he showed that it was possible to terminate pregnancy by withdrawal of progesterone. Using cases for termination of pregnancy, he showed that, following intraamniotic infusion of hypertonic saline there was a gradual but statistically significant progesterone withdrawal (Csapo, 1969 a). The fall in plasma progesterone was marked ten hours after saline infusion and during clinical abortion, a final withdrawal of 55.0% was measured. He also showed that a highly significant correlation between decreasing progesterone levels and increasing intrauterine pressure exists, indicating a causal relationship between these two factors.

There is also reliable evidence to show that labour is more readily induced in patients with low progesterone levels than in those with high levels.

The weakening of this defence mechanism at term has therefore been postulated by Csapo to be the main factor in initiation of labour. This fall in progesterone level prior to the onset of labour has also been the experience of other authors (Wiest, 1970; Pepe, 1972).

Based on this concept of progesterone withdrawal, Bengtsson (1965) used intra-myometrial injections of *Provera* (6 – alpha-methyl-17 alphaaceto-Progesterone) in different types of abortion in which effective uterine activity had started, and found that uterine activity could be completely extinguished.

Csapo believes that progesterone exerts a 'block' on uterine activity depressing the conductivity of the myometrial fibres and in this way, allows the continuance of pregnancy. Progesterone has no effects on the contractile elements of the myometrium (Turnbull and Anderson, 1971), but appears to influence the membrane potential of the myometrial fibres. The "progesterone block" is a result of direct spread of progesterone from the placenta into the muscle. There is an obvious local deposition in the myometrium adjacent to the placenta, but the rich blood supply to uterus would ensure that the progesterone content in the myometrial fibres would be evenly distributed (Theobald, 1968).

Possibly, declining plasma progesterone levels as term approaches, reflect diminishing biosynthesis of progesterone by the placenta (Wiest, 1970), related to the degenerative or ageing changes in the placenta near term when the uterus stops growing and disturbances of uterine circulation ensues (Greenhill, 1960) Then, according to Csapo's theory, the inhibitory effect on the myometrium is withdrawn and labour starts when the ratio between uterine volume and placental progesterone increases beyond a critical value.

ii) Oestrogen

The role of oestrogen probably rests on its regulatory effect on uterine function counteracting the influence of progesterone, by promoting the excitability and conduction of co-ordinated uterine contractions (Csapo, 1969 a). Oestrogen has been shown to increase the conductivity between muscle bundles in the myometrium (Csapo, 1960).

Bengtsson (1965) has shown that oestradiol therapy results in an increase in spontaneous uterine activity, as well as an increase in oxytocin sensitivity of the myometrium.

Masson and Klopper (1972) noted a tendency for unconjugated plasma oestriols to increase as labour approaches, reaching maximum values 2 to 4 days prior to the onset of labour.

Catala and Deis (1973), and Csapo (1969) observed that oestrogen was essential near term for normal parturition in experiments on rats. Yoshinaga (1969) described a rapid increase in oestrogen concentration in ovarian venous plexuses near term, the highest value being obtained on the day of parturition, falling to non-detectable levels on the day following delivery.

It is possible that critical steroid changes which brings on labour lies not in absolute changes in oestriol levels, but rather in the shift from a progesterone-dominated myometrium to an oestrogen-dominated myometrium. This is as reflected in the progesterone-oestriol ratios (Masson and Klopper, 1972).

The physiological effect therefore of a rise of oestrogens at the end of pregnancy could be related to an increase in sensitivity of the uterus to oxytocic substance (e.g. oxytocin, prostaglandins), and an increase in spontaneous uterine activity. The phenomenon is one of "oestrogen priming" of the uterus prior to the onset of labour.

iii) Oxytocin

The role of oxytocin in the onset of labour has been the subject of much controversy. Caldeyro-Barcia (1961) advanced the view that an increase in secretions of the neurohypophysis is one of the important factors causing the intensity and frequency of the uterine contractions during pre-labour. He also noted that a marked increase in the myometrial sensitivity to oxytocin is a pre-requisite for the onset of labour (Caldeyro-Barcia and Theobald, 1968).

Therefore, one would expect to find a rise in blood oxytocin levels prior to and during labour. Few studies, however, have been attempted in human pregnancy because of technical difficulties (Turnbull and Anderson, 1971). Chard, Boyd and Hudson (1970) found no circulating endogeneous oxytocin in human plasma during any stage of labour. Fitzpatirck (1966) and Chard et al (1970) failed to find any release of oxytocin during parturition in other species. Coch (1965) found "low oxytocin activity" in plasma during the first stage of labour, which increased markedly in the second stage. This has been the experience of Csapo (1960), Csapo and Ogata (1969), and Porter and Schofield (1966).

There is therefore no conclusive information on blood oxytocin levels in pregnancy prior to the onset of labour (Turnbull and Anderson, 1971). In the human, oxytocin is implicated only in the promotion of delivery already in progress. However this late involvement of oxytocin in human parturition does not minimise its therapeutic value.

Oxytocin promotes uterine activity by lowering the threshold, exerting its action on the cell membrane itself, bringing the membrane potential into the range most suitable for activity. Its action is instantaneous, promotes activity at all myometrial cell lengths and is rapidly reversible (Csapo, 1969 a).

Hence, despite its great therapeutic value there is no conclusive evidence for the essential involvement of oxytocin in the regulation of normal human uterine function and the initiation of labour.

iv) Oxytocinase

Oxytocinase, an enzyme capable of inactivating oxytocin was found to be present in high levels in plasma and placenta of women during pregnancy (Mathur and Walker 1968).

Increased oxytocinase activity has been reported in prolonged labours (Babuna and Yenen, 1966; Lambrinopoulus, 1964; Mathur and Walker, 1968). The maximum myometrial sensitivity to oxytocin occurs when the amount of oxytocinase in the blood is at its highest (Theobald, 1971).

The role of oxytocinase in the onset of labour is difficult to envisage. However, it might be logical to expect a fall in oxytocinase activity prior to the onset of labour but this has not been substantiated either in humans or in animal experiments.

v) Human Placental Lactogen (HPL)

The function of HPL in labour is unknown. Gillard (1973) showed that there was no change in the circulating HPL levels in the 14 days prior to onset of labour. Falls in HPL levels during labour are not great and not significant and are probably attributed to utero-placental ischemia associated with uterine contractions. There is no relationship between HPL levels and time of onset of labour.

vi) Corticosteroids and the Fetal Role

The role of cortisol in the initiation of parturition has been shown experimentally by Nathanielsz and Abel (1973). They found that cortisol administered into the rabbit on day 21 of pregnancy will initiate parturition. Shorter induction times were noted when cortisol was injected into the fetal sacs; this suggested that cortisol was more effective when administered into the fetus. However, while showing that adrenal steroids play a role in the onset of labour in rabbits there is no indication whether the steroids are secreted by the maternal or fetal adrenal.

It also appears that cortisol is unable to produce delivery in less than 60 to 70 hours over a wide range of infusion rates. This suggests that cortisol probably acts through a further step/steps which are indispensable for onset of labour, e.g.,

i) there is evidence that cortisol, in higher species, initiates certain metabolic reactions which produce hormonal changes necessary for parturition,

ii) in the sheep, one major secondary effect of cortisol infusion, is the production of prostaglandins (Liggins and Grieves, 1971),

iii) progesterone, in the rabbit, can inhibit cortisol induced parturition and this suggests that cortisol may also be exerting its effect by removing the 'progesterone block'.

The Fetal Role

Changes in function of the fetal adrenal cortex have been implicated in the initiation of labour in the sheep (Liggins et al, 1972), in the goat (Thorburn et al, 1972), and in the cow (Comline et al, 1973).

Josimovich (1969) reported that adrenalectomy in the fetal rat resulted in prolonged gestation. Liggins (1969) noted similar results with fetal hypophysectomy and bilateral adrenelectomy in the ewe. Conversely, ACTH administration, stimulating the fetal adrenals, provokes premature labour. This strongly suggests that the fetal adrenal may have something to do with the onset of labour (Theobald, 1971).

It has been shown that anencephalic fetuses, with adrenal hypoplasia secondary to pituitary deficiency, are often associated with prolonged gestation (Theobald, 1971; Turnbull and Anderson, 1971). Prolonged gestation has also been reported in women carrying a fetus affected by congenital adrenal hypoplasia, (O'Donohoe and Holland, 1968).

The fetal control of timing of its delivery is a highly advantageous biological adaptation (Nathanielsz, 1973). Preliminary evidence suggests that an increased concentration of cortisol in the fetal circulation causes a fall in progesterone production (Liggins, 1969), and onset of labour may be the result of withdrawal of the progesterone block in this way.

The control of the fetal adrenal is likely to reside in the hypothalamus. Inconclusive evidence suggests that the fetal hypothalamus may be responsive to stimuli well before term, thus allowing the possibility that increasing hypothalamic activity is the result of an increasing input of physiological stimuli as term approaches, rather than the result of maturation of the hypothalamic centres.

The timing of the onset of labour therefore appears to be an autonomous function of the fetus. It is the subject of continuing study in human pregnancy and in other species.

Conclusion

There is therefore a complex background of hormonal conditions determining the onset of labour. Groundwork for the preparation of labour seems to be accomplished by:

i) a fall in progesterone action and withdrawal of the "progesterone block",

ii) oestrogen "priming",

iii) changes in oxytocin concentration and myometrial sensitivity and probably oxytocinase activity,

and iv) changes in the function of the fetal adrenal gland with critical cortisol levels.

PART II: ROLE OF MECHANICAL AND NEURAL FACTORS

Both mechanical and neural factors no doubt influence myometrial function in their own ways, and are probably of importance in the onset of labour. Hippocrates in 460 B.C. commented that "when the child is grown big, he incontinently passes out into the outside world, free from any bonds". This was probably the earliest reference to a mechanical influence on the onset of labour. Theobald, discussing the nervous control of uterine activity, commented on a lighter strain that "the cow's uterus is said to contract when she casts eyes on the bull that is to cover her".

II.A. Role of Mechanical Factors

Research on the role of uterine volume shows it probably affects contractile function independently at multiple points through:

i) myometrial hypertrophy (Reynolds, 1949; Csapo, 1965).

ii) length-tension relationship (Csapo, 1955; Schofield and Wood, 1964).

iii) increase in pacemaker activity (Kuriyama, 1961, Csapo et al, 1963a, 1963b).

and iv) increase in conduction velocity (Csapo et al, 1963a, 1963b).

Clinical Examples

It has been long thought that the duration of pregnancy may be limited by the amount of stretch the uterine muscle can undergo. The frequent occurrence of premature labour when the uterus is over-distended and overstretched by hydramnios or multiple pregnancy lends support to this belief (Turnbull and Anderson, 1971; Greenhill, 1960; Csapo, 1969a).

The increase in uterine volume outstrips the myometrial progesterone concentrations and in addition enhances uterine activity. Onset of labour is imminent when the myometrial fibres are close to their optimal lengths for contraction.

Volume effects are further exemplified by the fact that post-menopausal women are capable of entering a process, hardly distinguishable from normal labour when delivering a submucous myoma by a futile effort (Kloosterman, 1960).

In intra-uterine death, there is a reduction of uterine volume which is considered by Csapo to be a significant factor in the continuance of missed abortions. Spontaneous evacuation occurs subsequently probably as a result of decreasing progesterone levels resulting in withdrawal of the "progesterone block". This is the likely mechanism for premature onset of labour in certain cases of toxaemia of pregnancy, placental infarction and abruptio placentae where there is placental insufficiency.

Experimental work

Volume effects have been shown experimentally by various authors.

Csapo (1969b) showed that ovariectomised rats first deliver from the uterine horn of greater volume. Volume a-symmetry between the uterine horns was also found by Csapo and Csapo (1969) to be a determining factor.

Csapo and Sauvage (1968) indicated that increasing stretch of the myometrium effectively promotes the "evolution" of uterine activity.

Certainly by late pregnancy, the myometrium is at its optimal length for contraction (Wood, 1964). Mosler (1967) has shown that the spontaneous onset of labour occurs only when the volume of the uterus has reached a critical point for maximal effective work and when wall tension is at its optimum.

Mechanism of Action

An increase of uterine volume in normal term pregnancies by intra-amniotic saline has been shown experimentally to increase uterine activity and may lead to labour (Csapo, 1963 c). Turnbull and Anderson (1968) has also shown that an artificial increase in the uterine volume at 18 weeks' gestation produces increased frequency of low intensity contractions.

Csapo (1961) postulated that another possible mechanism was that increasing uterine volume in pregnancy diminishes the "progesterone block" on the myometrium by increasing the non-placental uterine area. Spontaneous onset of labour occurs when the withdrawal of the "progesterone block" is adequate. Csapo formulated that the maintenance or termination of pregnancy is determined by the ratio $\frac{V}{PM}$, where V = uterine volume and PM = myometrial progesterone content.

There is therefore evidence supporting the theory that increasing distension of the uterus might initiate labour.

A counter argument against this theory lies in the fact that decreasing uterine volume following amniotomy might initiate labour. The mechanism here is however not related to volume loss which is shown by the lack of correlation between the volume of amniotic fluid removed at trans-abdominal amniocentesis and the onset of labour (Csapo et al). Amniotomy therefore increases uterine activity by a mechanism other than reduction of uterine volume: this is related to the Ferguson's reflex which will be commented on later.

Fundal Dominance

Before labour, the lower uterine segment is close to its optimal length for isometric contraction. During labour, this segment becomes over-stretched and the strength of contraction is reduced to between 10 – 35% of the maximum. This overstretch provides a natural mechanism for increasing the dominance of the upper segment over the lower uterine segment (Wood, 1964).

Role of Amniotic Fluid

The amniotic fluid may influence the onset of labour by means of active substances contained in the fluid, its ionic composition and its contribution to the uterine volume. The presence of oxytocics in human amniotic fluid has been demonstrated in vitro. However more recent work indicate that these oxytocic effects are largely due to ionic differences between the amniotic fluid and the perfusion medium. The importance of amniotic fluid oxytocics in the initiation of labour is doubtful, though the mechanical value of the bag of waters as a cervical dilator is considerable (Fuchs and Wagner, 1963).

II.B. Role of Neural Factors

It is established that all uterine activity is spontaneous and is but modified by hormones, nervous activity and impulses, electrolyte concentrations and membrane permeability (Theobald, 1968). This is exemplified by the fact that paraplegic women usually have normal labours and piglings and puppies

have been born normally after most of the maternal spinal cord has been cut (Csapo, 1960).

Establishment of Pathways

Unit activity in the hypothalamus and other diencephalic regions have been recorded, with a spontaneous firing rate varying from 0.1 sec. to more than 50 per second (Baraclough and Cross 1963). Probing of the cervix resulted in an acceleration of this firing rate, while progesterone administration resulted in selective depression of lateral hypothalamic neurones to cervical probing.

A neural connection therefore exists between the uterus and hypothalamus which is further evidenced by the precipitation of ovulation in the rabbit following coitus, an effect which could be mimicked by electrical or mechanical stimulation of the cervix and abolished by hypophysectomy (Csapo, 1960). Other similar confirmatory evidences include those of Theobald (1966), Theobald (1968), Cibils and Hendricks (1964) and Abrahams et al (1964). Abrahams commented that the specificity of the pathways from uterus to hypothalamus is however, open to doubt.

There is no doubt that pathways exist between the hypothalamus and pituitary gland, possibly commencing the efferent pathway. Fitzpatrick and Walmsley (1965) found that stimulation of certain nuclei and nervous pathways associated anatomically with the posterior pituitary gland could initiate labour or abortion.

Little work has been done on the regulatory effect of the autonomic nervous system of myometrial activity. Present knowledge is incomplete and confusing but there is no doubt that both parasympathetic and sympathetic elements exist. In the non-pregnant uterus there is a preponderance of noradrenetgic nerve fibres. As pregnancy progresses, this preponderance diminishes and a noticeable increase of adrenergic influences exists; this increase being about four fold. It is known that adrenaline has a depressive effect while nor-adrenaline has a stimulatory effect on the pregnant uterus. Wood (1969) therefore believes that the autonomic nerve influence on the human uterus changes in pregnancy to favour its maintenance. This is because during pregnancy, increasing levels of circulating adrenaline and a relative decrease in nor-adrenergic fibres supplying the uterus would both act to depress uterine activity.

It is therefore unlikely that the efferent autonomic pathway to the uterus plays any positive role in the onset of labour.

Contributions by Haterius and Ferguson (1938) and Ferguson (1941) showed that electrical stimulation of the neuro-hypophysis in rabbits resulted in increased uterine activity apparently due to some humoral agent. Stretching of the cervix evokes strong uterine contractions similar to those produced by oxytocin injections. These responses are abolished by mid-thoracic spinal or by destruction of the pituitary stalk.

The evidences suggest therefore that upon mechanical or electrical stimulation of the cervix, uterine activity is dependent on neurogenic impulses travelling along the afferent pathway from uterus to hypothalamus and higher centres and an efferent pathway to uterus via hormonal influences from the neurohypophysis rather than via autonomic efferents. This reflex forms the basis of "Ferguson's reflex", which probably explains the mechanism of induction of labour following amniotomy. The trigger for the reflex is related partly to the stretching of the cervix at amniotomy and partly to the direct mechanical stimulation by the fetal head on the pressure receptors in the cervix. Abrahams (1964) demonstrated that the relay between the uterus and hypothalamus is not only concerned with oxytocin release but also with effecting increased myometrial sensitivity to oxytocin.

Csapo (1960) commented that the myometrial (smooth muscle) cell contraction resembles rather than contrasts with that in striated muscle. Wansbrough et al (1967) demonstrated in addition the presence of alpha- and βeta-receptors in the human uterus. Continuance of pregnancy is associated with diminished conduction between muscle bundles, thereby reducing contractile activity. Progesterone reduces conduction velocity while oestrogen increases it. Excitation can also be related to alpha-receptor stimulation, a feature of oestrogen, while inhibition of uterine activity is related to βera-receptor stimulation, a feature of progesterone.

Therefore though all uterine activity is spontaneous, it is nevertheless modified to a great extent by hormonal influences, nervous activity and impulses, and even by volume effects.

CONCLUSION

Pregnancy therefore persists because of a fine

balance in "opposing" forces, those "holding" and those trying to expel the pregnancy. It seems that the effect of mechanical and neural factors in regulating myometrial function is super-imposed on a complex background of hormonal conditions – probably no single factor determines the onset of labour in human pregnancy.

PART III: ROLE OF POSTAGELANDINS

The name "prostaglandins" was given by von Euler in 1935 to a substance found in human seminal fluid. This substance stimulated smooth muscle and lowered blood pressure. It is now known that prostaglandins is not a single substance but a group of chemically related long-chain hydroxyfatty acids. They are not confined to the seminal fluid but are ubiquitous in mammalian tissues. In recent years, the role of prostaglandins in relation to parturition has been the subject of much research.

Karim (1971) suggested that prostaglandins may play a physiological role in the onset of labour. His arguments were based mainly on the following observations:–

i) the demonstration of a causal relationship between the level of prostaglandins in amniotic fluid and labour. Prostaglandins $F_{1\alpha}$ and $F_{2\alpha}$ were found to be present in amniotic fluid only during labour (Karim and Delvin, 1967). Prostaglandins E_2 was also found to be significantly higher in the amniotic fluid of patients in labour compared to patients at term but not in labour (Karim, 1971b). Prostaglandins E_1, though present, was not significantly higher in patients in labour.

ii) Prostaglandins $F_{2\alpha}$ was present in the maternal circulation only during labour (Karim, 1968), the highest concentration found at the peak of uterine contraction, with the second highest level just preceeding uterine contraction. Prostaglandins E_2 has recently also been identified in the maternal circulation during labour (Karim, 1971b).

iii) All four prostaglandins found in amniotic fluid during labour stimulated the pregnant myometrium is vivo. Prostaglandins E_2 and $F_{2\alpha}$ had been used successfully to induce labour at term (Karim et al, 1969; Embrey, 1969; Karim et al, 1970; Beazley et al, 1970).

iv) The pattern of uterine activity induced by prostaglandins E_2 and $F_{2\alpha}$ infusion was similar to that of normal labour.

Karim (1968) believes that prostaglandins is not released as a result of uterine contractions, but rather probably an increase in prostaglandins effects uterine contractions resulting in the onset of labour.

Liggins and Grieves (1971), experimenting on pregnant ewes suggested a causal relationship between prostaglandins $F_{2\alpha}$ and labour. In sheep, labour is controlled by secretion of cortico-steroids from foetal adrenals. In these experiments, dexamethasone was infused into three groups of sheep. In the first group where dexamethasone was infused for 24 hours but labour did not start, prostaglandins $F_{2\alpha}$ was noticed to be increased in the maternal cotyledons but not in the myometrium. In the second group, in which labour was initiated with 48 hours infusion of dexamethasone, a further increase in prostaglandins $F_{2\alpha}$ in both the maternal cotyledons and the myometrium was noticed. In the third group where dexamethasone was infused for 48 hours but labour was suppressed by progesterone injection, the level of prostaglandins $F_{2\alpha}$ was however, found to be the same as in the second group. It was concluded that prostaglandin $F_{2\alpha}$ precedes the onset of induced premature labour, indicating that it is probably not a consequence of labour. It was also postulated that the role of steroids in initiation of labour involves the release of prostaglandins.

Gillespie, Brummer and Chard (1972), have postulated that a release of prostaglandins from the decidua, heralding the onset of labour, causes release of oxytocin from the maternal neurohypophysis, the effect of which is enhanced in the myometrium by the local action of the decidual prostaglandins. A similar mechanism might act via the foetal pituitary. This involvement of the neurohypophysis may explain why spontaneous and prostaglandins induced contractions are inhibited by alcohol. Exogeneous pitocin induced labour is not inhibited by it.

Speroff (1973) has suggested that cortisol activation of placental enzymes is followed by oestrogen and prostaglandin production, both processes occurring within the same cell, possessing some sort of feedback effect upon each other.

Csapo (1973) has proposed that the myometrial

content of prostaglandins is stretch dependent. Therefore increasing uterine volume maintains a stimulation of uterine prostaglandins synthesis and release, but its oxytocic effects are suppressed by progesterone. As progesterone production diminsihes, the progesterone block is withdrawn and the increasing prostaglandins syr·' is resulting from uterine stretch predominates, thereby initiating labour.

Some authors however feel that the prostaglandins increase during labour may be a result rather than a cause of labour. Hibbard (1972) using serial sampling techniques found that peak prostaglandins release followed rather than preceded the peaks of contractions, a finding contrary to that of Karim (1968).

Brummer (1972) found that prostaglandins $F_{2\alpha}$ was higher in the maternal serum of women in labour than those at term but not in labour. The level of prostaglandins $F_{2\alpha}$ was not significantly different in women in spontaneous labour, labour induced by amniotomy and pitocin drip, and labour hastened by pitocin drip. Prostaglandins $F_{2\alpha}$ was also found to increase with cervical dilatation. He concluded that though prostaglandins was associated with labour, it was not the cause but rather a result of labour. He postulated that pressure, stretching and manipulation of the cervix caused the release of prostaglandins during labour. Poyser et al (1971) has noticed that distension of the guinea pig uterus in vitro will release prostaglandins $F_{2\alpha}$. Kierse and Turnbull (1973) measuring prostaglandins E_2 in amniotic fluid in women in spontaneous labour and oxytocin-induced labour produced a similar pattern of results. Their conclusion was almost identical.

CONCLUSION

This review of the literature shows that prostaglandins is in some way associated with labour. It is probable that prostaglandins is important in the complex chain of events that goes to initiate labour. Considering its success in the induction of labour, it is difficulty to believe that prostaglandins release is only the result of uterine contractions and in no way goes to initiate labour.

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