Today it is well established that the uterine body and the uterine cervix have to be considered as two entities closely related but with different functions.

The normal human cervix is a collagenous structure, that undergoes a dramatic and probably unique metamorphosis. In the nonpregnant state, the cervix is involved in the facilitation of sperm transport, prevention of invasion by micro-organism from vagina and outflow of menstrual blood and uterine secretions. While during pregnancy, cervix acts as a rigid sphincter for preserving the growing foetus in the uterus and for maintenance of pregnancy. At term, it dilates rapidly and effaces for easy passage of foetus.

Structurally, human cervix possesses all the components to meet the diverse demands throughout the reproductive cycle. Cervical canal is lined by columnar epithelium beneath which there are numerous glands (secretory units) to produce the cervical mucus. The main body of the cervix consists of stroma, made primarily of connective tissue which predominantly has collagen. The basic molecule of collagen is tropocollagen which is oriented in parallel and staggered in such a way that they create typical light and dark bands under electron microscope.

The cervical connective tissue at term shows widely scattered and dissociated collagen fibrils with
an increase in the ground substances when compared to the early pregnant or nonpregnant cervix (Danforth et al, 1960).

The collagen fibrils are embedded in a ground substance containing large molecule structure proteoglycan complexes containing a variety of glycosaminoglycans (GAGS). Hyaluronic acid binds least strongly of the GAGs molecules and will act to de-stabilize the collagen fibrils while GAGs containing iduronic acid and dermatan sulphate bind strongly and promote tissue stability (Obrink, 1973). The GAG slide chains of the proteoglycan then interact with further collagen, molecules and with each other. This relationship is important in orienting the collagen fibrils and thus providing mechanical strength (Lindahl and Hoo, 1978; Golichowski, 1980). The binding affinity of GAGs to collagen increases with increasing chain length and charge density.

The non-pregnant cervix consists of 80% water which increases to around 86% during late pregnancy (Liggins, 1978). In view of the highly hydrophilic property of the GAGs, these molecules may be important in determining the amount of tissue hydration, with increased hydration destabilizing the collagen fibrils and GAGs are produced by fibroblasts which constitute the major cellular component of the cervical connective tissue.

The collagen fibres are embedded in a ground substance containing large molecule structure proteoglycan complexes containing a variety of glycosaminoglycans (GAGs),
THE Dermatan Sulphate Proteoglycan & A Glycosaminoglycan

Protein core (30,000 daltons)

Oligosaccharide

Dermatan sulphate (25,000 daltons)

(2-O-sulfo) iduronic acid

4-O-sulfo-N-acetylgalactosamine
the most abundant being chondroitin sulphate and epidermatan sulphate (Von Mallot et al, 1979; Uldberg et al, 1983). There is change in glycosaminoglycan and water content, a relative increase in hyaluronic acid and a relative decrease in chondroitin sulphate and dermatan sulphate (Von Mallot et al, 1979). Hyaluronic acid has substantial hydrophilic properties influencing tissue hydration and thereby tissue tissue deformability causing an increased compliance. The increase in hyaluronic acid is due to breakdown of proteoglycan complexes by protease enzymes from the activated fibroblasts or leucocytes which infiltrate the connective tissue. The accumulation of hyaluronic acid and water between collagen fibres disperses them and increases distensability. A decrease in chondroitin sulphate concentration reduces the mechanical strength of the collagen fibriles and make them more prone to breakdown by proteolytic enzymes. The amount of soluble collagen in the tissue increases in parallel with the increased enzyme activities (Ito et al, 1979; Uldberg et al, 1983).

In addition to forming the ground substance of the tissue, proteoglycans invest collagen fibriles (Scott and Orford, 1981) with the protein ions attaching to the collagen.

Collagen is amenable to breakdown by only two enzymes, collagenase produced by fibroblasts and leucocytes and leucocytes elastase produced by macrophages, polymorphs
and eosinophils. Elastase causes breakdown of elastin collagen and proteoglycans. The collagen fragments produced by these enzymes is further broken down by non-
specific proteases such as neutral proteases and alkaline proteases. As the cervical collagen concentration decreases through pregnancy, the leucocyte elastase and collagenase activity increases (Uldberg et al., 1983).

Thus there is remodelling of collagen during pregnancy and parturition. The mature collagen with many cross links is broken down and is replaced with new collagen which has fewer cross links and can breakdown more rapidly during parturition.

Along with collagens and proteoglycans, a small amount of elastin is also present in the cervix. It is present as 20–30 micromole/l bands in a lamellar network forming a funnel-like structure in the cervix as compared to the fibrillar elastin fibres in the uterine corpus (Lappert and Yu, 1990).

During the days to weeks before the onset of labour, the consistency of cervix ordinarily changes so that it becomes softer and more readily distensible. The cervix also begins to shorten (Effacement) and the endocervical canal widens (dilatation), the process of cervical ripening. The changes associated with cervical ripening include a reduced collagen concentration within the tissue, an increase in water content and change in GAG content.
FACTORS INFLUENCING CERVICAL RIPENING

It appears that estrogens, progesterones, relaxin, prostaglandins, leucotrienes and catabolins, all may be the mediators for the regulation of synthesis and catabolism of connective tissue in the human uterine cervix.

ESTROGENS

Previous action of estradiol is necessary in order that progesterone and relaxin may later act upon the cervix. There is an increment of physiological phenomenon connected with the ripening of cervix (edema, increased vascularity and softening) (Pinto et al, 1965).

Estradiol has moderate oxytocic action upon the pregnant uterus at term and has an accelerating effect on the physiological phenomenon of cervical ripening (Pinto et al, 1965).

Estrogens promote cervical ripening probably by upregulation of collagenase and other proteolytic enzymes (Mochiesuki and Tojo, 1980). They also seem to contribute to the induction of phospholipase activity thereby increasing local production of PGE₂. Estradiol might be responsible for the influx of protease producing leukocytes which could induce ripening and which could not be evident in vitro.

PROSTAGLANDINS

Human semen was first noted to produce uterine contractions by Kursok and Lieb (1930) (Pickles, 1967).
The Arachidonic Acid Pathway for Prostaglandins (PG) and Leukotriene Production.

A A Membrane Phospholipids

Phospholipase A₂

Arachidonic Acid

PGG₂ / PGH₂

Thromboxane Synthetase

THROMBOXANE A₂ (TxA₂)

PG₂ / PGF₂α

Isomerase

PGI₂ Synthetase

PGI₂

AA - Arachidonic Acid
Subsequently the active ingredients were identified as prostaglandins.

Term prostaglandins was coined by Von Euler (1935). Prostaglandins are now known to exist in virtually every mammalian tissue and have important physiologic and pharmacologic activities. Prostaglandins are not stored in tissues but are formed from precursor fatty acids (diro-mogamma linolenic acid, arachidonic acid, eicosapentaenoic acid) which are freed from covalent bonding in phospholipids, triglycerides, cholesterol esters and other fatty acid compounds.

Depending on the precursor fatty acid prostaglandins of the 1, 2 and 3 double bond series are formed. In most physiologic systems, prostaglandins of the 2-series (PGF₂ and PGE₂) formed from arachidonic acid are most important.

Prostaglandins are naturally occurring substances of family of polyunsaturated 20 carbon fatty acids containing a cyclopentane ring and two aliphatic side chains chemically derivative of hypothetical prostanoic acid. Prostaglandins are divided into groups A, B, C, D, E, F, G, H and I, which are subdivided according to degree of unsaturation of side chains and a suffix denoting the number of double bond (e.g. PGE₁, PGE₂, PGE₃) when stereoisomerism exists its nature is shown by additional subscripts alpha or beta (PGF₂ alpha and PGF₂ beta). Only alpha isomer occurs naturally.
Prostaglandins are synthesized in vivo by cyclization of the centre of the carbon chain of 20-C(eicosaradic) polyunsaturated fatty acids, (e.g. arachidonic acid) to form a cyclopentane ring.

Arachidonic acid is a common constituent of phospholipid present commonly at \( C_2 \) position from which it is liberated by acylhydrolase phospholipase \( A_2 \). By the incorporation of two molecules of oxygen, arachidonic acid is converted to a highly unstable endoperoxide \( \text{PGE}_2 \), which then looses an oxygen radical to become \( \text{PGH}_2 \) from which all prostaglandins of the 2-series and thromboxane \( \text{A}_2 (\text{TXA}_2) \) are formed. Cyclooxygenase, the enzyme catalyzing the formation of \( \text{PGG}_2 \) from arachidonic acid. Mainly present in cells in an inactive form that is rapidly activated by substrate. The rate of prostaglandin synthesis is controlled by the rate of release of arachidonic acid from stores rather than by activity of cyclo-oxygenase (McDonald et al, 1978).

**Sites of Synthesis of Prostaglandins in Uterus**

It is found that uterine epithelium is the major source of \( \text{PGS}_2 \) alpha whereas the myometrium produces predominantly prostacyclin \( \text{PGI}_2 \) and a good amount of \( \text{PGF}_2 \) alpha. The endometrium metabolizes the arachidonic acid formed within endometrial cells and that from neighbouring tissues as amnion and chorion.

The main prostaglandins produced by the cervix are (\( \text{PGE}_2 \), \( \text{PGI}_2 \) and to lesser extent \( \text{PGF}_2 \) alpha. Their production
increases towards term and peaks during labour. Amniotic fluid concentration of PGE$_2$ and PGF$_2$ alpha also increases.

**CONTROL OF PG SYNTHESIS**

Effect of rising levels of cortisol in the fetal circulation is to divert progesterone synthesis towards estrogen synthesis, thus causing less progesterone and more estrogen to be secreted. Progesterone has a complex action on PG synthesis. On one hand it enhances the capacity to synthesize and on the other hand, it inhibits secretion.

Estrogen stimulates PG synthesis particularly from tissue previously exposed to progesterone. Thus the marked increase in estrogen progesterone ratio at term is a powerful stimulus for PG release. PGs act possibly by two ways:

1. They induce collagen breakdown.
2. They alter collagen binding and tissue hydration by altering GAG/proteoglycan composition.

Prostaglandin E$_2$ has double effect.

1. Regulate the C-AMP in the target cell.
2. Augment the activity of hyaluronic acid synthetase enzyme.

The increase in GAG production by PGs is by the increased hyaluronic acid synthesis within the fibroblasts under the influence of hyaluronic acid synthetase enzyme (Murota et al, 1977).

PGE$_2$ influences the cervical fibroblast production
of collagen and GAG. The production of these two substances is inversely related so that when collagen synthesis is reduced, an increase in GAG production occurs (Normstorm, 1984; Normstorm et al., 1985).

Secondly PGE$_2$ may induce proteolytic breakdown of proteoglycan complexes which causes increase in free hyaluronic acid content.

PGE$_2$ also causes release of stored collagenase/elastase from leukocytes. After treatment with PGE$_2$ these cells (leukocytes and fibroblasts) are enriched with vesicles localised close to the plasma membrane. They also contain long dendrite arms shortening the diffusion distance from the cell to any point in the tissue. Thus PGE$_2$ mediated cervical ripening easily explained by changes in GAG content which disperses and destabilise the collagen fibriles and increases tissue compliance.

RELAXIN

Relaxin is a polypeptide hormone similar to insulin, produced in the human corpus lutea, decidus and corion (Weis et al., 1977; MacLennan et al., 1980). Human fibroblasts exhibit relaxin receptors and relaxin has a mutagenic effect on fibroblasts (McMurtty et al., 1980). It stimulates cervical fibroblasts to release proteases which destroy the link proteins that hold the collagen framework together. This interaction may be dependent upon relaxin; interaction with estrogen and progesterone. Histologic
changes co-incident with cervical ripening induced by relaxin are indistinguishable from those induced by application of prostaglandins (MacLennan, 1980). Relaxin has been shown to have some effect on cervical ripening on women (MacLennan, 1981), and has been reported to increase collagenase activity. During pregnancy it seems to play a role in connective tissue remodelling at several anatomical sites (Evans et al, 1983).

**Oxytocin**

Oxytocin is secreted from both the maternal and fetal neurohypophysis during spontaneous labour.

Oxytocin is found in increasing concentration in amniotic fluid towards term (Dawood et al, 1978).

Oxytocin stimulates prostaglandins production in human uterine tissues. The decidua and amnion are the sites for the stimulatory action of oxytocin and not the myometrium, the classic target organ for oxytocin action (Fuchs et al, 1981).

There is high concentration of oxytocin receptors in the decidua at term. Myometrium also has a high oxytocin receptor concentration at term (Fuchs et al, 1981) but in the myometrium these receptors mediate only the contractile effects of this neurohypophyseal peptide (Fuchs et al, 1981), whereas in the decidua they serve a different function concerned with the biosynthesis of prostaglandins.
PROGESTERONE

It increases synthesis of prostaglandins in the cells but inhibits its release. Thus progesterone is an important physiological inhibitor of the ripening process in vivo by inhibiting neutrophil influx and activation (Jeffre and Koob, 1980). This possibility is supported by the ripening effects of anti-progestin on the cervix prior to termination of pregnancy (Gupta and Johnson, 1990; Radstead et al, 1990).

Progesterone seems to exert its influence on the myometrium by inhibiting sodium flux through the myometrium membrane and by raising the resting membrane potential.

EVALUATION OF THE CERVIX

A cervix that is unprepared and requires intervention and a cervix in which ripening process has already occurred must be differentiated before going in for induction of labour. The most readily used methods to make this assessment depend upon physical characteristics of the cervix. Bishop (1964) was the first to attempt to quantify the physical examination of the cervix by introducing a numeric scoring system. With their evaluation method one could predict an optimal time to begin induction as well as how long it would take a patient with a given score to go into spontaneous labour. When a high score is present, it is assumed that changes constituting cervical ripening have occurred and no further attempts to ripen
the cervix are needed (Bishop, 1964).

This was evaluated further by Friedman et al (1966) using the Bishop scoring system. These authors confirmed that the success or failure of induction correlates directly with the cervical score. With a score of 9 or more no one had failed induction. There was a 5 percent failure rate with a score of 6 to 8 and 20% failure of induction rate if the patient had a cervical score of 5 or less.

These authors also demonstrated that the pre-labour cervical score is directly related to the length of latent phase. As the pelvic score increases, while all other periods of labour are shortened the change is most apparent in the latent phase. The variation in the lengths of the latent phase in normal labour represent the variations of cervical preparedness.

Finally, of all the Bishop scoring parameters, the authors found dilatations to weight the most important and position of the cervix to weigh the least in determining the predictability of the score.

Calder et al (1977) and Wingerup et al (1978) have also published numeric rating system to evaluate the inducibility of the cervix.

Numerical scoring systems used to evaluate the inducibility of the cervix are given below.
<table>
<thead>
<tr>
<th>Factor</th>
<th>Score</th>
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A. Bishop (1964)

Dilatation (cm) 0-30 40-50 60-70 70+ 

Effacement (%) 0-10 20-50 60-70 70+ 

Station -3 -2 -1, 0 +1, +2 

Consistency Firm Medium Soft - 

Position Posterior Mid Anterior - 

No induction failure with pelvic score, more than or equal to 9. 20% induction failure rate when pelvic score less than or equal to 4.

0-5 unfavourable.

6-13 favourable.

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<th>Factor</th>
<th>Score</th>
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Dilatation (cm) <= 1 1-2 2-4 7-4 

Length (cm) 7-4 2-4 1-2 <= 1 

Consistency Firm Average Soft - 

Position Posterior Mid Anterior - 

Station of head from ischial spines (cm) 3 & above 2 and above 0-1; 0 <= 1, +2 

Cervical score of 3 or less has more complicated inductions including longer labours and increased rates of pyrexia and caesarean sections.
Factor

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<td>1</td>
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<td>2</td>
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C. Wingerup (1979)

<table>
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<th>Factor</th>
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<tr>
<td>Dilatation (cm)</td>
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<td>Effacement (%)</td>
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A pelvic score of 0-5 indicates that the cervix is unfavourable for induction, while a score of 6-10 indicates that it is favourable.

From the above account it is clear that cervical ripening greatly facilitates labour and ultimately influences the prospectives for a vaginal delivery, specially in multiparous patients. Failure of cervix to ripen significantly increases the chance of both post dated delivery and caesarean section, particularly when induction of labour is considered necessary. Under these circumstances, if measures are not taken to improve the cervical status before induction, oxytocin infusion alone may be relatively ineffective, resulting in prolonged induction, induction failure, an unacceptable rate of caesarean section (740%), prolonged hospital stay, increased medical costs and overall increase in maternal and fetal morbidity.
In search of an ideal priming agent, various agents and methods have been used over the years, which are broadly classified as mechanical and medical.

A. Mechanical

2. Balloon catheters and self retaining Foley’s catheters.
3. Hygroscopic
   Laminaria tents
   Laminical
   Dilapan.

B. Medical

1. Oxytocin
2. Oestrogen
3. Prostaglandins
4. Relaxin

**MANUAL DILATATION AND STRIPPING MEMBRANE**

Manual dilatation and insertion of foreign bodies into the endocervix and above the internal Os is the oldest methods available for ripening the cervix described in the writings of Hippocrates, serial digital dilatation of the unripped cervix is not done because of patient’s noncompliance but stripping or sweeping of the membranes is one of the most widely used mechanical methods for promoting cervical ripening and inducing labour. This is done by insinuating one or two fingers in the extra-amniotic space above the internal Os and then sweeping the fingers 360 degrees. Thereby separating the membranes from
the lower uterine segment. It is successful when pelvic score is good. With completely unripe cervix it fails and is inconsistent in its efficacy.

Excitation of the neural autonomic reflex and the release of oxytocin from the posterior pituitary may contribute (Fuchs et al, 1965).

The cervical ripening occurs because of local PG release, either PGE₂ from the chorio-amniotic membranes and adjacent decidua or PGF₂ from within cervix itself (Liggins et al, 1978 and Seilers et al, 1980). Direct effects of tissue stretching and disruption and the introduction of localized infection are the factor which initiate PG release.

**BALLOON CATHETERS AND HYGROSCOPIC CERVICAL DILATORS**

When the cervix is extremely unfavourable these are more advantageous for cervical ripening as they cause more gradual cervical dilatation and are associated with minimal patient discomfort. In addition, there is an increase in uterine activity which augments the local effects of the cervix and facilitates induction of labour with oxytocin.

Historically, various balloon catheters have been used to induce cervical ripening since the mid 1800's (Delee et al, 1966).

More acceptable, alternative method of cervical dilatation is the use of hygroscopic catheters (Rosenberg, 1980; Blue manthal et al, 1990).

In experienced hands they are a safe and reliable
method (Manabe et al, 1981). Though effective, the balloon catheters are cumbersome, archaic and aesthetically sub-optimal.

Several hygroscopic dilators are available. Laminaria tents made from dessicated stems of cold water sea weed (Laminaria Digitata, Japonica) available in various sizes, when placed in the endocervix for 6-12 hours, increase in diameter 3-4 fold without increase in length occurs. They appear to act primarily by expansive radical force to the cervical canal. But there is other mechanism which is not clear. Being natural products they have some disadvantages as it is difficult to control their content, and sterilization. Therefore, several synthetic hygroscopic dilators are introduced in which quality control can be done and they are equally effective safe and easy to use. Lamicel, a polyvinyl alcohol polymer sponge, impregnated with 450 mg of magnesium sulphate available as a sterile compressed, rigid cylinder 77.75 mm long and either 3 or 5 mm in diameter.

DILAPEN

Made from a stable, non tonic, hydrophyllc polymer of polycrylonitrite, available as sterile, rigid rods in various dimensions (4 x 65 mm; 4 x 55 mm and 3 x 55 mm) is safe and efficacious cervical dilator (Blumenthal et al, 1990).
MEDICAL METHODS

Oxytocin

A new milestone in the world of obstetric was reached when a posterior pituitary polypeptide known as oxytocin discovered by Sir Henry Dale was first used for induction of labour by Theobald (1956, 1959) and known as Pit drip.

It has been observed that in patients with an unripe cervix, infusion of oxytocin often fails to induce labour. In addition, this procedure does not prime the cervix (Wingerup et al, 1978).

Oxytocin for induction of labour in the presence of unripe cervix has led to a caesarean section rate for failed induction of approximately 50% (Prins et al, 1983; Shepherd et al, 1983).

Estrogens

Pinto et al (1965) described the oxytocin effect of high dose intravenous estradiol 17, as well as favourable effect on the cervical score.

Gordon and Calder (1977) concluded that local estradiol application was efficacious in priming and useful when placentual function is suspected. It has been theorized that estrogens act on the cervix indirectly via local stimulation of PG synthesis.

Tromens et al (1981) found that a local estradiol vaginal gel in cervical priming was associated with a significant absence of uterine activity.
Prostaglandins

Labour induction with prostaglandins was first reported by Karim et al (1968) using PGE₂ and P₂ alpha given by various routes have confirmed their value as oxytocic drugs for labour induction. Since then many trials (using various systemic and topical formulations) have documented the efficacy of PGE₂ in pregnancy termination, cervical ripening and labour induction. Numerous controlled and uncontrolled clinical trials were undertaken.

Using an intravenous infusion, Embrey and Karim (1968) found PGE₂ to be 5-10 times in inducing term labour.

In patients with a favourable cervical state prostaglandins given intravenously or orally have not been found superior to oxytocin. Moreover, systemic administration of prostaglandins has been associated with considerable number of side effects, specially of GIT and also as inflammation at the site of infusion (Graff et al, 1971).

But in patients with unfavourable cervixes, at term several investigators have found prostaglandins superior to oxytocin in inducing labour (Lindmark et al, 1975; Embrey et al, 1985). Even small doses of PGE₂ applied locally can provide significant improvement in cervical Bishop Scores, independent of uterine activity and with few systemic side effects (Calder et al, 1977; Bernstein et al, 1987).

These findings and reports from other clinical investigators suggest that PGE₂, in contrast to oxytocin and PGF₂ alpha may have a local priming effects on the
cervix. The results from the experience in vivo and in vitro in animals and in vitro studies in human cervical tissue by several investigators are also in accordance with these findings (Najaka et al, 1977).

Since PGs are categorised as locally acting hormones (Keirse et al, 1978) they should be administered preferably as close to the target organs as possible.

**LOCAL APPLICATION OF PGs**

Various routes are:

1. Extra amniotic route
2. Intravaginal route
3. Intracervical route

The ideal preparation for cervical ripening would produce a satisfactory effect on the cervix while not stimulating myometrial activity.

As the overall goal of such intervention is to induce labour, myometrial activity may not be a serious objection, however, myometrial activity in advance of a complaint cervix will result in increased stress for mother and fetus which may be particularly problematical in inductions where the fetus is compromised for example by intrauterine growth retardation.

**The Extra amniotic Route**

This was first to be studied by Calder and Embrey (1973). It involved transcervical passage of a Foley's catheter where, it was retained in the extra-amniotic space by the inflated catheter balloon. PGE₂
in the dose of 400-500 microgram was then applied extra-
amniotically, usually in a viscous gel such as tylose.
The technique is valuable in the most unripe and difficult
cases (Stewart et al, 1983). A number of controlled
clinical trials (Calder, 1986) have shown a significant
reduction in the induction delivery interval, caesarean
section rate, maternal pyrexia rate, and incidence of
babies born with low APGAR scores in women subsequently
induced with amniotomy and intravenous oxytocin. The
disadvantage of this technique is the invasiveness with a
theoretical risk of infection and possibility of bleeding
into the chorio-decidual space which could lead to uterine
hypertonus due to rapid uptake of the PG. Patients may
find the placement disagreeable.

Intracervical Route

Calder et al (1977) presented the first promising
results with the use of PGE$_2$ to hasten the ripening of an
unfavourable cervix in pregnant women prior to induction
of labour.

Following the studies by Ulmsten in Sweden
(Ulmsten, 1979; Ulmsten et al, 1979), endocervical
application of PGE$_2$ has become increasingly popular.

A variety of vehicles have been employed but the
most commonly used ones are the triacetin based gel marketed
as prepelil (Upjohn) and the starch based gel developed by
Ulmsten's group and marketed in Europe as cerviprost
(Organon). The dose administered is 0.5 mg with each
preparation.

The procedure is less invasive than the extra-amniotic space. It requires skilful placement of the gel accurately in the canal avoiding placement into the extra-amniotic space as well as leakage from the external Os.

Suspected side effects could be uterine hypertonicity, fetal heart rate variability and decelerations, incidence of fetal distress, nausea, vomiting, fever, peripartum infection, but they are very less.

Ulmsten et al (1983) carried out a study of endocervical application of PGE₂ gel combined with early intravenous infusion of oxytocin for induction of term labour in women with unripe cervix. and found favourable results.

Potentials benefits include fewer serial inductions, fewer failed inductions, fewer inpatient days, lower medical costs, better timing of delivery, lower maternal and fetal morbidity and a shorter interval to decision regarding the need for a caesarean section.

**Intravaginal Route**

Successful cervical ripening can also be achieved in majority of patients with vaginal preparations in the form of tablets or gel.

A much larger dose is required than that used extra-amniotically or endocervically and repeated applications may be required (Stewart et al, 1983; Greer and Calder, 1984).
Disadvantage being side effects due to greater dose and lesser efficacy (Ekman et al., 1983). Sophisticated hydrogel polymers (Embrey and Mackenzie, 1985) allowing slow sustained release of PGF₂ allow a major role, being easy to insert avoiding the more invasive techniques and avoiding the need for repeated application.

Relaxin

Several clinical trials conducted during the 1980s using purified porcine relaxin demonstrated its efficacy in promoting both pre-induction cervical ripening and labour in near term patients (MacLennan et al., 1985). Doses of 2 mg of relaxin in tylose gel administered as a single application either vaginally or intracervically promoted cervical ripening in 80% and labour in approximately one third of patients over 12 hour period.

The mean length of labour was significantly shorter and required less analgesic medicine with no significant maternal or foetal morbidity. Human relaxin has become available recently and clinical trials are underway in Australia (MacLennan, 1991).