REVIEW OF LITERATURE
of all the methods of termination of pregnancy in second trimester abdominal hysterotomy must be one of the easiest operation in the whole field of gynaecology and one in which the control of blood loss is total, but during past decade it has lost much of its popularity as other methods are being preferred in terms of avoiding scar, anaesthetic and operative complications and hospital stay. one of the advantage that is still there is the aminibility of the woman to accept tubectomy simultaneously with very little motivation.

In subsequent pregnancies complications due to scar are emphasized by Clow and Crompton (1973). As with a classical Caesarian section, there is a distinct possibility of a scar dehiscence or rupture occuring in any future pregnancy. Russel and Hewlett (1969) found radiographic evidence of deformity at the scar site in nearly 50 per cent of the cases investigated.

In a study of 50 cases carried out by Russel et al (1969) of patients who had hysterotomy for therapeutic termination of pregnancy fifty two per cent showed a normal Hysterogram. Forty eight percent showed some deformity at the scar.
Although much work has been done on induction of abortion with hypertonic saline, the method is still viewed with apprehension with regard to its safety. Since the time it was first introduced by Abuwal (1934 as quoted by Agarwal Savitro et al 1979) the method of termination of pregnancy by hypertonic saline has been extensively used by a number of workers in India and abroad - Wagner et al (1962), Ruttner (1966).

While most of the workers - Fuchs (1967), Schiffer (1966), and Mackenzie (1971) as quoted from Agarwal, Savitri et al (1979) used abdominal route for instillation of hypertonic saline others Ruttner (1966) claimed equal success by injecting it through vaginal route. Saline of different strengths has been used by different workers. Majority of workers used 20% saline (Wagner et al 1962), Mackenzie (1971). Except a few workers the amount of saline instilled was restricted to a maximum limit of 200 ml by majority of workers. Cameron and Dayan (1966) recorded 2 deaths due to massive cerebral infarction following instillation of saline.

(Csapo (1966) and Coworkers) believe that the hypertonic saline solution triggers the evaluation of uterine activity and abortion by increasing the uterine volume: plasma progestrone (V/P ratio).
Bengtsson and Csapo showed in 1962 that oxytocin had very little effect on midtrimester; after saline injections the uterus becomes much more sensitive to oxytocin. Wagner and colleagues (1962) and Schiffer (1966) investigated the effect of small dosages of oxytocin administered 24 hours after saline induced abortion and found that it had no effect.

Craft and Musa (1971) were able to demonstrate oxytocin effectiveness when the patients were aborted with intraamniotic instillation of urea. The study of Laurensen et al (1973) showed a significant faster mean abortion time when large dosage of oxytocin were given immediately after saline instillation.

<table>
<thead>
<tr>
<th>Oxytocin administration in relation to saline instillation</th>
<th>No. of patients</th>
<th>Mean abortion time in hours</th>
<th>S.D.</th>
<th>SEM</th>
</tr>
</thead>
<tbody>
<tr>
<td>No Oxytocin</td>
<td>202</td>
<td>35.6</td>
<td>± 14.18</td>
<td>.997</td>
</tr>
<tr>
<td>Oxytocin started within 2 hours</td>
<td>221</td>
<td>20.4</td>
<td>± 8.08</td>
<td>.543</td>
</tr>
<tr>
<td>Oxytocin in started between 2 and 24 hrs.</td>
<td>99</td>
<td>28.8</td>
<td>± 9.16</td>
<td>.925</td>
</tr>
<tr>
<td>Oxytocin started after 24 hrs.</td>
<td>160</td>
<td>45.2</td>
<td>± 17.19</td>
<td>1.355</td>
</tr>
<tr>
<td>Total</td>
<td>682</td>
<td>31.7</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
This analysis showed that abortion time was significantly lowered in patients who received oxytocin within 2 hours of saline instillation.

Various complications like post abortal fever, pelvic infection, retained placenta, maternal mortality have been reported by various workers. Wagner (1962) reported an incidence of 2.35% of pelvic infection which included the case of pelvic abscess, one case of paralytic ileus.

Post abortal fever was reported by Wagner et al, (1962), Weingold (1965) Kerenyi (1971) as quoted from Agarwal Savitri et al (1979) as 7.5%, 11.1% and 6.8% respectively. In the series of Agarwal Savitri (1979) the incidence for the same was noticed as 3.7% which responded to simple antipyretic measures.

Deaths reported by various authors were definitely either due to faulty technique adopted or wrong selection of cases with systemic disorders Haschizume (1950) as quoted from Agarwal Savitri et al (1979) from Japan. These were subsequently reviewed by Wagastuma (1968) and causes were attributed to (1) Technical failure which represented infection or direct injection into the blood stream or myometrium.
(ii) Aggravation of general complications already present due to improper evaluation of the illness. Pathak (1968) reported death in a known diabetic and with instillation of excessive hypertonic saline. Cameron Dayan (1966) reported death in which the technique was practised under G/A which is a disadvantage where the side effects cannot be elicited as compared to a fully conscious patient, so it is in fact that selection of cases and proper technique of administration of hypertonic saline is very important in order to avoid serious complications and side effects. Instillation of hypertonic saline has many advantages. It may be preferred to hysterotomy in as much as avoiding uterine scar, anaesthetic and operative complications and length of hospital stay.

Intrauterine injections via the cervix of soapy pastes actus/utus type have been used since 1930's and Barns (1971) as quoted by Green half (1971) enthusiastically reported a success rate of 80%.

Amniocentesis and the injection of 50% dextrose had been used with great success by Brosset (1958), Lewis et al (1969) but there remains the potential hazard of intrauterine infection and possibility of thrombolic complications if a part of injection is made intravenously.
<table>
<thead>
<tr>
<th>Author</th>
<th>No. of pts.</th>
<th>Dose of Oxytocin</th>
<th>Mean I/A interval (hrs.)</th>
<th>Failure Rate</th>
<th>Mean Hospital stay</th>
</tr>
</thead>
<tbody>
<tr>
<td>Craft and Musa</td>
<td>15</td>
<td>38 mu/min.</td>
<td>26.43</td>
<td>None</td>
<td>4</td>
</tr>
<tr>
<td>Rand and associates</td>
<td>7</td>
<td>None</td>
<td>49.60</td>
<td>None</td>
<td>not recorded</td>
</tr>
<tr>
<td>Greenhalf</td>
<td>50</td>
<td>Buccal after 24 hrs.</td>
<td>4800</td>
<td>10</td>
<td>5.5</td>
</tr>
<tr>
<td>Smith and Newton</td>
<td>50</td>
<td>app.265</td>
<td>22.79</td>
<td>5</td>
<td>not recorded</td>
</tr>
</tbody>
</table>

Hyperosmolar urea has been shown to be an effective midtrimester abortifacient and there is some evidence to suggest that with respect to safety it may have distinct advantages when compared to hypertonic saline. Whereas urea is considered to be extremely safe as an abortifacient agent. Certain complications comparable to that of saline have been documented.

Injection of urea into the myometrium just as saline is proved to result in muscle necrosis, as Parmley et al (1976) demonstrated in Rhesus monkeys. Recent literature also indicates the potentiality for coagulation defects in urea induced abortions. Burnett et al (1975) have demonstrated a fall in fibrinogen concentration approximately 15% after 6 hrs. of instillation of urea and lowest level recorded is 145 mgms.
The mean platelet count showed a drop of approximately 18% and the fibrinogen fibrin degradation products (FDP) were significantly elevated in 36% of patients.

Mackenzif and Linda (1975) reported changes consistent with intravascular coagulation (Rise in F.D.P., fall in plasma fibrinogen and reduction in platelet count) in patients aborted with prostaglandin in combination with urea.

The theoretical foundation for the use of prostaglandins in the induction of early and late abortions in human was the work on the induction of labour. Unlike oxytocin prostaglandins were found to have a stimulating effect on the myometrium in early as well as late pregnancies. Bygdeman et al (1967) Karim and Hillier (1970) identified significant levels of PGF₂α and PGE₂ in human amniotic fluid, in the decidua and in peripheral maternal circulation not only at the time of full term spontaneous labour but also during spontaneous abortion. Karim & Filshie (1970) reported a series of 15 patients who received a constant infusion of PGF₂α (15mg/min). Abortion was successful in 14 and complete in 13 Uterine contractions were monitored in 10 pts., which usually revealed an initial hypertonus which occurred 1-3 min after beginning the infusion and lasted 10-15 min until labour became established.
The only side effects noted were diarrhoea in 7 women, 3 of whom also vomited. Gestation ages were 9-22 weeks.

The simultaneous publication from Stockholm by Roth-Branådel et al (1970) concerning the use of prostaglandins to induce abortions in 11 women between the thirteenth and eighteenth weeks of pregnancy I/V infusions in various dose rate were used in 7 pts. and S/C injections in 4.

Both methods of administration caused an initial hypertonic uterine response with ultimate labour but were maintained long enough to induce abortion in 3 of 11 patients. Dose rates were regulated to invoke a uterine response without causing side effects.

In less than 2 years since these initial publications numerous clinical studies have been reported by Bygdeman and Wiquist (1971), Karim (1971), Embrey (1971), Gellespie (1971) Karim and Filshie (1970); Kaufman et al (1971): once again Karim had the most extensive experience. The success rate was 93% representing the most efficacious results thus far accomplished by any investigator.

Bygdeman and Wiquists (1971) cumulated experience with I/V PGF2α is summarized below. The infusion was given at a constant rate 25 - 100 ugms/min. and titrated against side effects. With a mean total dose of 30 mg, 94% of the early pregnancy (8 weeks or less) aborted. However only 10-30% of later pregnancies aborted despite prolongation of infusion to 13 hrs.
Results of cumulative experience using I/V PGE₂ for therapeutic abortion.

(Bygdemann and Wiquist 1971)

<table>
<thead>
<tr>
<th>Preg. (Wks)</th>
<th>No. of cases</th>
<th>Average infusion time (hrs)</th>
<th>Total dose (mg)</th>
<th>Complete or partial</th>
</tr>
</thead>
<tbody>
<tr>
<td>8</td>
<td>22</td>
<td>7.6</td>
<td>31.1</td>
<td>20</td>
</tr>
<tr>
<td>9-12</td>
<td>19</td>
<td>13.4</td>
<td>61.8</td>
<td>6</td>
</tr>
<tr>
<td>13-15</td>
<td>13</td>
<td>13.4</td>
<td>70.9</td>
<td>2</td>
</tr>
<tr>
<td>16</td>
<td>10</td>
<td>13.9</td>
<td>66.7</td>
<td>2</td>
</tr>
</tbody>
</table>

Wiquist and Bygdemann found that significant dysmenorrhoeic pain occurred in 50% of cases at a dose of 50 mg/min. whereas only 12% of cases had nausea or diarrhoea. At a rate of 75 mg/min. 80% complained of dysmenorrhoeic pain and 80% had nausea or diarrhoea. At 100 mgms/min. all subject developed significant dysmenorrhoeic complaints and it was concluded that the dose dysmennorhoic range which stimulates effective uterine contractions but does not cause generalized side effects is rather limited.

The lack of adequate efficacy and occurrence of clinically unacceptable side effects caused the investigators to turn to other possible routes of administration.
Karim noted uterine stimulation at term by using oral PGE\textsubscript{2} but found that large amounts required to stimulate the early pregnancy uterus caused unacceptable gastrointestinal side effects. Workshop conference on prostaglandins (1971). Wiquist and Bygdemar (1970) found that subcutaneous and intramuscular routes yielded a uterine response but caused excessive local pain. The only other route that showed promise was extraovular vaginal and intraamniotic. They investigated the extraovular route because of their limited success with more advanced pregnancies. It was hoped that the prostaglandins would have a local effect, thus giving maximum response with minimum side effects.

The intraamniotic route had been tried by Wiquist et al (1968). Using doses in the range of 75 ug/min in mid pregnancy uterus they noted no appreciable side effect on uterine contractility using higher dosages 5-15 mg PGE\textsubscript{2} administered at intervals of 3-14 hrs depending on contractile response. Bygdemar et al (1971) noted physiological contractions within 60 min. and nine patients aborted, 4 completely. The drug was injected through a transabdominal intraamniotic Catheter which was left in side to also allow recording of uterine contractions.
There is still great need for an easily available drug which will constantly induce second trimester abortion with certainly without ending up in incomplete expulsion of the products of conception or serious complications.

In recent years the role of Steroids in myometrial contractility and in labour has been under intense study. Mati et al (1973) could provoke premature labour in eves by intramuscular injection of Betamethasone. Craft et al (1975) successfully induced labour by betamethasone administered intramuscularly. Murphy (1973) indicated a relationship between cortisol levels and onset of uterine contracility in humans. Nwosu et al (1976) employed intraamniotic injection of 500 mg. cortisol to induce labour in prolonged gestation.

Parik (1978) in his series of 15 cases tried 400 mg of efoorlin - with 10 units of syntocinon. 13 cases (86.7%) aborted. The induction abortion interval was found to be 62 hrs. and 41 min. There was no incomplete abortion and failure was seen in 2 cases (13.3%).

The mechanism of cortisol induced labour is not fully understood. In the sheep Liggins (1972) has proposed that the sheep cortisol shower released by foetal lamb near term increases the levels of placental prostaglandins $F_2\alpha$ as well as oestrogens.
The increasing concentration of both these agents are thought to prime the uterus increasing its sensation to endogenous oxytocin. Whether a similar mechanism is applicable to human remains to be defined.

Midtrimester pregnancy termination was tried with intraamniotic distilled water by Rastogi K. et al (1981) in 100 cases. The amount of distilled water that could be instilled had no relation with the period of gestation, but had a very significant relation to outcome. The procedure was 100% effective when more than 100 c.c distilled water was injected.

The time of onset of uterine contractions varied from 0-12 hours in 5 cases, 12-25 hours in 25 cases, 24-48 hours in 70 cases. Thus in 70% cases contraction started in 24-48 hrs. The instillation abortion interval varied from 24-48 hours in 15 cases, 49-72 hours in 45 cases, 72-96 hours in 40 cases. In 10 cases, oxytocin drip was started and in 5 cases ARM was done. Only in 5 cases evacuation was done. Seventeen cases failed to abort and thus the success rate was 83%.

Complications reported excessive bleeding due to cervical tear, 1 case (1%) pyrexia, in 5 cases (5%) amniotic fluid embolism with mortality 1% and retained placenta 5 cases (5%).
The story behind the development of Japanese method begins with opening of Japanese doors to western civilization some 100 years ago. Japan learned modern medicine largely from Germany, and before the war German text books were generally used. Naturally, the techniques available for inducing labour at term were those which had been developed in Germany. These included rubber instrument insertion, such as Bougies between the membrane and the uterine wall known as Krause method (1855 as quoted from Hanebe, 1969) and introduction through the cervix or an infusion bag, e.g. the Colpoureynait or"Cari Brann (1851) as quoted from Hanebe (1969) and necreureynait of Champetier de Ribes (1887 as quoted from Hanebe 1969). Although American medical practise began to replace the methods after World War II, the time honoured use of rubber instruments persisted.

Hanebe, Y (1969) has reported upon the rise in uterine activity in necreureynait bougie induced abortion in mid-trimester extravular placement of rubber cube has been advocated by George (1978) as quoted from Misra, J. et al (1981) for mid trimester abortion. Prolonged abortion time being a major concern by Catheters a combined method of catheter and prostaglandins was advocated by Rajan et al (1979) Graud (1976) as quoted from Misra et al (1981) has used extravular rubber catheter only for termination of pregnancy with success.
The events of labour after induction by this method do not differ at all from those at term, so long the delivery is completed quickly without infectious complication and if foetus is near the middle of the 5th month it is normally delivered alive. Most foetuses however die shortly after delivery if foetal age is less than the middle of 7th month.

There seems no functional difference between Japanese methods and others including the use of hypertonic solutions. The common denominator is stimulation of the uterus in broad sense. Stretch is concentrated in the cervical region with metreurynter, while it is more widely spread from cervix to fundus in other methods. This suggests a lack of regional speciality for stimulation.

When mechanical stimulation is applied to the uterus the possibility of reflex release of oxytocin during treatment cannot be eliminated. It is known however that sensitivity of the uterus to the oxytocin is quite low at midtrimester and that it does not reach to physiological doses. Thus even if some oxytocin is released during treatment it can hardly be considered sufficient to start labour contractions. This has already been proved in metreurynter induced abortions. When the metreurynter is not used oxytocin treatment fails to start labour at mid pregnancy.
The study of Japanese methods indicates that placental dysfunction is not the cause of rise in uterine contractility, and the myogenic nature of uterine contraction has been postulated. The myogenic activity of uterine vessels is well recognized if the uterine muscle is stimulated mechanically its intrinsic myogenic activity is increased. Recent electrophysiological studies provide theoretical evidence bearing on this problem. When strips of pregnant uterus are passively stretched no tension on them increased, the membrane potential is reduced and spike frequently is increased.

The extraovular method which is based on the introduction of a solution into the uterus in an extraovular route has been known for a long time. In 1595 Avicenna, (as quoted from Nabriski 1971) devised aspecial apparatus for introduction of such solution into the uterus to cause abortion. In 1825 Schneehaus (as quoted from Nabriski 1971) advised the same method for the operation. The search for a safer solution led to the discovery of Rivanol or acrinol lactate.

Cohen in 1846 (as quoted by Rastogi et al (1981) first described the extraovulat injection for termination of pregnancy in second trimester. It is a derivative acridine, a yellow dye stuff with antiseptic action. It has been used as a 0.05 to 0.02% solution either locally
or as a surgical skin antiseptic or internally as disinfectant for the urinary tract. It is a 6,9 diamino - 2- oxyethyl acridine lactate.

In soviet union Pytel (As quoted by Rastogi. K., et al 1981) and associated reported 5 cases of acute renal failure after extraamniotic instillation of Rivanol. However, very large volumes (500 to 700 cc) of 0.1% solution of Rivanol were used in these cases. In Japan on the other hand no serious complications have been reported. However the volume used in that country were no more than 30-300 ml of 0.1% solution. The use of ethacridine lactate dates from 1949 but more extensive studies have been carried out only recently by Manabe (1969).

Nabriski and Kalmanovitch (1971) modified the original rivanol catheter technique by removing the catheter immediately after injection and their success rate was 94%. Carl Axel Ingemanson of Sweden (1973) compared the results of rivanol with extraamniotic injection of hypertonic saline and concluded that the overall results with rivanol were better and the initial success rate of 74% with saline induction as compared to 94% in rivanol catheter group with remarkably few complications.

Ethacridine lactate administered extraamniotically causes mechanical stripping of entire sac from the uterine wall.
It causes reflex release of oxytocin (Lewis and Still Well, 1971), it causes release of prostaglandins Gustavie (1974) suggested that any solution given extraovularly causes release of lysosomal enzymes within the decidual cells which help in release of prostaglandins precursors from the membrane phospholipids and thereby help in synthesis of the prostaglandins.

Anjaneyulu et al (1977) reported 81-4% abortion within 72 hours after first instillation and 100% after re-instillation. They used Unitocin (Spartment Sulphate) 150 mg I.M. 1 hourly for 3 doses to assist the process of expulsion.

In the series of Gupta et al (1977) the success rate with Emoredyl was 28% in 48 hours and total 92% in 72 hours and method failure was 4%.

There is disagreement on the nature of change produced on the placenta and membrane after intraamniotic injection of hypertonic solutions. The lesions described have included necrosis of amnion (Stamm and De-Watteville 1954) as quoted from Christie et al (1966), an intense "necrotising placentitis" (Bengtsson and Stormby, 1962) intervillous and thrombosis of chorionic vessels with chorioamnionitis (Scianera et al, 1964), as quoted from Christie et al (1966) other workers did not detect any change in the placenta and membrane (Wood et al : 1962).
However, Jaffiöön et al (1962) did not find any microscopic evidence of deciduitis but did describe intervillous thrombosis in subchorionic zone. Klopper et al (1966) also found bulk of placenta normal but for superficial coagulative necrosis. Christie et al (1966) observed oedematous membranes in all and thin irregular zone of red thrombus in 5 out of 7 placentae of hypertonic saline abortions on microscopic examination.

Kunders and Hemlatha (1972) as quoted from Salhan Sudha et al (1979) on histological examination of placenta and membrane could only attribute mild inflammation with polymorphonuclear leucocytosis to I/A saline injection. The histological findings of Salhan Sudha et al (1979) were similar to those reported by Gustavie and Brunk (1971). They observed that decidual cells underneath nitabuck membrane showed extensive digestive alterations. Brunk and Gustavie (1973) as quoted from Salhan Sudha et al (1979) came to the conclusion that the saline diffuses out through membrane and acts on decidua which lies in the extra amniotic space. It is therefore, possible that the decidua is the target in the action of hypertonic saline. The damage to the decidua causes release of prostaglandin $F_2\alpha$ into amniotic fluid exerting its abortifacient activity (Gustavie and Brunk 1971).
Vassilakos et al (1974) were also able to demonstrate a surprising vulnerability of decidua during saline abortion by observing degenerative changes as early as 2 hours after saline instillation. Myers et al (1974) upheld this findings Llewellyn et al (1975) recorded a steady rise in prostaglandins $F_2\alpha$ levels after intraamniotic saline injection. Similar findings were reported by Gustavie and Green (1972).