SURVIVAL OF EMBRYOS TRANSFERRED INTO THE IUD-BEARING UTERUS OF THE RAT

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Summary. An IUD is thought to exert a contraceptive effect either by (1) inducing the premature expulsion of embryos, (2) preventing the uterus from accepting the embryo for implantation, or (3) causing the death of the unimplanted embryo. The intrauterine environment of rats with an IUD was tested for embryotoxic effects on embryos introduced into the uterus, using the technique of double transfer of embryos. Exposure of embryos to an IUD-bearing uterus for 2½ to 4 hr resulted in failure to recover 85% of them. Even the few embryos recovered after 2½ to 4 hr showed greatly increased mortality when transplanted into a normal pseudopregnant recipient. Removing the IUD 6, 24, 48 or 72 hr before embryo transfer increased both the recovery and survival rates over those obtained with the IUD in situ. The recovery rates were not equal to those from the controls, however, until 72 hr elapsed between IUD removal and embryo transfer. Embryos were transferred into the IUD-bearing horn of bilaterally ovariectomized rats treated with progesterone. The recovery rate of these embryos was intermediate between that of intact controls and non-ovariectomized, IUD-bearing animals. The survival rate of these embryos, however, was higher than that of the controls. The results of the embryo transfer experiments indicate that an IUD inhibits pregnancy in the rat by directly causing the death of embryos within 4 hr.

INTRODUCTION

Recent studies on the rat (Parr, Schaedler & Hirsch, 1967) and several other species, e.g. ferret (Marston & Kelly, 1969a), rabbit (Marston & Chang, 1969), mouse (Marston & Kelly, 1969b), cow (Hawk, Conley & Brinsfield, 1968) and sheep (Hawk, 1969), suggest pathological changes in the uterine milieu as the primary mediator of anti-implantation effects of an intrauterine device (IUD). It is not clear if this anti-implantation effect is on the uterus or on the embryos. The technique of double transfer of embryos, which is well suited for distinguishing uterine effects from embryonic effects, was used to determine embryotoxic effects of the intrauterine environment of rats having an IUD. The embryos were subjected to the environment of the IUD-bearing uterus for only a few hours before retransferring them.
The only previous report of the transfer of ova in investigations of IUDs was by Hawk (1965). He transferred unfertilized ova from IUD-bearing ewes to the oviducts of intact ewes. After mating these recipients, the transferred ova became fertilized, indicating that an IUD did not deleteriously affect them.

MATERIALS AND METHODS
The overall plan of our experiments was to transfer normal embryos into the uterus of rats, one horn of which contained an IUD while the other served as a control horn. At various intervals after transfer, the rats were killed, and the embryos recovered. The embryos were immediately retransferred into the uterus of a second, normal, pseudopregnant host to determine if residing in the uterine environment with an IUD had damaged the embryos. Embryonic survival in this second recipient was determined at mid-gestation.

Holtzman-derived rats (Sasco, 5309 North 24th Street, Omaha, Nebraska) were maintained as previously described (Anderson, Melampy & Chen, 1967). Daily vaginal smears were taken by lavage. Day 1 of pregnancy was the day on which spermatozoa were found in the vaginal smear. Pseudopregnancy was induced by stimulating the cervix of pro-oestrous or oestrous rats for 20 sec with a vibrating rod held in an electric engraver (DeFeo, 1966). Rats were stimulated on the morning of each day on which the vaginal smear contained cornified cells. Day 1 of pseudopregnancy was the last day of cornification.

A silk (No. 5-0) thread IUD was inserted in the mid-portion of the right uterine horn of cycling rats by using the technique of Parr et al. (1967). A 1.5-cm length of the thread lay within the lumen. Before use as an IUD, the thread was washed in running tap-water for 12 hr and then autoclaved. Animals were not used as donors or recipients of embryos for at least 2 weeks after inserting the IUD.

The technique of embryo transfer was similar to that of Dickmann & Noyes (1960) and Dickman & DeFeo (1967). Phosphate-buffered saline (pH 7.3) and rat plasma in a ratio of 2:1 were used as the medium for collection and transfer of embryos. The medium was preheated to 35°C in an incubation chamber for the microscope. All manipulations and observations of embryos were carried out in this chamber. Embryos were exposed to the conditions in vitro for 10 to 15 min. All equipment that came into contact with either the embryos or the uterine lumen was sterilized; otherwise, clean technique was used. Embryos were transferred between 10.00 and 19.00 hours on Day 4.

Four series of experiments were included: (1) effect of an IUD on oviducal embryos, (2) effect of duration of incubation of embryos in an IUD-bearing horn on embryonic survival, (3) reversible effects of IUDs, and (4) effects of ovariectomy and an IUD on embryonic survival. Table 1 shows the treatments of all groups.

Effect of an IUD on oviducal embryos
Rats having an IUD in the right uterine horn were mated. On Day 4, oviducal embryos were transferred into the right and left uterine horns, respectively, of intact rats at Day 4 of pseudopregnancy. These recipients were killed on
Day 13, and the number of live embryos was determined. Only embryos with heartbeats were considered alive. The survival rate percentage was calculated for each horn as the number of live embryos at Day 13 divided by the number of embryos originally transferred into that horn multiplied by 100. There were twelve recipients in this group.

**Table 1**

**Experimental treatments of transferred embryos and embryo recipients**

<table>
<thead>
<tr>
<th>Group</th>
<th>No. of rats</th>
<th>Experimental treatment of Recipient I</th>
<th>Hr embryos incubated in uterus of Recipient I</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Recovery of embryos from the oviduct</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>12</td>
<td>Normal Day-4 pp; embryo donor with IUD†</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Effect of duration of embryos in an IUD-bearing horn on recovery and survival of embryos</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>I</td>
<td>12</td>
<td>Day-4 pp; IUD†</td>
<td>1</td>
</tr>
<tr>
<td>II</td>
<td>12</td>
<td>Day-4 pp; IUD†</td>
<td>1½</td>
</tr>
<tr>
<td>III</td>
<td>12</td>
<td>Day-4 pp; IUD†</td>
<td>2</td>
</tr>
<tr>
<td>IV</td>
<td>12</td>
<td>Day-4 pp; IUD†</td>
<td>2½</td>
</tr>
<tr>
<td>V</td>
<td>12</td>
<td>Day-4 pp; IUD†</td>
<td>3</td>
</tr>
<tr>
<td>VI</td>
<td>12</td>
<td>Day-4 pp; IUD†</td>
<td>3½</td>
</tr>
<tr>
<td>VII</td>
<td>12</td>
<td>Day-4 pp; IUD†</td>
<td>4</td>
</tr>
<tr>
<td>VIII</td>
<td>12</td>
<td>Normal Day-4 pp; control</td>
<td>4</td>
</tr>
<tr>
<td>IX</td>
<td>12</td>
<td>Day-4 pp; IUD†; both horns ligated before transfer</td>
<td>2½</td>
</tr>
<tr>
<td>X</td>
<td>12</td>
<td>Day-4 pp; IUD†; embryos washed before second transfer</td>
<td>2</td>
</tr>
<tr>
<td>Effect of removing the IUD on recovery and survival of embryos</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>A</td>
<td>12</td>
<td>Day-4 pp; IUD†, removed 72 hr before transfer</td>
<td>3</td>
</tr>
<tr>
<td>B</td>
<td>12</td>
<td>Day-4 pp; IUD†, removed 48 hr before transfer</td>
<td>3</td>
</tr>
<tr>
<td>C</td>
<td>12</td>
<td>Day-4 pp; IUD†, removed 24 hr before transfer</td>
<td>3</td>
</tr>
<tr>
<td>D</td>
<td>12</td>
<td>Day-4 pp; IUD†, removed 6 hr before transfer</td>
<td>3</td>
</tr>
<tr>
<td>Effect of ovariectomy on recovery and survival of embryos</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>9</td>
<td>Ovariectomized and progesterone injected; IUD†</td>
<td>3</td>
<td></td>
</tr>
</tbody>
</table>

* Day-4 embryos were transferred to Day-4 recipients in all groups except that Day-5 blastocysts were transferred to Day-4 recipients in the ovariectomized group. † IUD was inserted only in the right uterine horn of these rats. pp = pseudopregnant.

The effect of the duration of incubation of embryos in an IUD-bearing horn on embryonic survival

Ten groups of animals were established in a randomized block design, with each treatment consisting of a double transfer of embryos. There were twelve replicates in each group. The first recipient of embryos (Recipient I) had an
IUD in the right uterine horn. In all groups, the embryo donors and both recipients (Recipients I and II) were at Day 4 of pregnancy or pseudopregnancy, respectively.

In Group I, embryos were transferred into the uterine horns of Recipient I. One hour after transfer, Recipient I was killed, and both uterine horns flushed separately to recover the embryos. The recovery rate percentage was calculated for each horn as the number of embryos recovered, divided by the number of embryos transferred into that horn multiplied by 100. The recovered embryos were immediately transferred into the corresponding uterine horns of a second recipient, also at Day 4 of pseudopregnancy (Recipient II). At Day 13, the second recipient was killed, and the number of living embryos in each uterine horn was determined.

The same experimental regimen was used for Groups II to VII as for Group I except that the duration of residence of embryos in the uterus of Recipient I was increased by ½-hr intervals.

Group VIII was a control group in which Day-4 embryos were transferred into a Day-4 pseudopregnant host that did not bear an IUD. After a 4-hr incubation, embryos were recovered and transferred into another normal Day-4 pseudopregnant host.

In Group IX, both horns of Recipient I were ligated at the cervical end to prevent expulsion of embryos. Then embryos from Day-4 donors were transferred to the Recipient-I rats. After 2½ hr, the embryos were recovered and transplanted to Recipient-II animals for embryonic development to Day 13.

Preliminary results indicated that flushings obtained from the IUD-bearing horn contained a greater amount of cellular exudate and débris than was found in the opposite, intact horn. Possible embryotoxic effects of uterine fluids were determined by separating the embryos from the uterine fluid in Group X. Day-4 embryos were transferred to the Day-4 pseudopregnant animal (Recipient I) that had an IUD in the right horn. After 2 hr, the embryos were recovered and separated from the uterine fluid by micropipetting them into a watchglass containing 1 to 2 ml of fresh medium. The embryos were then transplanted to Recipient II for foetal development to Day 13.

**Reversibility of IUD effects**

To test if the uterine environment might be improved by removing the IUD, double transfer of embryos was done in four groups. Embryos were incubated in both horns of Recipient I for 3 hr in all groups. Before embryo transfer, the IUD was removed at various times from Recipient I. In Group A, the IUD was removed 72 hr before embryo transfer, i.e. at Day 1 of pseudopregnancy. In Group B, the IUD was removed on Day 2 of pseudopregnancy, 48 hr before embryo transfer. The IUD was removed on Day 3 of pseudopregnancy, 24 hr before embryo transfer in Group C. Embryo transfer was carried out 6 hr after the IUD was removed in Group D. There were twelve animals in each group.

**Effect of ovariectomy and an IUD on embryonic survival**

A preliminary experiment was conducted to determine the effects of progesterone on the embryotoxicity of an IUD-bearing uterus in spayed rats.
Again, double transfer of embryos was employed. The embryo donor in this group was at Day 5 of pregnancy, and Recipient II at Day 4 of pseudopregnancy. Nine animals were used as Recipient I and were bilaterally ovariectomized when they were 60 days old. Laparotomies were performed on these animals 30 days later and a No. 5-0 silk thread was inserted into the right uterine horn. The following day (designated Day 1), progesterone injections were begun and continued for 8 days. Rats received 2.5 mg progesterone daily on Days 1 to 4 and 5 mg progesterone/day, subcutaneously, on Days 5 to 8. Also on Day 8, blastocysts were transferred into both uterine horns. After 3 hr, the first recipient was killed and the blastocysts recovered and immediately transferred to Recipient II for further development to Day 13.

RESULTS

EFFECT OF AN IUD ON OVIDUCAL EMBRYOS

The number of embryos recovered from the oviducts adjacent to an IUD was similar to that recovered from the contralateral oviduct, thus confirming the findings of others (Doyle & Margolis, 1964; Greenwald, 1965; Craig, 1969;

<table>
<thead>
<tr>
<th>Embryos in oviduct</th>
<th>No. of embryos transferred</th>
<th>Survival of embryos in uterus of intact recipient rat at Day 13</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ipsilateral to IUD</td>
<td>61</td>
<td>39, 63.9</td>
</tr>
<tr>
<td>Contralateral to IUD</td>
<td>60</td>
<td>38, 63.3</td>
</tr>
</tbody>
</table>

* Embryos were transplanted to an intact recipient rat.

Ishihama & Miyai, 1969). A high percentage of these embryos was viable (Table 2), indicating that an IUD does not adversely affect embryos within the oviduct.

THE EFFECT OF THE DURATION OF INCUBATION OF EMBRYOS IN AN IUD-BEARING HORN ON EMBRYONIC SURVIVAL

Effect on the recovery rate

The percentage of embryos recovered from the non-IUD horn after 1 to 4 hr did not differ significantly from the recovery rate in the controls (Group VIII, Table 3). Thus, an IUD in one horn did not affect the ability to recover embryos from the opposite horn.

The relationship between hours of incubation in Recipient I and the percentage of recovery of embryos is shown in Text-fig. 1. The percentage of recovery
was converted to arcsines (Snedecor & Cochran, 1967) and subjected to analysis of variance and regression analysis. The slope of the line for the non-IUD horn did not differ significantly from zero ($P>0.05$).

### Table 3

RECOVERY AND SURVIVAL RATES OF RAT EMBRYOS IN AN IUD-BEARING HORN

<table>
<thead>
<tr>
<th>Group</th>
<th>Treatment</th>
<th>Hr embryos incubated in Recipient I</th>
<th>% recovery in Recipient I at Day 4</th>
<th>% survival in Recipient II at Day 13</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>IUD right horn</td>
<td>1</td>
<td>49-4 (38)*</td>
<td>37-9 (11)*</td>
</tr>
<tr>
<td>II</td>
<td>IUD right horn</td>
<td>1½</td>
<td>44-1 (41)</td>
<td>34-3 (12)</td>
</tr>
<tr>
<td>III</td>
<td>IUD right horn</td>
<td>2</td>
<td>36-7 (29)</td>
<td>38-4 (10)</td>
</tr>
<tr>
<td>IV</td>
<td>IUD right horn</td>
<td>2½</td>
<td>14-9 (13)</td>
<td>25-0 (3)</td>
</tr>
<tr>
<td>V</td>
<td>IUD right horn</td>
<td>3</td>
<td>13-7 (11)</td>
<td>27-3 (3)</td>
</tr>
<tr>
<td>VI</td>
<td>IUD right horn</td>
<td>3½</td>
<td>11-8 (9)</td>
<td>11-1 (1)</td>
</tr>
<tr>
<td>VII</td>
<td>IUD right horn</td>
<td>4</td>
<td>14-3 (11)</td>
<td>9-1 (1)</td>
</tr>
<tr>
<td>VIII</td>
<td>Intact control</td>
<td>4</td>
<td>59-0 (36)</td>
<td>41-2 (14)</td>
</tr>
<tr>
<td>IX</td>
<td>Both horns ligated; IUD right horn‡</td>
<td>2½</td>
<td>66-2 (29)</td>
<td>28-5 (13)</td>
</tr>
<tr>
<td>X</td>
<td>Embryos washed; IUD right horn§</td>
<td>2</td>
<td>30-5 (25)</td>
<td>33-3 (8)</td>
</tr>
</tbody>
</table>

* No. of embryos per group in parentheses.
† No IUD.
‡ Uterine horns of Recipient I ligated before embryo transfer.
§ Embryos washed free of cellular débris after recovery from Recipient I.

**Text-fig. 1.** Effect of the time of exposure to an IUD-bearing uterine horn on the recovery rate of embryos. O, IUD horn; •, non-IUD horn.

The amount of time that embryos were incubated in an IUD horn did, however, significantly affect the recovery rate. The slope of the line for the IUD horn was significantly different from zero ($P<0.01$). The quadratic
component of this regression was not significant \( (P>0.05) \). After 2 hr of incubation in an IUD-bearing horn, the recovery rate \((36.7\%)\) was seen to be significantly depressed when compared to that from the controls \( (P<0.05) \). By 2½ hr, 85% of the embryos could no longer be recovered. Thus, these results show that an IUD environment caused loss or degeneration of embryos within 4 hr. Embryos in the opposite, control horn developed to Day 13.

**Effect on the survival rate**

*Non-IUD horn.* Embryos recovered from the non-IUD horn of Recipient I and transferred into Recipient II survived equally as well as the controls (Table 3). In Text-fig. 2, the linear regression coefficient for time of incubation in the non-IUD horn on percentage of survival did not differ significantly from zero \( (P>0.05) \). This indicates that the effect of a unilateral IUD in the rat is localized within that horn.

*IUD horn.* The percentage of survival at Day 13 decreased linearly with the time that embryos had remained in the IUD horn of Recipient I (Text-fig. 2 and Table 3; \( P<0.05 \)). Exposure of embryos to an IUD-bearing uterus for 1, 1½ or 2 hr did not decrease survival, whereas after 2½ hr exposure, the survival rate was significantly reduced \( (P<0.05) \). The decrease in survival rate with increasing time of incubation was similar to that of the recovery rate (Text-fig. 3).

The survival rate of embryos recovered from the ligated IUD horn in Group IX was 28.5%, similar to that obtained from unligated horns at 2½ hr \( (25\%\); \( P>0.05 \); Group IX versus Group IV, Table 3). This survival rate, however, was below that of the control animals \( (P<0.05\); Group IX versus Group VIII, Table 3).

The results in Group X show that washing the embryos free of the cellular
débris generated by an IUD had no effect on their subsequent survival (Table 3). The survival rate of these washed embryos (33.3%) was similar to the survival rate of those obtained from IUD horns after 2 hr of incubation (Group III, 38.4%).

The embryonic losses in Recipient II were not caused by postimplantation resorption in any of the groups. The total number of dead or resorbing foetuses observed in Recipient II at Day 13 in any group ranged from 0 to 5 in the IUD-horn and 0 to 9 in the opposite control horn.

**REVERSIBILITY OF IUD EFFECTS**

*Effect of removing the IUD on the recovery rate*

Removing the IUD significantly increased the recovery rate of embryos compared with that obtained when the IUD remained *in situ*. This effect, however, was dependent on the interval between IUD removal and embryo transfer (Table 4). In Group A, the recovery rate was similar to that of intact control animals. The recovery rates from the IUD horns in the 48- and 24-hr groups (Groups B and C) were below ($P<0.05$) those of controls, but above ($P<0.05$) those obtained when the IUD remained *in situ*. The recovery rate from the horn in which the IUD had been removed 6 hr before transfer (Group D) was less than that of Group A ($P<0.05$). This recovery rate, however, was higher than the corresponding rate in animals in which the IUD had not been removed (Group V, Table 3).

The recovery rates from the non-IUD horn of all four groups did not differ from controls ($P>0.05$).
Effect of removing the IUD on the survival rate

Non-IUD horn. In all groups, the survival rate in the non-IUD horn was similar to that found in the non-IUD horns in Table 3. Since the control horn had been subjected to trauma 6 to 72 hr before receiving embryos by transplantation, the high survival rates indicate that trauma per se had little effect on the subsequent viability of the recovered embryos.

IUD horn. Embryonic survival was higher among embryos recovered from uterine horns in which the IUD had been removed than among those recovered from horns with an IUD in situ. After removal of the IUD, the survival rate of embryos in all four groups was similar to that of the control with double transfer of embryos (P>0.05).

EFFECT OF OVARIECTOMY AND AN IUD ON EMBRYONIC MORTALITY

Embryos transferred into the IUD-bearing uterus of progesterone-treated, spayed rats showed a higher recovery and survival rate than those transferred into intact rats with an IUD (Table 5). Forty-seven blastocysts were transferred into the IUD horn of ovariectomized, progesterone-treated rats (Recipient I).
After 3 hr, thirteen were recovered from four of the nine recipients. Thirty-nine blastocystst were transferred into the opposite control horn, of which sixteen were subsequently recovered from five of the nine recipients. The difference between the recovery rate in the control versus the IUD horn was not significant \((P > 0.20)\). The percentage of recovery in the control horn was not lower than the recovery rate from the non-IUD horn of intact animals \((P > 0.05)\).

Of the thirteen blastocysts recovered from the IUD horn of Recipient I and transferred into Recipient II, nine were living at Day 13. Nine of the sixteen recovered from the non-IUD horn of Recipient I survived to Day 13. These survival rates were higher than those obtained from double transfers of Day-4 embryos involving intact animals without an IUD (Group VIII, Table 3).

**DISCUSSION**

It is becoming increasingly clear that, at least in the rat, an IUD prevents implantation by causing the uterus to become hostile to embryos. Several investigators have shown that embryonic mortality is not increased by an IUD before the embryos leave the oviduct and enter the uterus on Day 4 of pregnancy (Doyle & Margolis, 1964; Greenwald, 1965; Craig, 1969; Ishihama & Miyai, 1969). In this report, it has been conclusively shown that oviducal embryos are still fully viable on Day 4 (Table 2). Normal blastocysts cannot be recovered from the IUD-bearing uterus on the morning of Day 5 (Doyle & Margolis, 1964; Greenwald, 1965). The loss of rat embryos must, therefore, occur after the evening of Day 4 and before noon on Day 5. Following ligation of the cervical end of the IUD-bearing uterus, the number of embryos that could be recovered on Day 5 was nearly restored to the number that could be recovered from the controls, although 95% of the embryos were abnormal or degenerated (Greenwald, 1965).

The nature of the changes in the intrauterine environment produced by an IUD is almost totally unknown. Parr et al. (1967) believed that an IUD in the rat uterus caused inflammation, the products of which caused destruction of the embryos. Parr (1968) postulated that the toxic factor that killed the embryos was produced by polymorphonuclear leucocytes. Extracts of polymorphonuclear leucocytes were capable of killing rat morulae *in vitro* (Parr, 1969). Furthermore, Parr (1969) calculated that the embryotoxic factor was present in the uterus in the same concentration as that which killed embryos *in vitro*. Extracts of several cell types (e.g. L, HeLa, thyroid, and liver cells), however, were also capable of killing rat embryos *in vitro*, indicating that perhaps a component of damaged cells might also be embryotoxic (cf. Parr, 1968, 1969).

Batta & Chaudhury (1968) transferred fluid obtained from IUD-bearing uteri into mated rats and observed a sharp reduction in embryonic survival by Day 10. These authors postulated that an embryotoxic factor that caused embryonic death was produced. DeBoer, Anderson & Melampy (1970) obtained similar results with fluids from IUD-bearing rat uterine horns. Physiological saline alone, however, containing no products from an IUD-bearing uterus, also decreased embryonic survival in mated rats.

Recently, Sağiroğlu & Sağiroğlu (1970) noted large numbers of viable
IUD and embryonic survival in the rat 385

macrophages accumulating in the IUD-bearing uterus of women. They suggested that these macrophages phagocytosed the blastocysts within the uterus, accounting for the action of the IUD in women.

We have shown (Table 3) that exposure of normal embryos to the intra-uterine environment with an IUD for 4 hr or less resulted in loss of over 85% of the embryos. This rapid and stringent embryotoxicity alone is capable of explaining the anti-implantation effect of an IUD in the rat. This loss of embryos was the result of two factors: (1) the apparent expulsion of the transferred embryos from the uterus into the vagina, resulting in failure to recover them in an IUD-bearing uterine horn, and (2) physiological damage of the embryos by exposure to some uterine factor that caused embryonic death. Removal of the IUD from Recipient I before embryo transfer prevented the production of the embryotoxic factor responsible for decreasing embryonic survival (Table 4).

It is possible that increased uterine motility caused by the presence of an IUD resulted in the inability to recover embryos. Parr (1965, 1968) and Zambrana & Greenwald (1969), however, have shown that uterine motility, if it is increased at all, is probably not important in causing embryonic loss at Day 5 of pregnancy in the rat. We have shown (Group IX, Table 3) that ligating the cervical end of the IUD-bearing uterus before embryo transfer restored the recovery rate to control levels. The survival rate of these recovered embryos, however, was significantly lower than the rate of those from the controls.

Embryonic loss and embryonic mortality may both be caused by the same mechanism, which is not dependent on uterine motility. We postulate that some factor produced by an IUD-bearing uterine horn is detrimental to the metabolism of the unimplanted embryo and causes, initially, alterations in the adhesiveness of the zona pellucida. Due to altered metabolism and loss of normal adhesiveness, embryos might be passively expelled from the uterus. If embryos have not been exposed to the deleterious uterine factor for too long (<2 hr) and have not yet been expelled from the uterus, they may still undergo normal development in a non-IUD-bearing host. After more than 2½ hr exposure, other aspects of embryonic physiology may be permanently damaged and the embryos fail to develop, even when removed from the deleterious environment and transplanted to a normal host.

The recovery rate of embryos from the IUD-bearing horn of ovariectomized, progesterone-treated rats was higher than that from the IUD-bearing horn of non-ovariectomized rats (Table 5), but lower than that from the controls. The survival rate of the blastocysts recovered was higher than in any control group. Whether this was the result of suppression by progesterone of uterine embryotoxic factors, decreased uterine motility, or other mechanisms is not clear. This is the first clear demonstration of an improvement in embryonic survival in an IUD-environment in rats. Further studies may elucidate the reasons for the attenuation of embryotoxicity.

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REFERENCES


