Arch. Biol. Med. Exp. *24:* 403-410 (1991)
Printed in Chile

Hormonal control of ovum transport through the rat oviduct

Control hormonal del transporte ovular por el oviducto de la rata

HORACIO B. CROXATTO, MARIA ELENA ORTIZ, MARIA LUISA FORCELLEDO, BLANCA FUENTEALBA, GABRIELA NOE, GRACE MOORE, FRANCISCO MORAN and HUGO CARDENAS

Pontificia Universidad Católica de Chile, Facultad de Ciencias Biológicas, Unidad de Reproducción y Desarrollo, Casilla 114-D, Santiago, Chile

The rat offers several advantages to analyze the hormonal control of ovum transport since it responds to exogenous estrogen (E_2) at all times with a reproducible and dose-related acceleration of oviductal transport in contrast with the mixed responses of other species. In addition, the rate of transport differs markedly in mated and non-mated animals, independently of the condition of the eggs and it is insignificantly affected by stress or manipulation of viscera. A body of evidence, based on the effects of E_2 synthesis inhibitors, the antiprogestin RU486 and immunoneutralization of progesterone (P), indicates that, at physiologic levels, endogenous E_2 accelerates oviductal transport and P has the opposite effect. Dose-response comparisons between local and systemic delivery showed that E_2 accelerates transport by a direct action on the oviduct.

Experiments using synthetic ovum surrogates delivered to the oviductal infundibulum at various times relative to ovulation, followed by detailed analyses of their location in control and E_2 treated animals have disclosed a gate-like behavior of the ampullary-isthmic junction largely unaffected by E_2. Accelerated transport occurs once the eggs enter the isthmus and this is associated with increased frequency of back and forth movements of the luminal contents.

INTRODUCTION

One of the prominent roles of the oviduct in reproduction is to capture the eggs released from the ovarian follicles and to transport them to the uterus. These are mechanical functions accomplished by the interplay of muco-ciliary currents that take place in the luminal surface and contractions of the smooth muscle layers of the oviductal wall. Undoubtedly the rheological properties and volume of the fluid present in the lumen determine the responsiveness of the luminal contents to the mechanical action of ciliary and muscular cells.

From a physiological standpoint, one can anticipate that if the rate of transport is a regulated process, the ultimate targets of the regulatory signals would be the muscular, ciliated and/or secretory cells of the oviduct. A direct endocrine control implies that these cells would be the immediate target of the circulating hormones involved in the regulation of this process, whereas an indirect form of control would imply that the hormones involved act primarily on neurons innervating the oviduct and/or on local paracrine cells.

The aim of this presentation is to examine whether or not oviductal transport of eggs is in fact under regulation, what are the regulatory signals and the mechanisms through which they operate. This was previously reviewed by Fuentealba *et al.* (1983). The mouse, rabbit and rat are the three species in which these issues have been studied most extensively and there are notable differences between them. For our studies, we choose the rat as animal model because very early in this story it became evident that, while the same hormone could elicit opposite responses of oviductal transport in other species depending on the dose and time of administration, the rat exhibited a single, reproducible and dose-related response to the same hormone. Thus the rat afforded a much simpler stimulus-response situation for studying the mechanism involved in the control of the mechanical function of the oviduct.

MATERIAL AND METHODS

Animals were reared locally and were kept under controlled environmental conditions as previously described (Moscoso *et al.*, 1984, Ortiz *et al.*, 1986, 1989). Female Sprague-Dawley rats weighing 200-220 g were subjected to daily vaginal smears and were used after two 4-days estrous cycles. Mating was confirmed by the finding of seminal plug or spermatozoa in the vaginal smears. Pseudopregnancy was induced by cervical stimulation in the evening of proestrus or by mating with vasectomized males. The days of the cycle, pregnancy or pseudopregnancy are numbered considering as day one the day of ovulation (day of estrous smear and day of mating, respectively).

Female golden hamsters weighing 100-140 g were used after observing the vaginal discharge for two cycles.

Female mice of the BALB/c strain were caged with males and checked each morning for the presence of vaginal plug indicative that mating had taken place.

In order to assess the number, location and condition of eggs in the genital tract, the animals were killed and oviducts and uterine horns were dissected and flushed separately into embryologic culture dishes. In some experiments the oviduct was straightened and divided into segments under an operating microscope prior to flushing. The flushings were examined under a stereomicroscope to count and classify the eggs as per fertilization and developmental status.

The design of each experiment is described in the next section.

A given treatment was considered to accelerate oviductal transport when the mean number of eggs present in the oviducts of the treated group was significantly decreased in comparison with vehicle-injected controls killed at the same time post-ovulation. A concomitant increased number of uterine ova was not a requisite since ova arriving prematurely into the uterus are often expelled very quickly into the vagina.

A treatment was considered to delay oviductal transport when the mean number of eggs recovered from the oviducts or the ratio of oviductal to uterine ova in treated animals was significantly increased in comparison with the vehicle-injected group killed at the same time post-ovulation. Since all treatments were given after ovulation it is assumed that the timing of ovulation should be comparable in treated and control groups.

RESULTS

I. Characterization of the rat as a model

Rats, mice and hamsters were treated with a single s.c. injection of estradiol (E_2) dissolved in olive oil or with vehicle alone on day one of pregnancy, and were killed at appropriate times to assess the occurrence of accelerated or delayed oviductal transport (Ortiz *et al.*, 1977). The results summarized in Fig. 1 show that the rat is more sensitive to E_2 than the other two species and responds only with accelerated transport over a wide dose range.

Mice responded with delayed transport to a wide range of low doses and with accelerated transport to high doses. When the timing of treatment instead of the dose was changed, opposite responses were also elicited (not shown here, see Moscoso *et al.*, 1984). Hamsters were the least sensitive and responded to a narrow range of

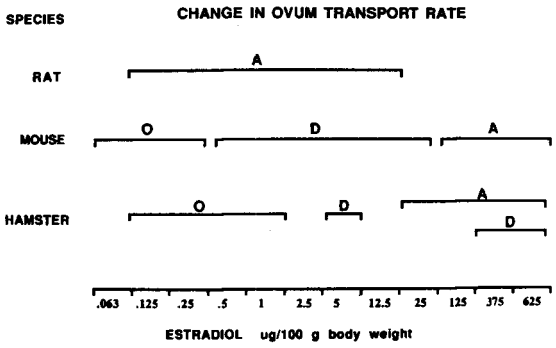

Fig. 1: Changes in egg transport rate through the oviduct induced by estradiol injected s.c. on day 1 of pregnancy in the rat, mouse and hamster. A, D and 0 indicate the range of doses that accelerate, delay or do not affect respectively, oviductal egg transport. The rat is more sensitive and responds only with acceleration. The quality of the response is dose dependent in mouse and hamster. Some eggs are accelerated and others delayed by the higher doses in the hamster.

low doses with delayed transport. Higher doses produced mixed responses, with some eggs entering the uterus prematurely and others being retained in the oviduct beyond the normal timing of transfer to the uterus.

A more detailed assessment of the time-course of accelerated transport and dose-response relationships to E_2 in the rat are presented in Fig. 2. In the rat the sojourn of the embryos through the oviduct normally lasts between 80 and 90 h. A single dose of E_2 in the range of 0.5 to 25 μg per rat given at 12:00 on day 1 of pregnancy caused a progressive decrease in the number of oviductal embryos which started approximately 11 hours after treatment, although maximum serum levels of E_2 were observed 10-60 min after treatment. Expulsion of eggs from the oviduct ended within the next 12 hours and compromised from 25 to 94% of the ova. All accelerated ova were expelled from the uterus. With each dose tested some eggs were not accelerated and their number tended to be smaller the higher the dose. In all groups these eggs remained in the oviduct until the normal time of passage into the uterus and their rate of implantation was normal (Ortiz *et al.*, 1979). Thus the accelerating effect of E_2 given on day 1 of pregnancy had a latency period of several hours, was transient and did not disturb subsequent steps of the reproductive process.

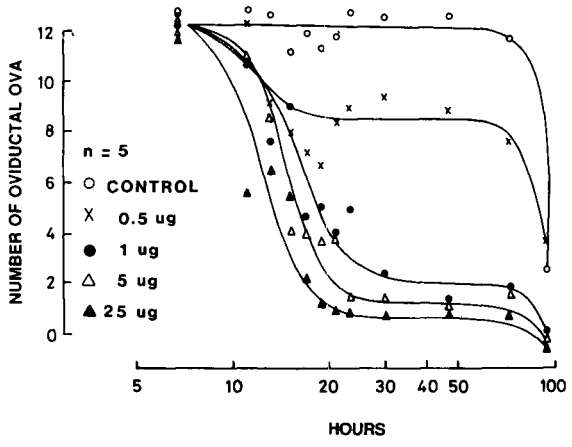

Fig. 2: Mean number of eggs recovered from the rat oviduct at various times after a single s.c. injection of estradiol-17 β in 0.2 ml oil or vehicle alone (Control) given on day 1 of pregnancy. Each point is the average of values for 5 animals. Note logarithmic time scale.

Further experimental analysis disclosed that oviductal sensitivity and responsiveness to this treatment is significantly increased between the evening of day 2 and the evening of day 3 of pregnancy (Ortiz *et al.*, 1985). In addition, concomitant treatment with progesterone (P) blocked the accelerating effect of exogenous E_2 (Fuentealba *et al.*, 1987).

The above features of the response of oviductal egg transport to E_2 in the rat indicate that this is a suitable animal model to investigate the chain of cellular, biochemical and physiologic events that links the rising plasma levels of E_2 with the mechanical changes leading to accelerated transport.

II. Physiologic significance of sex steroids in the regulation of ovum transport

A fundamental question is whether or not estrogens and progestins (and perhaps androgens) at their physiologic levels in plasma indeed influence the rate of oviductal transport of ova. It is often difficult to find appropriate experimental paradigms to answer this type of questions.

The fact that administration of these hormones, in doses which produce supraphysiologic levels in the circulation, changes the rate of transport can only suggest, but not prove, that ovum transport is normally under their control. It was important therefore to examine ovum transport under conditions in which the endogenous hormones were produced at different rates but within the physiologic realm or at subnormal rates or under conditions in which the action of these hormones was partially prevented.

Since reports from several laboratories indicated that sex steroid levels in plasma differ among cycling, pregnant and pseudopregnant rats, ovum transport rates were assessed in these three reproductive states, which for this purpose can be considered to represent physiologic conditions. Eggs were found to pass from the oviduct to the uterus between day 3 and 4 in cycling rats and between day 4 and 5 in pregnant

and pseudopregnant rats. On the other hand, P plasma levels became much lower and the E_2: P molar ratio in plasma became much higher from day 3 to day 4 in cycling rats in comparison with the other groups (Forcelledo *et al.*, 1981).

Since cycling and pseudopregnant rats transport unfertilized eggs and pregnant rats transport embryos and little or no difference was found in the transport of fertilized and unfertilized eggs in pseudopregnant rats (Villalón *et al.*, 1982), we inferred that the differences in ovum transport rates through the oviduct between cycling and pregnant or pseudopregnant rats should be attributable to their different endocrine milieu rather than the type of egg being transported. Thus, the above study provided definite evidence that the time of passage of ova from the oviduct to the uterus is subject to physiologic regulation and supported the concept that postovulatory changes in the levels of sex steroids in plasma may contribute to this regulation.

In order to examine the effects of sex steroid defficiency on ovum transport, three approaches have been explored. In the first, organ ablations such as hypophysectomy (Wu *et al.*, 1971a, 1971b) ovariectomy and/or adrenalectomy (Forcelledo *et al.*, 1982) with or without hormone substitution therapy were performed. Ovariectomy was followed by a rapid and deep fall in circulating P and by loss of some eggs. Nearly half of those remaining were retained in the oviduct on day 5. Progesterone subdermal implants that provided normal P levels in the circulation were able to prevent both the loss of ova and their retention in the oviduct. From the results of these experiments it can be concluded that after ovulation there is a continuous requirement of, at least, progesterone secreted by the ovary for normal oviductal embryo transport in the rat. However, ablation of endocrine glands entails not single but multiple endocrine changes and the effects of single hormone substitution therapy can be quite different in an abnormal as compared to an otherwise normal endocrine milieu. Thus single hormone deficits, although more difficult to attain, represent the ideal condition and this was attempted in the other two approaches.

In order to simulate a specific deficit of progesterone rats were treated with the antiprogestin RU486 (Roussel Uclaf, Paris) which binds to the progesterone receptor and prevents the hormone from acting on its target cells. Cycling and pregnant rats were treated from day one at 09:00 with RU486 4 mg/day or vehicle delivered continuously from an ALZA osmotic pump implanted s.c. (Fuentealba *et al.*, 1987). Treatment with RU486 accelerated oviductal transport in both states but while in cycling rats this effect started 24 h after the onset of treatment, in pregnant rats it was not apparent until day 4 at a time when RU486-treated pregnant rats behave as cycling rats in terms of increased E_2 secretory rate, balooning of the uterus and vaginal cornification. Thus, these results suggest a different requirement of postovulatory progesterone action on the oviduct for normal egg transport in cycling and pregnant rats and in the case of pregnant rats they apparently contradict the previous conclusion drawn from the effects of ovariectomy and progesterone replacement. The main difference between the two approaches lays in multiple versus single hormone deficit achieved in the two situations and no coherent explanation is yet available.

The different response of oviductal transport to RU 486 in cycling versus pregnant rats is also difficult to explain and is further emphasized by the fact that treatment with progesterone 5 mg/day s.c. since day one delayed oviductal transport in cycling but not in pregnant rats (Fuentealba *et al.*, 1987). An unproved but possible explanation is that in this particular set of experiments control cycling rats had higher E_2 levels than pregnant controls on day 2 and that with progesterone treatment E_2 levels had decreased on day 4 by 55% in the former and by 23% in the latter. Thus the effects of progesterone action and therefore of its antagonist may depend on prior or concomitant E_2 levels.

Additional evidence for the role of progesterone in delaying embryo transport through the oviduct of pregnant rats was obtained by means of immunoneutralization of P in the circulation (Noé *et al.*, unpublished). A monoclonal antibody raised against progesterone ($P_5 D_6 F_2$ kindly donated by Prof. P. Talwar, New Delhi, India) was injected i.v., as a single dose on day 2 of pregnancy. Progesterone binding capacity of serum and P plasma levels, but not tissue levels, were significantly increased 48 h following treatment. Under these conditions a dose related acceleration of embryo transport was found (Fig. 3). This observation indicates more clearly than the results obtained with RU486 that progesterone action in the postovulatory period is essential for normal embryo transport.

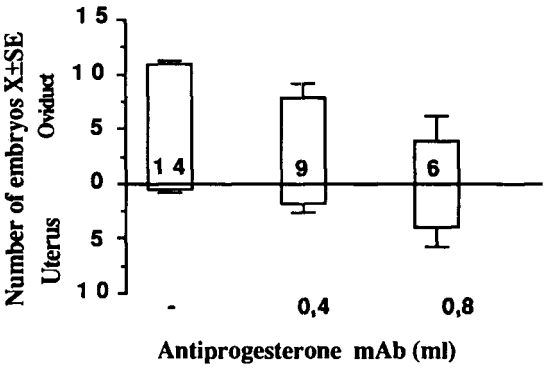

Fig. 3: Mean number of embryos recovered on day 4 of pregnancy from the oviducts or uterus of control rats and rats injected with an antiprogesterone monoclonal antibody (mAb) i.v. on day 2. Figures inside bars indicate number of animals.

The third approach to produce a single hormone deficit consisted in treating cycling and pregnant rats with the aromatase inhibitor 4-hydroxy-4-androstene-3, 17-dione (4-OH-A) which inhibits the synthesis of E_2 (Forcelledo and Croxatto 1986a, 1988). In both conditions continuous treatment with 4-OH-A since day 2 decreased E_2 ovarian secretion and increased testosterone (T) secretion with no changes in P production. This was accompanied by delayed oviductal transport of ova in both conditions (Fig. 4). By way of estrogen substitution experiments or

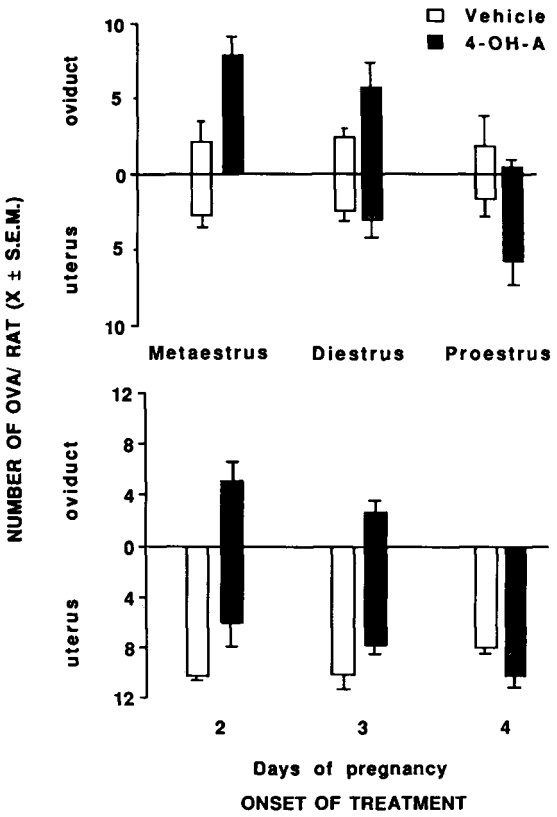

Fig. 4: Effect of treatment of rats with 4-hydroxy-4-androstene-3,2 dione (4-OH-A) 1.66 mg s.c. every 4 h or vehicle starting at various times after ovulation on the distribution of ova on day 4 of the cycle or day 5 of pregnancy. Values are mean ± S.E.M. of groups of 3 to 13 animals.

treatment with T it was possible to determine that the effects on ovum transport were solely accounted for by the hypoestrogenic state of the animals treated with the inhibitor. The results of these experiments convinced us that postovulatory estrogen secretion has a crucial role in timing the passage of oocytes or embryos to the uterus in cycling and pregnant rats, respectively. Here again this conclusion is in apparent disagreement with the effects of ovariectomy in which estrogen levels were presumably decreased, yet administration of progesterone alone was sufficient to attain normal timing of embryo arrival to the uterus.

Situations in which the rate of secretion of sex steroids change in response to stressful stimuli have provided additional opportunities to explore the relationship between oscillations of endogenous hormones within physiologic limits and

oviductal embryo transport. When rats were given an i.v. infusion of E_2 under anesthesia, it was found that for a constant total dose, the duration of the infusion was critical to accelerate ovum transport (Forcelledo *et al.*, 1986b). Infusions lasting 150 min or less were totally ineffective while longer infusion were as effective as s.c. injections. With a short i.v. infusion, elevated E_2 levels in the circulation lasted for much shorter interval than after a s.c. injection of the same dose. Nonetheless, the oviductal content of E_2 attained after a short infusion of 5 μg was higher than after a s.c. injection of 5 μg. Further investigation of this lack of response of oviductal transport to a short i.v. infusion of E_2 revealed that P levels in the circulation increase transiently, several fold, during i.v. infusion of E_2 or vehicle. When this P rise was prevented by hypophysectomy or adrenalectomy or P action was prevented by concomitant treatment with RU486, short i.v. infusions of E_2 became effective in accelerating oviductal embryo transport (Morán *et al.*, 1990). Thus, a physiologic response to stress which involves an increase in P levels was able to counteract the effect of an excess of E_2 derived from an exogenous source.

Pregnant rats, forced to swimm in cold water, experience a stress reaction evidenced by increased secretion of corticosterone. In this situation there are minor but significant increases in the E_2 : P molar ratios in plasma which are accompanied by a slight but statistically significant acceleration of egg transport (Cárdenas, 1988).

The bulk of these data strongly supports the concept that transport of ova through the rat oviduct is normally under the influence of the circulating levels of estradiol and progesterone. The former tends to accelerate the passage of eggs into the uterus and progesterone antagonizes this effect. The basis of this antagonism is discussed below.

III. Mechanism involved in the changes in the rate of oviductal egg transport induced by estradiol and progesterone

A key question is which are the cells that detect the rising levels of E_2 or P in plasma and whose response leads to accelerated or delayed egg transport, respectively. Our working hypothesis to search for an answer to this question is that E_2 and P change the rate of transport as a consequence of a direct action on cells located within the oviduct.

As a first step to test this hypothesis efforts were directed to examine the presence of estrogen and progesterone receptors in the oviduct and possible relationships between their fluctuations and egg transport. These studies (Fuentealba *et al.*, 1982, 1988a, 1988b) showed that in whole oviducts of cycling and pregnant rats, about 12 h before the eggs enter the uterus, there is a transient increase in nuclear estrogen receptor level, slightly preceding a peak of nuclear progesterone receptor level (Fig. 5). Treatment with RU486 which advanced the passage of embryos to the

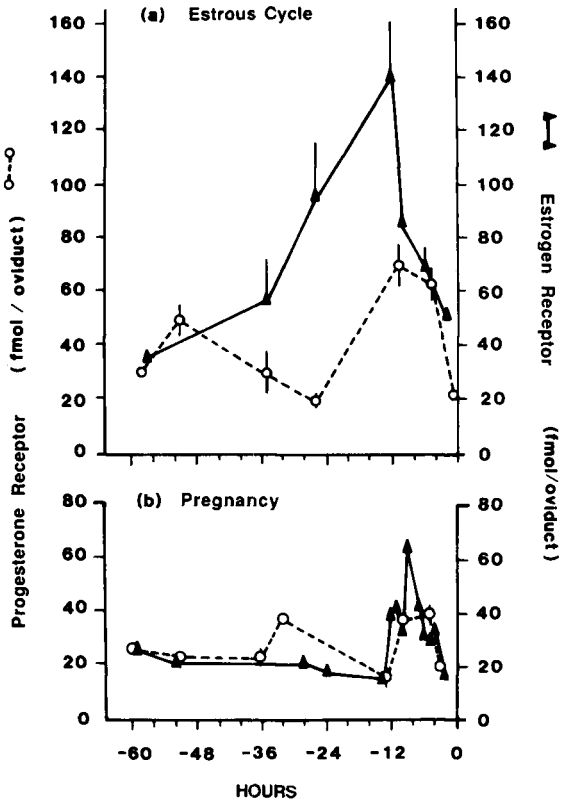

Fig. 5: Temporal relationship between the passage of the eggs to the uterus (Time 0) and nuclear estrogen (triangles) and progesterone (circles) receptor peaks in the rat oviduct during the estrous cycle (a) and pregnancy (b). Values are mean ± S.E.M. of 2-3 determinations, each from pooled oviducts of 6-8 rats.

uterus also advanced estrogen receptor accumulation in the oviduct. The same happens after treatment with E_2 (Croxatto *et al.*, 1982). Conversely treatment with P which blocks the accelerating effect of E_2 greatly reduced the increase in total oviductal estrogen receptor induced by exogenous E_2 and shortened the retention time of nuclear estrogen receptors. These results indicate that the effects of E_2 and P on ovum transport are the result of receptor mediated actions of these hormones on oviductal cells.

Further exploration of the site of action of estradiol was carried out by comparing the minimal effective dose of E_2 required to accelerate transport by local or systemic administration. To this end, E_2 was given by direct injection into the oviductal lumen or s.c. Single doses of 25 to 50 ng per oviduct were effective by local administration while the systemic route required from 10 to 20 times as much (Forcelledo *et al.*, unplublished).

Concerning the biochemical events that link the hormone-receptor interaction with the final mechanical response there is still much to be learned. Our approach to advance in this area has been two fold. On one hand to explore possible extracellular mediators acting distally on the mechanical effector cells as well as intracellular mediators operating in the E_2-responsive cell. Concomitant treatment with E_2 and a variety of alpha and beta adrenergic agonists and antagonist as well as cholinergic agonists and antagonists have failed to change in any direction the accelerating effect of E_2 (Croxatto *et al.*, unpublished) whereas protein synthesis inhibitors (Fuentealba *et al.*, 1983) as well as prostaglandin synthesis inhibitors (Ortiz *et al.*, 1984) blocked the accelerating effect of E_2. On the other hand efforts were directed to identify the type(s) of mechanical effector cells involved in the accelerating action of E_2. By performing segmental flushings of the oviduct and using synthetic microspheres whose transport through the rat oviducts mimicks the transport of native ova (Moore and Croxatto, 1988a) and whose movements within the rat oviduct can be followed by direct visual observation it was possible to establish that E_2 only accelerates transport of eggs located in the isthmus and this is associated with increased frequency of back and forth movement of the luminal contents (Moore and Croxatto, 1988b). This observation clearly indicates that one of the mechanical effector cells whose activity is changed as a consequence of increased receptor-mediated action of E_2 on the oviduct is the smooth muscle cell of the oviductal isthmus.

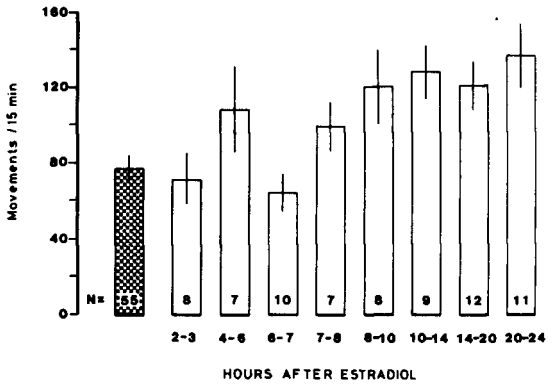

Fig. 6: Frequency of movements of dextran blue microspheres in the isthmus of the rat oviduct. Four microspheres were transferred to the infundibulum of each oviduct on day 1 of pregnancy. Estradiol 5 μg was injected s.c. on day 1 or 2 into 72 rats (open bars) and 55 served as controls (solid bar). Frequency of back and forth movements of the microspheres were determined at various times after estradiol. Values are mean ± S.E.M. for the number of rats indicated at the foot of each bar.

Our current view is that E_2 acting through its receptor on cells located in the endosalpinx of the isthmus elicits gene expressions which lead to the secretion of paracrine signals that activate mechanical effector cells such as smooth muscle and possibly ciliary and secretory cells. Progesterone counteracts E_2 action mostly at the beginning of this chain by reducing intracelullar E_2 receptor levels.

ACKNOWLEDGEMENTS

Previously unreported work was supported by Grant RF 88077. We are grateful to Mrs. Emma Muñoz for typing this manuscript.

REFERENCES

CARDENAS, H. (1988) Ovum transport under stressful conditions. Ph. D. Thesis. Pontificia Universidad Católica de Chile. Santiago, Chile.

CROXATTO, H.B.; ORTIZ, M.E.; FORCELLEDO, M.L.; FUENTEALBA, B. (1982) Transporte del huevo por el tracto genital y su regulación. *Arch. Biol. Med Exp. 15:* 309-314.

FORCELLEDO, M.L.; VERA, R.; CROXATTO, H.B. (1981) Ovum transport in pregnant, pseudo-pregnant, and cyclic rats and its relationship to estradiol and progesterone blood levels. *Biol. Reprod. 24:* 760-765.

FORCELLEDO, M.L.; MORALES, P.; VERA, R.; QUIJADA, S.; CROXATTO, H.B. (1982) Role of ovarian and adrenal progesterone in the regulation of ovum transport in pregnant rats. *Biol. Reprod. 27:* 1033-1041.

FORCELLEDO, M.L.; CROXATTO, H.B. (1986a) Ovum transport in cyclic rats rendered hypo-estrogenic by treatment with 4-hydroxy-4-androstene-3, 17-dione. *J. Reprod. Fertil. 76:* 325-330.

FORCELLEDO, M.L.; DE LA CERDA, M.L.; CROXATTO, H.B. (1986b) effectiveness of different estrogen pulses in plasma for accelerating ovum transport and their relation to estradiol levels in the rat oviduct. *Endocrinology 119:* 1189-1194.

FORCELLEDO, M.L.; CROXATTO, H.B. (1988) Effects of 4-hydroxyandrostenedione and exogenous testosterone on blood concentrations of oestradiol and oviductal embryo transport in the rat. *J. Endocrinol. 118:* 93-100.

FUENTEALBA, B.; VERA, R.; NIETO, M.; CROXATTO, H.B. (1982) Changes in nuclear estrogen receptor levels in the rat oviduct during ovum transport. *Biol. Reprod. 27:* 12-16.

FUENTEALBA, B.; FORCELLEDO, M.L.; ORTIZ, M.E.; CROXATTO, H.B. (1983) Regulación hormonal del transporte ovular. *Rev. Méd. Chile. 111:* 1057-1060.

FUENTEALBA, B.; NIETO, M.; CROXATTO, H.B. (1987) Ovum transport in pregnant rats is little affected by RU486 and exogenous progesterone as compared to cycling rats. *Biol. Reprod. 37:* 768-774.

FUENTEALBA, B.; NIETO, M.; CROXATTO, H.B. (1988a) Progesterone abbreviates the nuclear retention of estrogen receptor in the rat oviduct and counteracts estrogen action on egg transport. *Biol. Reprod. 38:* 63-69.

FUENTEALBA, B.; NIETO, M.; CROXATTO, H.B. (1988b) Estrogen and progesterone receptors in the oviduct during egg transport in cyclic and pregnant rats. *Biol. Reprod. 39:* 751-757.

MOORE, G.D.; CROXATTO, H.B. (1988a) Synthetic microspheres transferred to the rat oviduct on day 1 of pregnancy mimic the transport of native ova. *J. Reprod. Fertil. 82:* 735-742.

MOORE, G.D.; CROXATTO, H.B. (1988b) Effects of delayed transfer and treatment with oestrogen on the transport of microspheres by the rat oviduct. *J. Reprod. Fertil. 83:* 795-802.

MORAN, F.M.; FORCELLEDO, M.L.; CROXATTO, H.B. (1990) Increased secretion of adrenal progesterone explains the lack of response of oviductal embryo transport to a short intravenous infusion of estradiol in the rat. *Arch. Biol. Med. Exp. 23:* 299-305.

MOSCOSO, H.; ELLIES, J.; VERA, R.; CROXATTO, H.B. (1984) Varying responses of ovum transport in mice related to dose and time of administration of oestradiol. *Acta Physiol. Pharmacol. Latinoam. 34:* 253-261.

ORTIZ, M.E.; VILLALON, M.; MOSCOSO, H.; SOZA, X.; VERA, R.; FUENTEALBA, B.; CROXATTO, H.B. (1977) Effect of estradiol upon ovum transport in hamsters, rats and mice. *Arch. Biol. Med. Exp. 11:* R164 (Abstract).

ORTIZ, M.E.; VILLALON, M.; CROXATTO, H.B. (1979) Ovum transport and fertility following post-ovulatory treatment with estradiol in rats. *Biol. Reprod. 21:* 1163-1167.

ORTIZ, M.E.; CAMPUSANO, C.; CANESSA, G.; GAETE, C. (1984) Effect of prostaglandins (PGs) and estradiol-indometacin interactions on ovum transport in the rat. *Arch. Biol. Med. Exp. 17:* R165 (Abstract).

ORTIZ, M.E.; DARRIGRANDE, O.; BASTIAS, G. (1985) Mechanisms of variation of oviductal response to estradiol. *Arch. Biol. Med. Exp. 18:* R155 (Abstract)

ORTIZ, M.E.; BEDREGAL, P.; CARVAJAL, M.I.; CROXATTO, H.B. (1986) Fertilized and unfertilized ova are transported at different rates by the hamster oviduct. *Biol. Reprod. 34:* 777-781.

ORTIZ, M.E.; LLADOS, C.; CROXATTO, H.B. (1989) Embryos of different ages transferred to the rat oviduct enter the uterus at different times. *Biol. Reprod. 41:* 381-384.

VILLALON, M.; ORTIZ, M.E.; AGUAYO, C.; MUÑOZ, J. CROXATTO, H.B. (1982) Differential transport of fertilized and unfertilized ova in the rat. *Biol. Reprod. 26:* 337-341.

WU, J.T.; DICKMAN, Z.; JOHNSON, D.C. (1971a) Effects of ovariectomy or hypophysectomy on day one of pregnancy on development and transport of fertilized rat eggs. *J. Endocrinol. 49:* 507-513.

WU, J.T.; DICKMAN, Z.; JOHNSON, D.C. (1971b) Effects of estrogen and progesterone on the development oviductal transport and uterine retention of eggs in hypophysectomized pregnant rats. *J. Endocrinol. 51:* 569-574.