Myoelectrical activity and transport of unfertilized ova in the oviduct of the mouse *in vitro*

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**Summary.** The relationship of myoelectrical activity to locations and movements of eggs was analysed in 12 mouse oviducts *in vitro*. When the eggs were in the ampulla the ampullary activity did not spread through the ampullary–isthmic junction (AIJ), and a narrow region of activity of lower frequency separated the ampullary and isthmic activities. When the eggs were in the isthmus the activity beginning on the isthmic side of the AIJ spread towards the uterus for progressively longer distances. Eggs were near or at the front of the plateau formed by this activity. A separate activity arising in one or more areas of the uterine side of the plateau often spread in the ovarian direction, thus opposing movements of eggs and fluid in the uterine direction. Transport of unfertilized eggs appears to be regulated by a small number of relatively stable pacemakers in the mouse oviduct.

**Introduction**

Knowledge concerning the mechanism of egg transport in the oviduct has increased rapidly during the past few years. Unfortunately, however, most studies have been of the rabbit in which eggs are transported through the oviduct by ciliary activity and muscular contractions. The ciliary transport through the ampulla is rapid in the absence of contractions (Halbert, Tam & Blandau, 1976). Contractions result in to-and-fro movements of eggs superimposed on the linear, smooth ciliary transport (Verdugo, Blandau, Tam & Halbert, 1976). In many species, there are few cilia in the isthmus and their beat may not be only in the uterine direction as in the ampulla (Gaddum-Rosse & Blandau, 1976). The role of the contractile activity therefore seems to be of crucial importance. A clear correlation has been found between movements of small plastic spheres and the spread of myoelectrical activity in the rabbit oviduct (Hodgson, Talo & Pauerstein, 1977). Although movements of eggs have not been compared with the spread of activity, their location after experiments seems to be related to the activity characteristics (Talo & Hodgson, 1978; Hodgson & Talo, 1978). Simulation experiments (Portnow, Hodgson & Talo, 1977a) suggest that changes in myoelectrical activity alone could explain even the delay of transport at the ampullary–isthmic junction.

Eggs can be seen throughout the oviduct in the mouse (Humphrey, 1968) and mice would be useful to study the relationship between myoelectrical activity and ovum transport. This is the subject of the present paper.

**Materials and Methods**

Virgin NMRI mice aged at least 2 months were housed 10–12 per cage. A vaginal smear was taken in the mornings to determine the day of the oestrous cycle. Mice in oestrus and metoestrus were killed by cervical dislocation and the ovariés, oviducts and uterine horns were removed and...
placed in oxygenated Ringer solution (9 g NaCl, 0.42 g KCl, 0.6 g NaHCO3, 0.24 g CaCl2, 0.025 g MgCl2 and 0.5 g glucose in 1000 ml H2O) at about 20°C. The oviducts were carefully freed of mesentery but the uterus and bursa ovarica were left attached. The presence and location of the eggs were ascertained visually. There were 4 oviducts in which the eggs were in the ampulla (Mice 1–4), and in 2 of these (Mice 3 and 4) the eggs were still surrounded by cumulus cells. In 8 oviducts (Mice 5–11) the eggs were in various parts of the isthmus. Both oviducts from Mouse 11 were studied.

For electrical recordings the oviduct was transferred to a thermostatically controlled tissue chamber in which Ringer solution was maintained at 37 ± 0.5°C. The solution was oxygenated continuously (95% O2, 5% CO2) and slowly changed. The bursa ovarica and ovarian end of the uterus were fixed by pins to the bottom of the chamber so that the oviduct was slightly stretched. Although this probably led to a partial displacement of the fluid in the isthmus it was considered necessary for accurate determination of the locations of the electrodes. Six small suction electrodes (Talo & Hodgson, 1978) with an external tip diameter of approximately 0.15–0.2 mm were attached to the oviduct and each recording lasted for 15–30 min. The distances between the electrodes were measured using a calibrated ocular graticule. Electrical potentials were recorded against a common silver–silver chloride reference electrode. Recordings were made on a 6-channel Grass 7P Polygraph using AC coupled preamplifiers. The typical high-pass filter position was 0.15 Hz. In this position the 0.15 Hz signals were attenuated by 50%.

In a few oviducts movements of eggs were filmed through a Wild M5 stereo microscope on a Philips N1500 VRC video tape simultaneously with recording. Approximate locations of eggs were subsequently marked on the recording chart. Only relatively crude determinations of the locations of eggs with respect to the electrodes could be made during the spread of activity.

Results

The relationship between myoelectrical activity and the ovum locations is shown by representative examples at different phases of egg transport in Text-fig. 1. In Text-fig. 1(a), representing Mouse 3, the eggs were located in the ampulla and were still surrounded by cumulus cells. The myoelectrical activity began over the eggs and spread in both directions. It ceased at about 0.5–1.0 mm from the ostium and did not spread past the ampullary–isthmic junction. Between the areas of ampullary activity and high frequency activity in the isthmus there was a region which showed contractions of low frequency only. In the oviducts of Mice 1, 2 and 4 there was no inactive region in the distal isthmus. In the oviducts of Mice 1 and 2 containing eggs freed of cumulus cells, the isthmic frequency was lower, and the activity of the ampulla began on the ovarian side of the eggs but did not spread past the ampullary–isthmic junction. When the eggs were in the distal isthmus (Mouse 5; Text-fig. 1b), the frequency was highest in the ampulla. Plateau values were seen in the ampullary–isthmic junction region on the ovarian side of the ova and in the middle of the isthmus; the activity starting in the latter area spread only in the ovarian direction. The 3 successive recordings in the same oviduct of Mouse 6 are shown in Text-fig. 1(c) as the eggs passed down the oviduct. During the first recording the activity began near the ampullary–isthmic junction and spread in both directions. The eggs were at the front of the frequency plateau. During the second and third recordings the plateau extended more towards the uterus and the eggs were again at the front of the plateaux. A similar situation is illustrated in Text-fig. 1(d): the eggs remained near the uterine end of the oviduct throughout 4 successive recordings. Activity began in the distal isthmus and spread only a short distance in the ampullary direction but through nearly the whole isthmus in the uterine direction. The eggs were at the front of the frequency plateau. A separate activity arising at the site of the eggs spread in the uterine direction with a lower frequency but did not displace the eggs. A short portion of the original recordings from this oviduct is illustrated in Text-fig. 2.
Text-fig. 1. Relationship of the locations of eggs to frequency and spread of myoelectrical activity. Each panel represents the oviduct of one mouse and the position of the 4–7 eggs in each oviduct is indicated by the ovoid. Dots indicate the sites where electrical activity began, and the arrows the direction and distance of its spread. Each sequential recording lasting a minimum of 15 min is distinguished by different symbols for the 4–6 electrode sites. In (c) the activity spread progressively further towards uterus during a period of 45 min. In all three recordings ova were at the front of the plateau. The oviduct length is shown on a percentage scale, where 100% indicates the utero-tubal junction; the ampullary–isthmic junction (AIJ) is indicated.

The approximate locations of a group of eggs in relation to the spread of electrical activity are shown in Text-fig. 3. This figure was selected to illustrate how the activity on the uterine side of the area showing plateau frequency activity was slightly different in frequency from that in the plateau and opposed the spread of activity and movements of eggs. While the activity on the uterine side of the plateau closed the lumen and prevented the fluid flow into that segment, the contraction in the plateau area was unable to close the lumen when the wave of activity spread past the eggs. Consequently, the eggs were moved backwards rapidly with the flow of fluid and were located at the tail of the plateau rather than the front.

The number of pacemakers was usually only 3 or 4, as illustrated in Text-fig. 1(d); 1 or 2 in the ampulla and 2 in the isthmus, one near the ampullary–isthmic junction and the second near the uterine end where the eggs were located. In the early phases of egg transport the isthmic activity was less co-ordinated and the number of pacemaker areas was larger and difficult to identify exactly.
Text-fig. 2. A portion of two successive recordings of the same oviduct as that in Text-fig. 1(d). The 2 recordings are separated by a line but electrode sites 5 and 6 were common to both records. Lines are drawn between activity waves in the centre of the recordings to indicate the direction of the spread. The activity started in the upper recording between electrodes 3 and 4. Eggs were located between electrode sites 9 and 10. Vertical scale 100 µV.

Text-fig. 3. Approximate sites of a group of 3 eggs, shown by circles, in relation to myoelectrical activity. Activity spreads from electrodes 1 to 4 and from 6 to 5. The distance between electrodes 1 and 6 was 4.3 mm and the relative distances between the electrodes are correct as illustrated. Electrode 6 was 2.5 mm from the utero-tubal junction. Activity spreading from electrode 1 spreads past the eggs. Backward movements of the eggs were fast and were caused by fluid flow. Vertical scale 100 µV.
**Discussion**

Eggs are transported into the rat oviduct by the ciliary current (Blandau, 1969). Ciliary activity transports them through the preampulla (infundibulum) to the dilated ampulla, in which they are moved by contractions (Humphrey, 1968). The present study analysed the mechanism of ovum transport from the middle of the ampulla to the area above the utero-tubal junction. The observation that contractions do not spread from the ampulla to the isthmus (Blandau, 1969) was confirmed in this study. However, this may be true only when eggs are destined to remain in the ampulla because spread through the ampullary-isthmic junction in both directions was often recorded. Eggs are probably transported through the ampullary-isthmic junction by ampullary activity. This was in fact observed in one of the oviducts but when one electrode was placed at the junction to see the direction of the spread better the activity changed and the eggs returned to the ampulla. The narrow region of lower frequency in the distal isthmus or at the ampullary-isthmic junction suggests that excitability in this area is lower than on both sides of it. When the eggs are in the isthmus the ampullary frequency declines but a frequency plateau is formed behind the eggs. The activity initiates near the ampullary-isthmic junction and spreads progressively further, pushing eggs towards the uterus. The present recordings did not indicate whether this progress took place gradually or in phases but Humphrey (1968) observed that rushes of activity pushed eggs to the next segment. The results of the present study suggest that the whole isthmus is active during egg transport and that there is an area of spread towards the ovary on the uterine side of the eggs which prevents premature transport too far along the oviduct or into the uterus. In this regard the mouse oviduct appears to differ from that of the rabbit. Experiments in vitro have suggested that the proximal isthmus is inactive in the rabbit and that this inactive region gets shorter at the time of entry of eggs into the uterus (Talo & Hodgson, 1978). However, Talo & Hodgson (1978) made no recordings at the very proximal portion of the oviduct, where it is partly covered by the muscle layer extending longitudinally from the ovarian end of the uterus over the oviduct. Thus the presence or absence of the activity in this area was not determined.

The present study is the first in which the location and movements of eggs were observed simultaneously with recording of electrical activity in the mammalian oviduct. Its results suggest that the transport from the ampulla to the isthmus and through the isthmus is controlled by electrical (contractile) activity, as concluded for the rabbit oviduct (Talo & Hodgson, 1978; Portnow et al., 1977a). This means that no sphincteric mechanism is required to explain the features of the transport. In the mouse oviduct fluid displaced by contractions spreading in the uterine direction did not enter the segments that appeared to be closed and in which activity spread in the opposite direction. The present results do not indicate whether this is due to the recorded activity, some form of tonic contraction or passive elastic properties of these segments.

Verdugo *et al.* (1976) applied stochastic principles in the analysis of the study of egg movements and suggested that movements of eggs have a random component. Portnow, Talo & Hodgson (1977b) showed that completely random movements can lead to directional transport in the oviduct since the ciliary activity prevents them from returning to the abdominal cavity and the proximal isthmus (due to its inactivity) and uterus act as barriers to prevent return to the rest of the oviduct. Verdugo, Lee, Blandau & Halbert (1977) included ciliary activity in a model in which egg transport was presented as a one-dimensional random “walk” in an external field of force. These models apply in the rabbit oviduct after ovulation because the activity begins at practically any point and spreads in both directions for various distances and frequency (Talo & Hodgson, 1978). The number of points at which activity arises nearly simultaneously is much higher than in the mouse oviduct, and the random component is apparently far greater. In the mouse oviduct, the number of pacemaker regions may be only 3 in the simplest situation: one in the ampulla, the second in the distal isthmus and the third in the proximal isthmus. The pacemaker in the distal isthmus is fairly stable. It therefore seems that egg transport in mouse is far simpler than in the rabbit and that the concept of randomness probably does not apply.
References


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