CYCLICAL CHANGES IN THE EPITHELIUM OF THE FALLOPIAN TUBE

Studies with scanner electron microscopy (SEM)

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SUMMARY

By means of SEM the existence of cyclical changes has been demontsrated on the surface of the tube that is of paramount importance in the biology of reproduction. The frequency of ciliary cells increases under the influence of estrogens, producing erect cilius. Under the influence of progesterone, they are frequent once again, but due to the disappearance of secretory activity of the secretory cells. The days preceding and immediately following ovulation (days 13 to 17) the maximum cellular secretion is observed by virtue of apocrine secretion, characterized by the elimination of part of the cellular cytoplasm, and merocrine secretion brought about by multiple and coarse microvilli. The fluid that is produced during these days serves as a vehicle of sperm transport and prevents the descent of the fertile egg.

INTRODUCTION

The suspicion of the existence of cyclical changes in the tube is as old as the understanding and description of endometrial changes.

Histologically, it seemed that the appearance of the existence of changes in the secretory cells ([43]) consisted in an increase of their cytoplasmic secretion or of changes in the height reached by the epithelium ([22, 57, 62, 76, 79, 82, 83]). The changes in the ciliated epithelium, on the other hand, were doubted or not accepted.

The introduction of morphological techniques of high resolution such as transmission electron microsopy ([6, 7, 11, 12, 13-16, 21, 39, 40, 52-56, 59-61, 68, 72, 75, 77]), enzymehistochemistry ([2, 4, 10-12, 20, 25, 32-36, 42, 45, 46, 62, 71, 74, 78, 80]), autoradiography ([8, 24, 48]) and of scanner electron microscopy ([9, 27-30, 37, 49, 50, 58-61, 69, 73]) have confirmed and expanded the conventional studies of optical microscopy in this field.

MATERIAL AND METHODS

Entire tubes coming from surgical operations of genital pathology having no relation to the oviducts have been studied with optical microscopy and SEM. For a complete datation of the hormonal cycle, studies were made using optical microscopy of the endometrium as well as hormonal determinations.

The tubes were examined with SEM in their four histological parts. Multiple biopsies were performed in 7 cases during the following periods:

post-menstruation (days 4 to 7); middle estrogen phase (days 8 to 11); pre-ovulation phase (days 12 to 14); post-ovulation phase (days 15 to 17); middle progesterone phase (days 18 to 22); and premenstrual phase (days 23 to 28). Lastly, two biopsies were made during menstruation.

The biopsies, after being repeatedly washed in physiological serum, were fixed in a 2% solution of glutaraldheid in cacodital 0.1 M (pH = 7.4) for 1 hour. The two solutions became isomolar with the first, with the addition of sacarose. In order to dehydrate the biopsies, the "critical point" technique was employed using freon-11. The samples were covered in a vacuum chamber with an evaporator at 5 times 10^{-5} torr, with

the endosalpinx begin their growth in the cellular periphery, later occupying the entire surface, eventually making it impossible to see its microvilli in the endometrium; their growth is centralized, thus the microvilli remain visible in the periphery.

Ciliated cells

Under the initial effect of the estrogens (post-menstrual phase) (figs. 1-2) the mucosa of the endosalpinx is thin, the ciliated cells are scattered and are more scarce than during the rest of the cycle. Their ciliae appear slightly fallen. In that the estrogen effect increases (fig. 3) (middle estrogen phase) the number of ciliated cells becomes greater and the ciliae become erect, clearly stand out in the mucosa surface. In the secretory phase (fig. 4), a few days after ovulation the ciliated aspect again becomes dominant, even though the ciliae are once again fallen. This cellular domination is due to the disappearance of the secretion in the upper pole of the secretory cells. At the end of the secretory phase, the ciliated cells once again have a very similar aspect to that of the post-menstrual phase.

Secretory cells

Cyclical changes manifest themselves much more in the secretory cells than in the ciliated cells. In the post-menstrual phase (figs. 1 and 2), these cells are low and cubical, with a large intercellular space defining very well the limits between them. Their surface is covered with many fine and regular microvilli. As ovulation approaches (fig. 4) a sudden development of its cytoplasm appears, that produces a protrusion of the surface of the cells on the inner wall of the tube. These cells are then dominant on the inner wall, and it can be seen how the ciliae go out between them as if they were compressed.

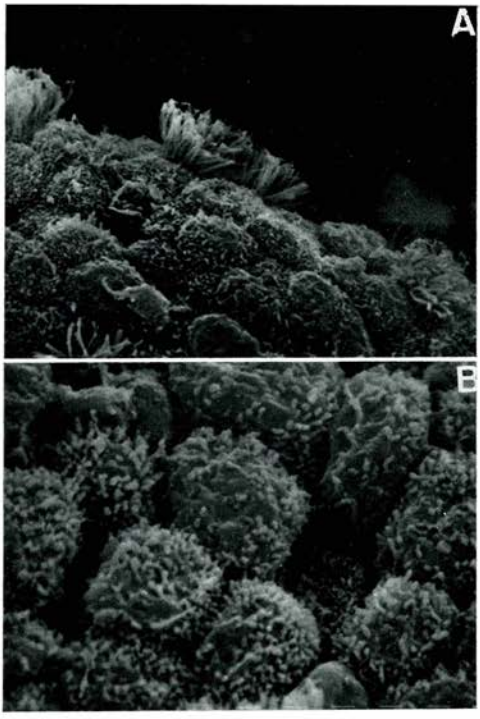

Fig. 1. — The two most common cellular types in the epithelium of the fallopian tubes as seen with SEM. Above two ciliated cells are prominent, below the secretory cells with typical microvilli on the surface (3000-5000 ×).

carbon and gold. The samples were examined with a model JSM-50A SEM with an acceleration voltage of 10 kW.

RESULTS

The SEM has allowed the study of a wide range of the surface of the endosalpinx with high magnifications. The cyclical changes differ morphologically in intensity depending on the segment of the tube studied as well as the distinctive cellular type.

Augmented slightly, the ciliated cells can be observed in rows or as isolated cells (fig. 1), predominantly in the ampullae and fimbria zones. In contrast to what occurs in the endometrium, the cilia of

With low amplification, the height of the endosalpinx reached thanks to the secretion makes the delimitation between the cytoplasms of the secretory and ciliated cells difficult, and the ciliae reach the same level as the secretion granules.

The microvilli, in this stage, become much more numerous acquiring a rough aspect (fig. 4 D), covering much of the cellular surface.

Immediately before the ovulation and during the following days, many globular protrusions are seen (fig. 4 A, B and C) some with very numerous microvilli and others with very few which correspond to the apocrine secretion, that flow into the lumen, taking with it part of the cytoplasm. The rest of the microvilli which are not eliminated as a part of the cytoplasm brake its surface eliminating tube fluid as merocrine secretion. Therefore, during the periovular period it is common to observe on the surface of the lumen tube cellular remains and mucus fibers that cover the mucosa (fig. 6). As a result of this the ciliae remain adherent with one another, greatly decreasing their motility.

Between the 17th and 20th days of the cycle the surface of the mucosa shows large hollows which correspond to exausted secretory cells. The ciliated cells return to appear above the epithelium and the ciliae emerge anew.

These hollows are only temporary (fig. 5), in that the recuperation of the surface

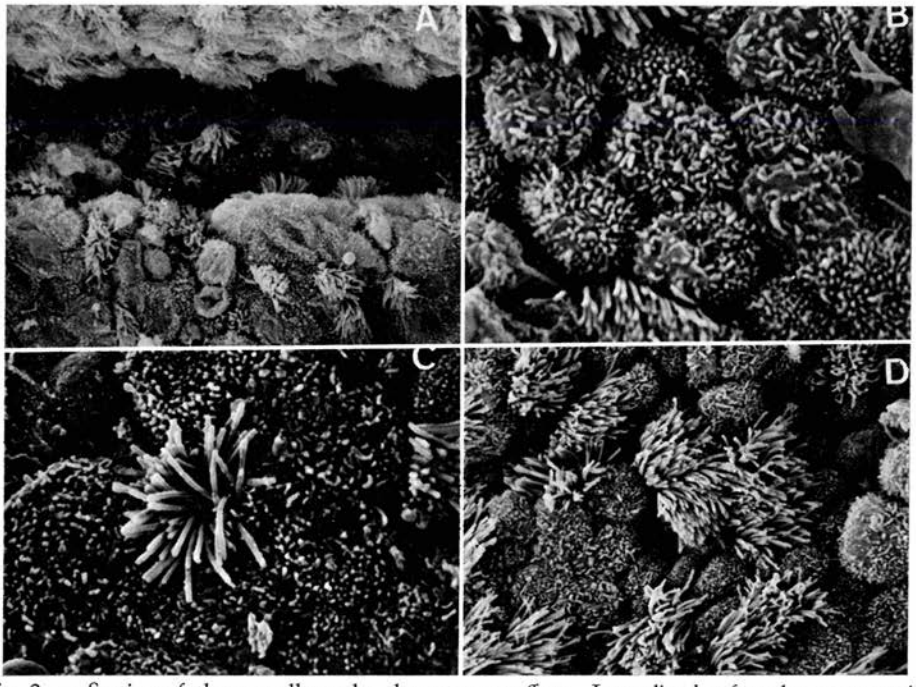

Fig. 2. — Section of the ampulla under the estrogen effect. Immediately after the menstruation a low epithelium can be observed, with scarce ciliated cells and fallen cilio. The secretion cells reach little height (A). These cells possess scarce microvilli which are homogeneous, and the cells are well defined between one another. As the estrogen action increases (C) the ciliated cells become dominant, and their cilium appears erect, standing out clearly over the surface of the secretory cells (D). (1000; 5000; 5000; 2500 ×).

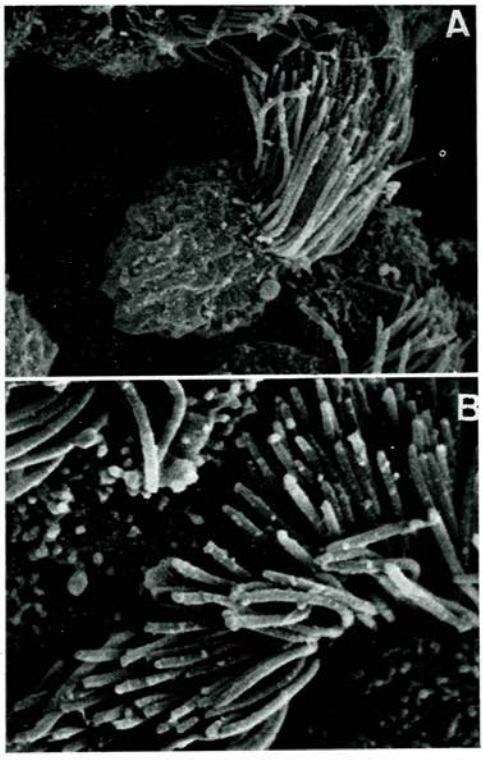

Fig. 3. — Around the 10th day of the cycle, the ciliogenesis activity is at its maximum. The cilium occupying the whole surface of the cellular membrane, they are erect and separated between one another (7000-10,000 ×).

of the secretory cells is very rapid, remaining from that moment on a thin mucosa formed by low cubic secretory cells endowed with scarce microvilli but with its membrane intact.

During the menstruation, as well as in the immediate puerperium (fig. 6) it is common to observe blood elements that cover the surface of the mucosa as well as the remains of the cellular detritus. All of these arise from the endometrium.

DISCUSSION

Only the SEM has been able to show the importance of the cyclical changes in the fecundation mechanism and ovum transport. The enzymehistochemical studies by now classic, were not very conclusive; thus the majority of the Authors that study the glycogen content didn't find cyclical changes ([25, 42, 45, 62, 80]), they found only a decrease in the ciliated cells after ovulation ([10, 35]), others are found in the secretory cells ([25]), or during pregnancy ([32]).

The fatty content ([20, 42, 45]), the alcaline phosphatase activity ([2, 4]), the resistence to the diastases ([25, 46, 71, 74]) to the periodic acid schiff reactive ([78]), or the polysacharidase content ([33]) do not afford conclusive data.

The autoradiographic studies, on the other hand, have clearly shown that the synthesis of DNA only exists under the estrogen effect ([8, 24, 48]), which has a special importance at the time of performing microsurgery.

With transmission electron microscopy two cyclical phases classically, have been accepted, as in the case of the endometrium ([7, 21, 23, 39, 40, 54, 55]), although there are some who denied these alterations ([84]): during the follicular period the cytoplasm of the secretory cells show ever increasing concentrations of granular endoplasmatic reticulum and mitochondria which are not prominent, located in the basal pole. Because of this, this phase is called "ergastoplasmic" ([72]). As the date of the ovulation approaches a large increase in number and size of the mitochondria appeared, and during the luteal phase the highest concentration of voluminous mitochondria, migrated to the upper pole, were observed. These organels were eliminated through a secretion system, basically apocrine, but also, more infrequently, merocrine; because of these, this phase was called "mitochondrial" ([72]).

Nevertheless the "secretory concept" throughout the second phase of the cycle is not accepted thanks to the investigations with SEM.

The ciliated cells, on the other hand, were hardly investigated, many Authors denied the existence of cyclical chan-

ges ([21, 39, 40, 54, 55, 69, 75]). More recently a group of publications affirm that the ciliae suffer periodic degeneration and regeneration ([17, 18, 23, 63, 64, 74]), in the same way in post-partum and in the climacterium decilation has been observed, with recuperation by way of new estrogen production

On the contrary, it has been shown, that the progesterone decreases the population of ciliated cells in the fimbriae, to the point of making them disappear from the isthmic part of the tube ([63, 64, 69]).

Concretely, it can be concluded that during the prolipherative phase there exist

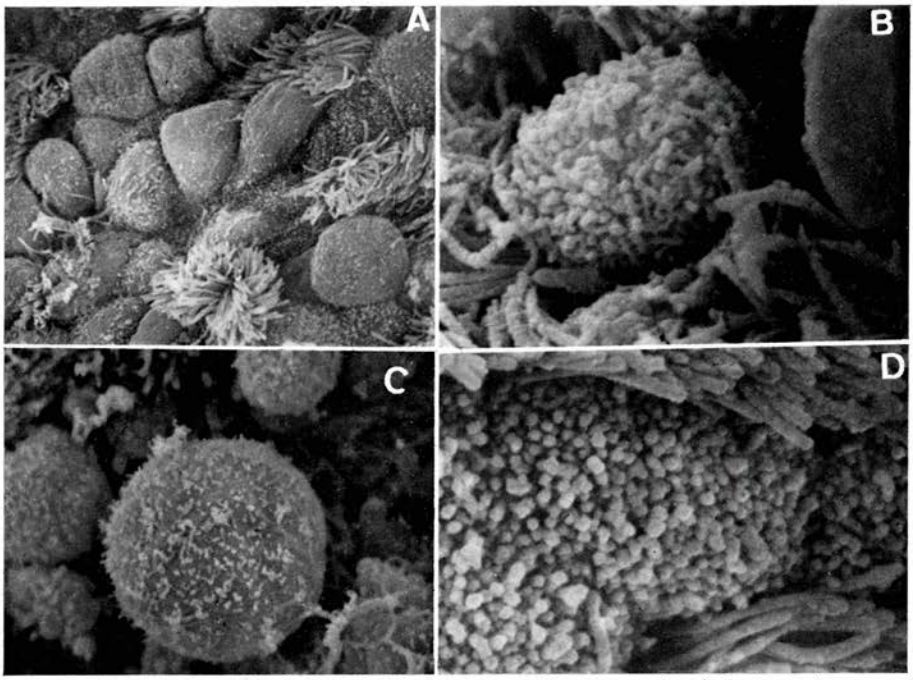

Fig. 4. — Days 12 to 16 of the cycle. An extraordinary growth of the cytoplasm or the secretory cells can be observed that protrudes into the lumen, taking on a oval and globular aspect (A). The ciliated cells appear compressed between these, and the secretion attaches to the cilium avoiding their motility. The microvilli of the secretory cells are very coarse, irregular and of large size. Two types of secretion can be observed, apocrine (C), with desquamation of large globes, that include parts of the cytoplasm, and merocrine (D), in the form of very numerous coarse and irregular microvilli, which end "in the form of drum-sticks", that eliminate in this form their secretion. The maximum production of tube mucus occurs during ovulation (3000; 7000; 5000-10,000 ×).

or by way of the estrogen administration ([3, 37, 69, 81]). The trophic effect of the estrogens on the ciliae has also been shown if they are administered continuosly to the women in the hormonally active period, conducting the ciliated cells to their highest development with the presence of erect ciliae ([50, 69]).

cellular prolipheration (with or without ciliogenesis, according to different Authors) and in the secretory phase the appearance of secretion, in periods identical to the endometrium.

The SEM has been able to define these changes, at the level of the cellular membrane, clearly specifying the moment of

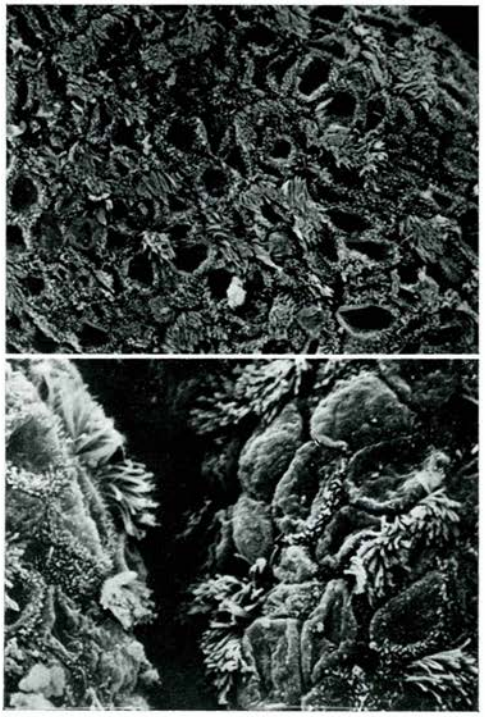

Fig. 5. — In the phase of initial secretion (days 16 to 18), the fallopian tube epithelium appears covered by hollows, that correspond to the cytoplasm of the examined: in secretory cells due to the process of secretion (above). The cytoplasmic recuperation is very rapid. In the two hours immediately after the secretion the membrane of the surface has been restored once again. From this moment on (below) the ciliated cells once again become dominant, standing out above a low epithelium (3000-5000 ×).

their appearance, and their intensity ([8, 21, 23, 26, 27-30, 31, 37, 38, 39, 40, 44, 47, 49, 50, 51, 58-61, 65, 69, 70, 73, 77]):

1) There exist changes in the content of the ciliar elements in the distinct tube segments, dominating in the ampullar and fimbriae portions ([9, 38, 47, 66, 67]).

2) There is an increase in the ciliogenesis in the first phase of the cycle, especially at the beginning, and again dominant at the end of the same, upon the disappearance of the secretory effect by the secretory cells ([44, 49, 50]).

3) The maximum secretion occurs only immediately before, during, and immediately after ovulation ([44, 49, 50]), characterized by the appearance of multiple irregular and coarse microvilli (merocrine secretion), and the elimination of really "cytoplasmic globes" (apocrine secretion). It can be concluded that the fundamental result is that the maximum production of tube mucus coincides with ovulation and with the two days after. This phenomenon produces basic consequences for the biology of the fecundation and ovum transport:

– the tube mucus, such as the cervical, will be the principal transport vehicle of the spermatozoa;

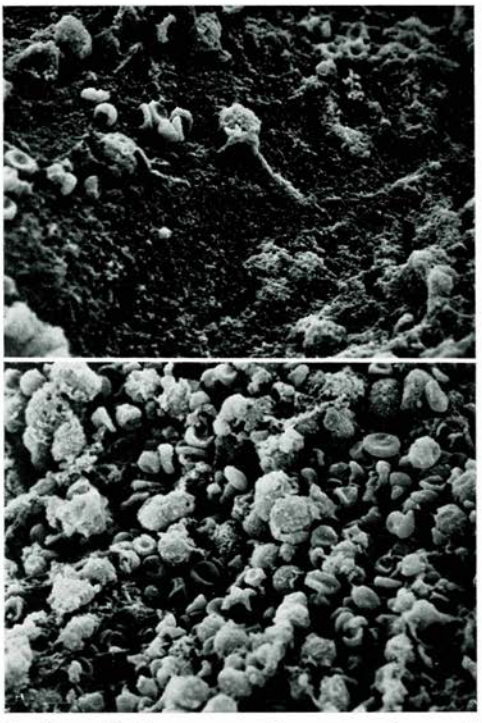

Fig. 6. — During menstruation, puerperium, and occasionaly ovulation, the epithelium surface can be observed to be covered by a mixture of mucus and blood elements. It is not difficult to encounter, as in the above image, degenerated spermatozoa linked to the mucus (2000-2000 ×).

– produces as the cervical, a new natural selection of the non capacitated spermatozoa;

– eliminates, or greatly reduces, the motility of the cilius, whose spacial orientation, in the human being, applies only to the uterine cavity. Without this effect, the spermatozoa would never be capable of ascending, in that the cilius move at the frequency of 1191 beats/min ([1]), which represents an excessively intense resistence;

– the tube mucus creates a really "intramural and istmic cap", which has the function of preventing the ascent of germs and the descent of the ovum into the uterine cavity during 3 or 4 days after its fecundation, permitting its development ([44]).

There is no doubt that the cyclical changes which occur in the fallopian tube epithelium play a decisive role in the biology of the fecundation and ovum transport.

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