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On the Lympho-Epithelial Relationships in the Human Oviduct

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Summary. In order to study the lympho-epithelial relationships in human oviducts, lymphocytes situated in the epithelium were counted and the values found were correlated with differing physiological and pathological changes. In this process the following observations were made:

1. In the secretory phase there are significantly more lymphocytes to be found in the epithelium than during the proliferative phase.

2. In nonspecific purulent salpingitis the number of lymphocytes is not significantly different from that in a normal proliferative phase.

3. The values for fallopian pregnancy are significantly lower than those of a normal secretory phase and do not differ significantly from those of a normal proliferative phase.

4. The values observed for the reproductive period are significantly higher than those found postmenopausally.

Examination by electron-microscopy showed that the lymphocytes in the epithelium of the uterine tube are intercellular. Pointers towards degenerative changes were not seen.

It is presumed that the number of lymphocytes appearing in the epithelium of the fallopian tube depends on the hormonal activity of the ovaries.

Key words: Fallopian tube – Lymphocytes – Lympho-epithelial relationships.

Introduction

Various authors have dealt with the question of the function and fate of lymphocytes which enter epithelia. Koburg (1965) reported on lympho-epithelial relationship in the tonsils, and Andrew and colleagues (1947-1949) carried out similar examinations on the epidermis, trachea and gut. Bohle et al. (1970)

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examined the behaviour of lymphocytes in the renal tubules of human kidneys under physiological and pathological conditions. With the electron-microscope they were able to prove that lymphocytes in the renal tubules are situated intercellularly in the epithelium, and that their position is almost exclusively in direct contact with the basement membrane. Similar findings for the gut were reported by Meader (1967). In contrast to these observations Shields and colleagues (1965) found in their light-microscopic examination that lymphocytes in endometrial glands are situated in an intracellular position.

Opinions differ on the function of these lymphocytes, situated in the various epithelia in an intercellular or intracellular position. Carrel, who noted increased growth in epithelial cell and fibroblast cultures when lymphocytes were present, considered a trephocyte function possible (from the Greek, trephein, to nourish). Bohle and colleagues (1970), who had observed an increased number of lymphocytes in the tubular epithelium in certain kidney complaints, discussed the possibility of lymphocytes participating in the resorption processes of the epithelium. They considered that a transfer of antigens to the lymphocytes situated in the epithelium was possible. Finally, it seems possible that, as Fichtelius (1969) presumes, lympho-epithelial relationships form part of the immunising system, analogous to the Bursa Fabricii in birds.

In order to gain further insight into the function of lymphocytes which enter epithelia, we extended our examination to the *fallopian tubes,* after initial studies had shown the probability of the so called "reserve cells" at the base of the mucous membrane epithelium being lymphocytes.

The individual points of interest were as follows:

1. The exact position of the lymphocytes in the epithelium;
2. the problem of whether they might be influenced by hormonal factors;
3. the nature of their behaviour under pathological conditions.

Materials and Methods

Our examinations were concerned with:

1. Lympho-epithelial relationships of the fallopian tubes of women ($n=29$) of reproductive age. The tubes were removed during sterilisation operations. No information was available about the state of the endometrial cycle at the time the tubes were removed.

2. Lympho-epithelial relationships in the fallopian tubes of post-menopausal women ($n=27$). Here the tubes were removed during hysterectomy. In these cases the endometrium was atrophic.

3. Lympho-epithelial relationships in the fallopian tubes of women ($n=36$) during the proliferative phase. Some of the tubes in this group were removed in the course of hysterectomy, and some partly resected for sterilisation, with curettage at the same time. In all cases we had at our disposal endometrium which enabled us to assess the state of the cycle.

4. Lympho-epithelial relationships of the fallopian tubes of women ($n=12$) whose endometria showed signs of a secretory phase at the time the tubes were removed.

5. Lympho-epithelial relationships in the fallopian tubes of women ($n=14$) in tubal pregnancy.

6. Lympho-epithelial relationships in the fallopian tubes of women ($n=12$) with nonspecific purulent salpingitis. In these cases we had no knowledge of the phase of the endometrial cycle.

Paraffin sections 2–3 µm thick were examined after staining with Giemsa. For electron-microscopic studies 2 mm thick sections were taken from the healthy fallopian tube of a woman who at the time of removal of the tube was in the second cycle phase; the sections were taken immediately after operative removal and pre-fixed in phosphate-buffered 4% Formalin.

Post-fixation followed in Osmium tetroxide (2%). The tissue was embedded in Araldite and section contrasting carried out with lead citrate.

On the paraffin sections, 2000 epithelial cells per fallopian tube on the luminal aspect of the epithelial basement membrane were counted and the number of lymphocytes lying among these 2000 cells was determined. Counting was carried out in the ampullary portion of the tubes exclusively and only in vertical sections. A distinction was made between a basal, intermediary or apical position of the lymphocytes when referred to the total height of the epithelium. A division into infranuclear, intermediary and supranuclear (as undertaken by Bohle and colleagues in their examination of the lympho-epithelial relationships of the renal tubules) could not be made here because of the differing positions of the epithelial cell nuclei in cross section.

The individual results were expressed in permil and for each group an average value ($\bar{x}$) and a standard deviation (s) were worked out. Significance was tested with Students t-test (p=or less than 0.05).

Results

The results are presented in Tables 1 and 2, for which the observed values were converted to apply to 1000 epithelial cells.

Table 1. Number of lymphocytes amongst 1000 tubal epithelial cells

Diagnosis	n	$\bar{x}$	s
Reproductive age (no knowledge of cycle phase)	29	66.37‰	±31.05
Postmenopausal	27	21.81‰	±10.74
Proliferative phase	36	43.40‰	±14.86
Secretory phase	12	95.04‰	±33.58
Fallopian pregnancy	14	47.75‰	±13.78
Salpingitis (average age 32.4)	11	54.45‰	±25.71

Table 2. Position of the intra-epithelial lymphocytes

Diagnosis	Basal	Intermediary	Apical
Reproductive age	98.17%	1.4%	0.43%
Postmenopause	96.56%	3.44%	–
Proliferatve phase	96.36%	3.26%	0.38%
Secretory phase	94.57%	5.43%	–
Fallopian pregnancy	94.91%	4.79%	0.30%
Salpingitis	94.82%	4.67%	0.51%

From the results the following can be deduced:

1. The number of lymphocytes in tubal epithelium is significantly higher in the reproductive period than postmenopausally.

2. In the secretory phase there are significantly more lymphocytes in the epithelium than during the proliferative phase. The values observed for the proliferative phase are significantly higher than the values for the postmenopausal period.

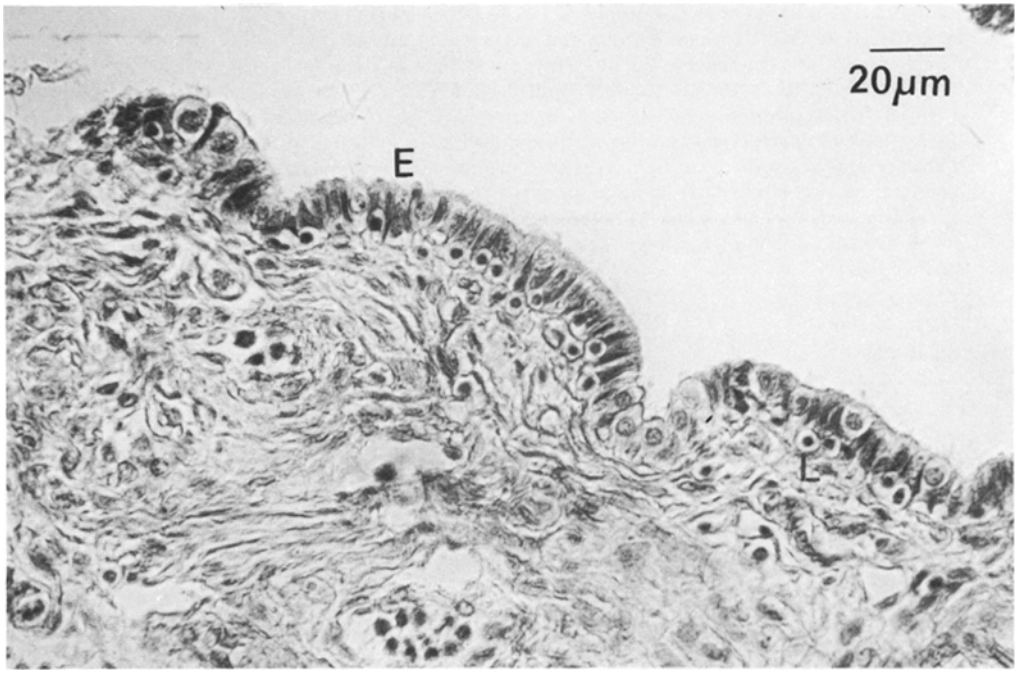

Fig. 1. Tubal mucous membrane with numerous lymphocytes in the epithelium (secretory phase of the endometrium), for the most part in a basal position. *L* lymphocytes, *E* epithelial cells. Light microscope, × 500

3. Neither salpingitis nor fallopian pregnancy effect an increase in the number of lymphocytes entering tubal epithelium. On the contrary, in a fallopian pregnancy the number of lymphocytes is significantly lower than that in a normal secretory phase.

With regard to the position within the epithelium, it can be seen that the lymphocytes were situated basally almost without exception; this can be observered especially easily with the light microscope during the secretory phase. During this phase, lymphocytes appear in such great numbers that in places one can find lymphocyte alongside lymphocyte at the base of the epithelial cells (Fig. 1). During the proliferative phase they are seldom seen.

Their basal position can also be identified with the electron microscope (Fig. 2) and the cells lie exclusively in an intercellular position. This can be seen clearly in Figure 3; the surface of the lymphocyte is here surrounded by cytoplasmic portions of several epithelial cells. Nevertheless it would seem obvious to assume that intracellular lymphocytes are found in isolated cases, as Farr and De Bruyn (1975) were able to show in the endothelium of the postcapillary venules of lymph nodes. Thus the lymphocyte in Figure 4 is almost completely surrounded by the processes of a single epithelial cell. In Figure 5 narrow invaginations of the epithelial cells can be seen in the cytoplasma of

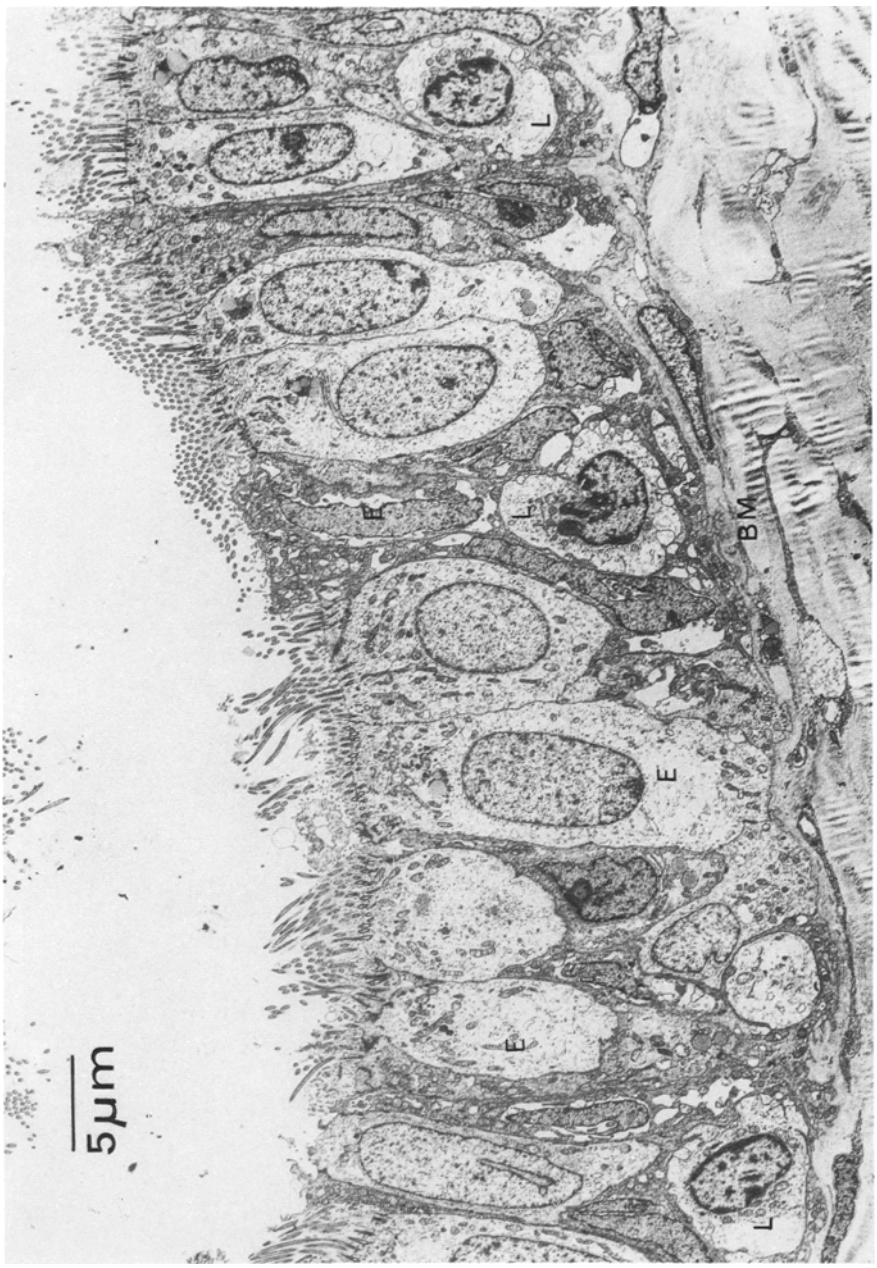

Fig. 2. Tubal mucous membrane with clear ciliated epithelial cells beside dark cells without cilia with longish narrow cell nuclei. In the basal portion of the mucous membrane small rounded clear cells with nuclei rich in chromatin, which in part have deep (clear lymphocytes). *L* lymphocytes, *E* epithelial cells, *BM* basement membrane. Electron microscope, ×2500

a lymphocyte, which may serve to increase the contact surfaces between the epithelial and lymphocyte cells. These invaginations are deep in places and contain portions of the endoplasmatic reticulum of the epithelial cells. A striking feature of Figure 4 are membrane-edged vacuoles in the peripheral cytoplasmic portions of the lymphocytes, which presumably correspond to sectional profiles

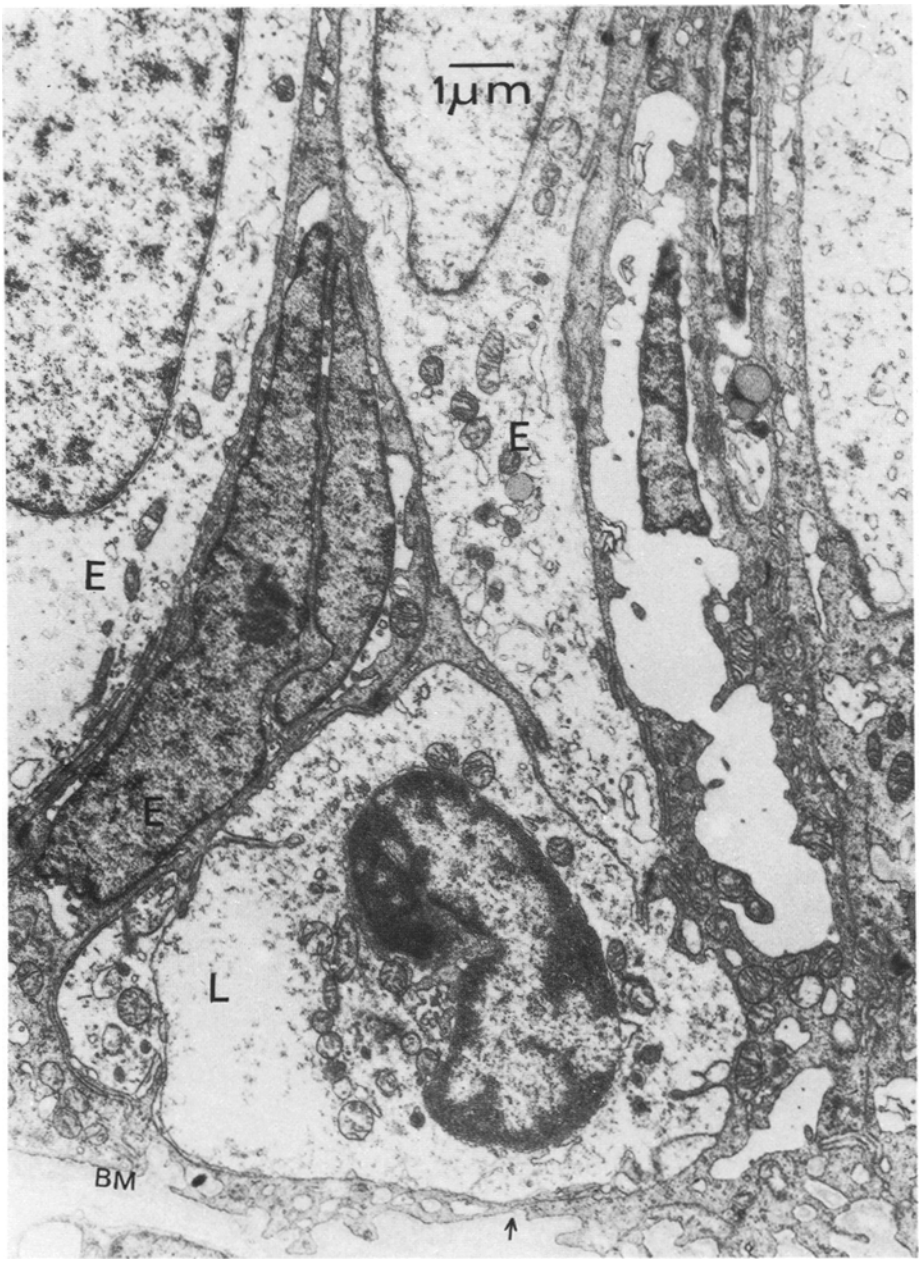

Fig. 3. Section of the tubal mucous membrane. Lymphocyte surrounded by cell processes of several epithelial cells. Arrow shows thin plasma processes of the epithelial cells, touching each other. *L* lymphocyte, *E* epithelial cells, *BM* basement membrane. Electron microscope, × 8700

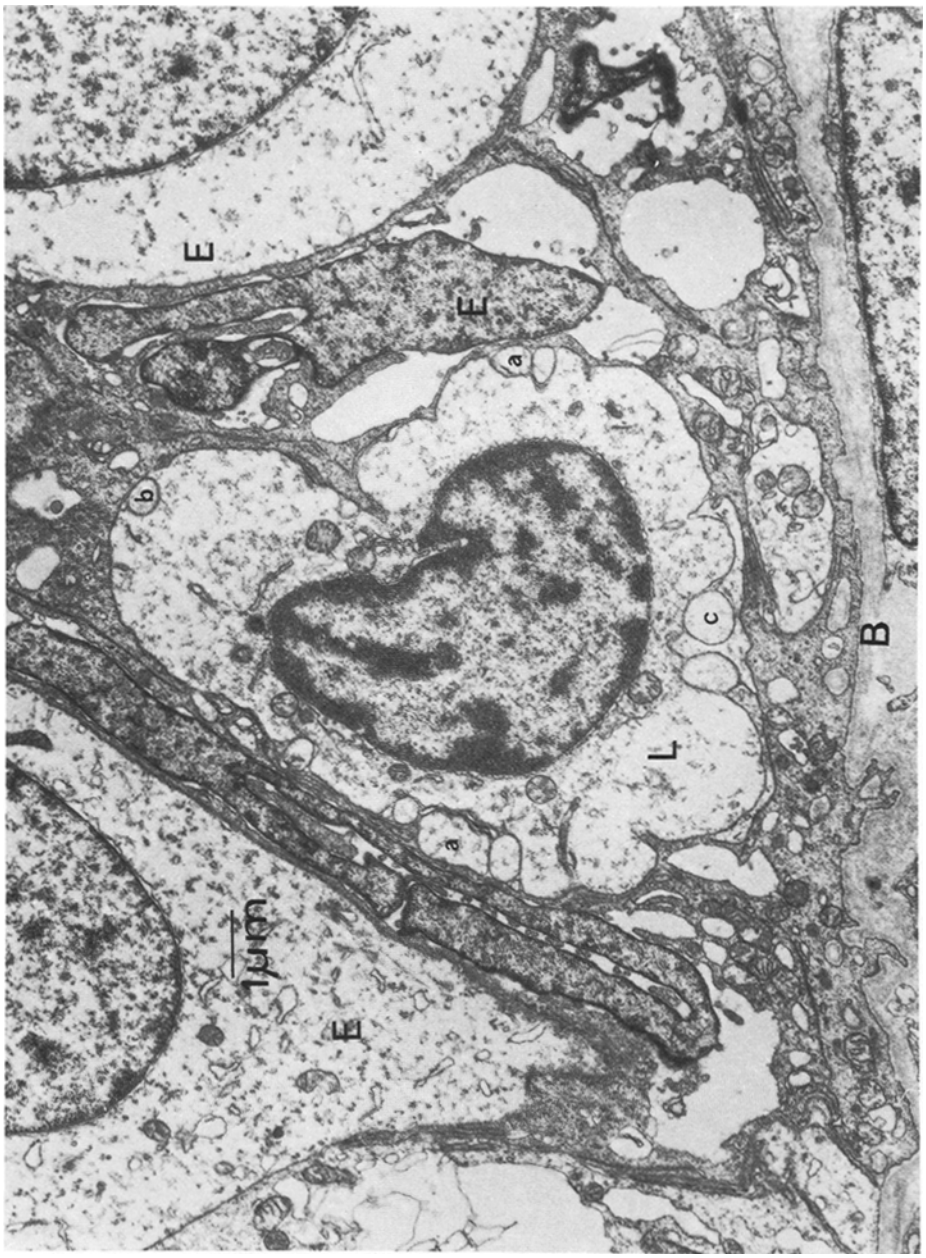

Fig. 4. Section of the tubal mucous membrane. Lymphocyte almost completely surrounded by the process of a single epithelial cell. Striking are membrane-edged vacuoles on the periphery of the lymphocyte, presumably invaginated section profiles of club-shaped processes of the same cell (Cf. sketch in Fig. 6). *L* lymphocyte, *E* epithelial cells, *BM* basement membrane, *a*, *b*, *c* section profiles of invaginated processes. Electron microscope, ×8400

of club-shaped invaginations of the lymphocytes. These membrane-edged "vacuoles", lying near to the surface, have a varied relationship to the rest of the cytoplasm of the lymphocyte according to the angle at which the section is cut (a, b, c): In situation a, the cell processes are almost completely surrounded by the cytoplasm of the neighbouring epithelial cells; in situation b, the processes

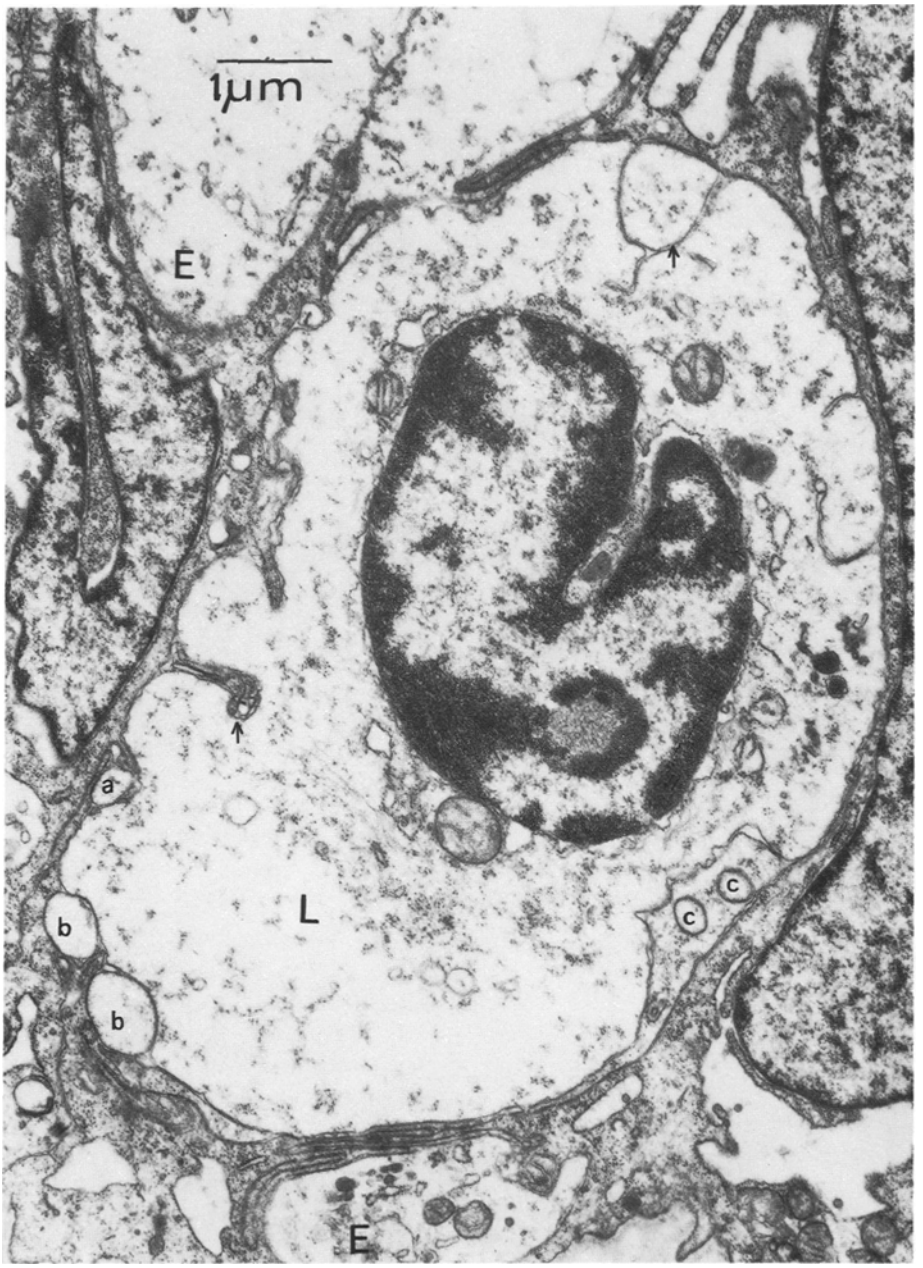

Fig. 5. Section of the tubal mucous membrane. Bar-shaped invaginations of the cell plasma of epithelial cells on the periphery of the lymphocyte in the places marked by arrows. *L* lymphocyte, *E* epithelial cells, *a, b, c* section profiles of invaginated cell processes of the lymphocyte. Electron-microscope, ×15,000

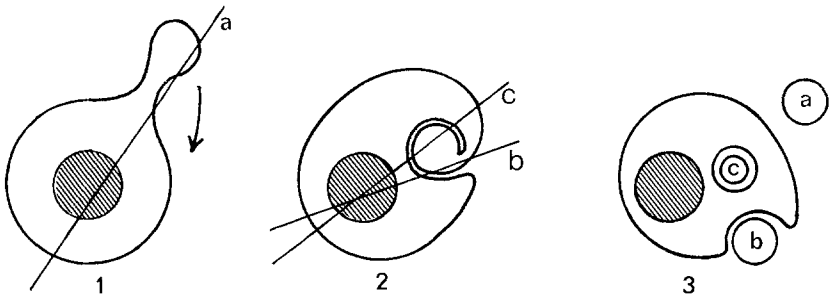

Fig. 6. 1 Lymphocyte with club-shaped cell process. **2** Invaginated cell process. **3** Resulting sections of cell processes when cut at the angles marked in 1 and 2

lie straight along the outside of the lymphocyte membrane and press it slightly inwards; in situation c, the invagination is so deep that the section profiles are completely surrounded by cytoplasm of the lymphocyte.

In addition to this, electron microscopy showed that the cells situated in the tubal epithelium, such as blood lymphocytes (Bessis, 1973) and the lymphocytes of the lymph nodes (Yoshitaka and Lennert, 1969), have nuclei of a rounded or kidney-shaped basic form and a high chromatin content with lumpy thickenings on the nuclear membrane. Unattached ribosomes and few mitochondria are found evenly distributed in the cytoplasm. The majority of the cells correspond to the so-called "clear lymphocytes."

Discussion

As can be seen from our results, lympho-epithelial relationships in the fallopian tube are dynamic relationships, which are influenced by hormones. The question as to whether the lymphocytes in the epithelium of the tuba uterina are dependent on the plasma level of the oestrogenes and/or progesterones or on other humoral factors, requires further experimental examination. A factor which perhaps argues in favour of a dependence on the normal ovarian function, is the clear reduction in number of lymphocytes in the postmenopausal period which accompanies the general atrophy of the mucous membrane of the uterine tubes.

Further, it is conceivable that the lymphocytes entering an epithelium which forms an inner surface serve to set up an immunological defence mechanism and that this function might be weakened with age (menopause). It might be presumed that antigenic information sent out by sperms or by the fertilised ovum is received by these cells. This fact could explain an, as it were, more pronounced defence readiness during the secretory phase. The clear reduction in the number of lymphocytes during fallopian pregnancy compared with the secretory phase does not contradict this interpretation. This reduction could be determined by the fact that a large number of the lymphocytes has already left the epithelium in order to report the special situation "fallopian pregnancy".

Also, the fact that the number of lymphocytes does not increase in salpingitis, as well as the circumstance that essentially they are situated basally, would speak against a transfer, carried out under physiological conditions, of lymphocytes from the stroma into the lumen of the fallopian tube.

In our view pathologists must abandon the suggestion that these basal cell elements in the epithelium serve as reserve cells for its regeneration (Pauerstein and Woodruff, 1967). In view of the vast number of cells found by us, intermediary stages in the phase of differentiation to the epithelial cell should have been found. This was, however, not the case.

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