THE CYCLICAL VARIATION IN THE PERCENTAGE OF CILIATED CELLS IN THE NORMAL HUMAN ENDOMETRIUM

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Summary. The percentage of ciliated cells in the luminal and glandular epithelia of endometrial samples from sixty-eight normal women has been studied. Although the concentrations of ciliated cells found in the luminal epithelium tended to lag behind and below those found in the glandular epithelium, no significant difference was found between the absolute percentages of ciliated cells in each site.

The number of ciliated cells increased during the proliferative phase to reach a maximum of around 20%. This was maintained during the ovulatory phase, and then declined. The hormonal basis of this variation is discussed.

INTRODUCTION

Ciliated cells have been recognized as a component of human endometrial epithelium for a number of years (Benda, 1894). Although originally believed to occur only in pathological conditions (Novak & Rutledge, 1948), ciliated cells are now accepted as being present also during the normal menstrual cycle (Schueller, 1968, 1973; Armstrong, More, McSeveney & Chatfield, 1973). The dynamics of the population of such cells during the menstrual cycle, however, is a matter of dispute. Some workers have suggested that they are only seen in the proliferative endometrium (Fruin & Tiche, 1967) while others have described them also in the secretory endometrium (Fleming, Tweeddale & Roddick, 1968; Schueller, 1968, 1973). Differences have also been noted between the prevalence of ciliated cells in the luminal and in the glandular epithelium. The purpose of the present study was to quantify accurately the variations, if any, in the ciliated cell population during the menstrual cycle and to investigate any differences in this respect between the luminal and the glandular epithelia.

MATERIALS AND METHODS

Tissue was obtained by curettage from sixty-eight healthy women between the ages of 17 and 44 years. The biopsy material was obtained from thirty-five
of the women during laparoscopic sterilization. A further twenty women were undergoing investigation of minor menstrual irregularities and thirteen were being investigated for primary or secondary infertility. In each case, care was taken to ensure that an adequate biopsy representative of the body of the uterus had been obtained. The tissue was divided into two portions. The first was fixed in buffered 4% formaldehyde (pH 7-3) and, after dehydration and embedding in paraffin wax, 5 µm sections were cut and stained for routine examination in the light microscope.

For detailed study of the ciliated cells, the other portion of tissue was cut immediately into 1-mm cubes, fixed in buffered glutaraldehyde (pH 7-3), post-fixed in buffered osmium tetroxide, dehydrated and embedded in Araldite. Sections (1 µm thick) were cut on an LKB ultramicrotome and stained by toluidine blue at high pH. They were then examined under oil immersion in a Leitz Orthomat microscope and at least ten frames of epithelium from each of two unselected blocks were photographed. From the prints, a count was made of epithelial and of ciliated cells and the percentage of the latter was calculated. By this method, at least 500 cells from both the glandular and the luminal epithelia were examined from each specimen.

RESULTS

Routine light microscopic examination showed no significant abnormality in any biopsy specimens.

The ciliated cell in the araldite sections stained with toluidine blue was identified as a shield-shaped cell with a pale-staining and relatively clear cytoplasm compared with the surrounding non-ciliated glandular cells. It appeared to be confined to the basal layer of the epithelium and free luminal cilia were not always identifiable.

![Text-fig. 1. The percentage of ciliated cells in the luminal (•) and glandular (○) epithelia of the human endometrium at various stages of the menstrual cycle. For detailed explanation see text.](image-url)
The percentage of ciliated cells in the luminal and glandular epithelia at the various stages of the menstrual cycle is shown in Text-fig. 1. To facilitate statistical analysis, results have been grouped arbitrarily into 4-day periods but the mean for each day is also given along the base of the figure. The percentage of ciliated cells in both the glandular and the luminal epithelium increased to a maximal value during the ovulatory phase. There was no significant difference between the maximal values for the percentage of ciliated cells in the glandular epithelium (22.0%) and the luminal epithelium (20.6%) ($t = 1.391; 0.20 > P > 0.15$). The curve for the luminal epithelium, however, tended to lag behind and below that for the glandular epithelium throughout the proliferative phase so that the maximal percentage of ciliated cells in the luminal epithelium was achieved 1 day later than that found in the glandular epithelium. The percentage of ciliated cells in both sites then fell steadily throughout the secretory phase although even on Day 28 a significant population was still present.

DISCUSSION

A variation in numbers of ciliated cells, expressed as a percentage of the epithelial cell population, in different areas of the endometrium has been established quantitatively for some time. Several authors (Schueller, 1968; Johannisson & Nilsson, 1972; Ferenczy, Richart, Agate, Purkerson & Dempsey, 1972) have shown that ciliated cells are found in greatest numbers around the ciliated isthmus and at the cornua. Several authors have noted that a cyclical variation occurs in the percentage of ciliated cells in the body of the uterus during the normal menstrual cycle. It has been established subjectively from these studies that ciliated cells are most frequently identified during the mid-cycle but the subsequent behaviour of the cells is a matter of dispute (Fruin & Tiche, 1967; Fleming et al., 1968; Schueller, 1968, 1973; Ferenczy et al., 1972). Although Fleming et al. (1968) attempted to quantify the percentage of ciliated cells against an empirical 'basal value' and Ferenczy et al. (1972) produced values for the percentage of ciliated cells in the luminal epithelium, the present study is the first that has been specifically designed to attempt an accurate quantification of this phenomenon.

The steady rise in the percentage of ciliated cells in both the glandular and the luminal epithelia during the proliferative phase to maximal levels which were maintained throughout the ovulatory phase supports the hypothesis that ciliated cells may be important in fertilization or nidation.

The curve for the luminal epithelium showed a constant displacement to the right compared with the curve for the glandular epithelium. When this shift was taken into consideration, there was no significant difference at any stage of the cycle between the percentage of ciliated cells in either of these sites. This may suggest that the ciliated cell population is derived from stem cells which are located in the bases of the uterine glands. During differentiation, the maturing ciliated cells may migrate, leaving the glands to become components of the luminal epithelium. The increase in ciliated cells in both sites during the proliferative phase suggests that the precursor cells are sensitive to oestrogen.
stimulation. Further evidence for this is found in the work of Fleming et al. (1968), who showed that there was an increase in the expected percentage of ciliated cells in conditions when oestrogen was present in excess, such as endometrial hyperplasia. The fall in numbers during the secretory phase of the menstrual cycle may be attributed to the negative influence of progesterone since it has been established that after a mid-cycle plateau, the concentration of circulating oestrogen continues to rise with progesterone to reach a peak around Day 24 (Dallenbach-Hellweg, 1971). The morphological basis for this decline in numbers is uncertain. The ciliated cells may undergo necrosis in situ, although evidence for this, such as an increase in pyknotic ciliated cell nuclei, has not been noted in the present study. Alternatively, the ciliated cells may develop some secretory capability (Schueller, 1968), thus losing their histological characteristics. The investigation of these points demands further histological and ultrastructural analysis of the ciliated cell of the human endometrium and a study of these aspects is in progress.

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REFERENCES


