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»PALE CELLS« IN THE UTERINE MUCOSA

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Irregular bleeding is the most frequent cause for histologic examination of the uterine mucosa and the task of histologists trying to explain the most intricate process of bleeding from morphological conclusions is extraordinarily difficult.

In the following, only those irregularities of bleeding will be discussed which occur without a thoroughly defined histologic change (tumour, inflammation). In the majority of cases, the origin of such bleedings can seldom be disclosed by histology, in order to explain the irregular bleeding. In the course of time, the correlation between the structure of the mucosa and the bleedings has been considered from different angles. There was a period when stress was laid on glandular hyperplasia assumedly due to inflammation. However, since the problems of hormonal control had been cleared, the mucous membrane and its anomalies, later the more delicate structure of the stroma, and the correlation between glands and stroma have formed the points of chief interest.

Studies of the vascularization and blood supply of the uterine mucosa called attention to changes in the structure of the vessels. No doubt can, however, arise that consideration of the mucous membrane, or even the entire uterus, from either of the above angles, and any endeavour to explain the process of uterine bleeding solely by those factors, could lead to conclusions that are incorrect, being partial and organoperspectivical.

Menstruation and the cyclic change of endometrium present an outstanding example of organ function regulated by the neuro-endocrine system. The influence of hormones on the cyclic change of the uterine mucosa has been proved. Any kind of neuro-endocrine functional disturbance may cause disorders in menstruation and in the cyclic transformation of the endometrium.

Changes in the structure of the endometrium clearly reflect all disturbances inherent to the neuro-endocrine system. However, the correlation between isolated structural changes and disorders of the regulatory function is not yet wholly clear. The mechanism of hormonal action has not yet been

solved, nor have the effector cells and tissues been detected. It had been assumed at an earlier time that hormones do not exert their effect directly but through the endocrine cells in the organs. Therefore attention has been called to the characteristic type of cell of uterine mucosa, i. e. the »pale cells«.

The so-called endocrine cells of organs were first investigated by *Feyrter* [1] who observed these cells first in the pancreas and in the uterus. He regarded them in his monograph subsequently published as cells of a »diffuse endocrine epithelial organ«. Similar cells which may be observed on various mucous surfaces are considered by most authors, in accordance with *Feyrter*, as having some kind of endocrine function.

It is presumed that the so-called pale or chromophobic cells of the uterine mucosa are similar local cells with endocrine properties. As *Feyrter* has himself declared later on, the pale cells of endometrium are a special kind of ciliated epithelium. The ciliated epithelium and secretory epithelium are only a functional appearance of the same type of epithelium. In his work published in 1949, he points to a certain correlation between the numerical variation of chromophile cells and periods of the menstrual cycle, demonstrating an absolute increase of the chromophobe cells in the cystic and polypous hyperplasia. Finally he raised the question of a correlation between chromophile cells, cervical metaplasia, and adenoconcroid tumours. In 1949 *Flerkó* has corroborated the statement of *Mihalik* that ciliated epithelium is formed by so-called replacing cells. To this paper of *Flerkó* [2], I remarked that replacing cells are, according to my opinion, identical with chromophobic cells (Pathologist's Session, 1949, in Debrecen).

In 1951, *Hamperl's* paper on »pale ciliated epithelium of the uterine mucosa« was published. The author herein confirms the statements of *Mihalik* and *Flerkó*. In his opinion it is new that ciliated cells originate from chromophobe cells.

My examinations, based on 2000 specimens of curettage material have concerned the morphology of pale cells and their relation to the cyclic and morbid changes of endometrium.

Pale cells can be found in every part of the uterine mucosa, their number being highest in the glands of the fundus. Usually they are situated near the basal membrane, intercalated between other cells and they gradually rise (»grow«) toward the lumen (Fig. 1). The cells arriving at the surface are nearly invariably ciliated whereas in cells approaching the lumen each phase of cilium formation may simultaneously be present. There are, on the other hand, cells, especially in the deep layers, in which no sign of cilium formation can be noticed.

The question brought up by *Hamperl* also arises, whether all ciliated cells of the uterine mucosa are pale and whether all pale cells are ciliated. Concerning the first question *Hamperl* contends that all ciliated cells are chromophobe.

My opinion differs in this item, having found many ciliated cells which have no common feature with the typical pale cells.

The second question, whether all pale cells are ciliated, is more difficult to answer. There is no doubt that many unciliated pale cells exist and it is difficult to determine into what cells they may develop.

I would add a third question to the former ones: is the pale cell identical with the replacing cell? My answer to this is in the affirmative. One should certainly speak of replacing cells instead of pale ones. Very likely, replacing cells are liable to differentiate to either ciliated or secretory cells.

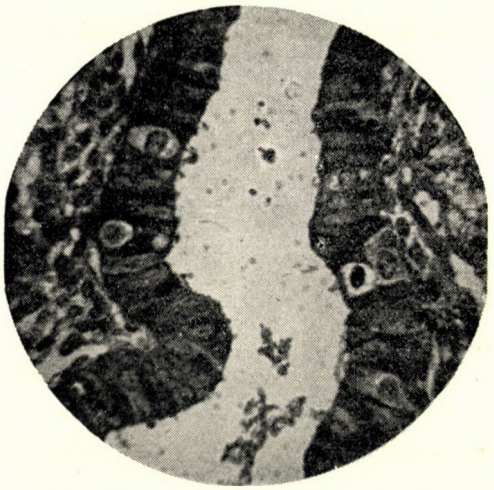

Fig. 1

Chromophobic cells in various situations. Age : 40 years (hyperplasia glandularis partim cystica endometrii).

On the other hand, the endocrine properties of these cells have not at all been proven and this is the same case with the entire »diffuse endocrine cell system«. In my examinations, no morphologic sign in favour of the hormonal function of pale cells was found. Yet a certain correlation was disclosed between these cells and endocrine function, first of all gonadotropic and ovarian hormone function.

Flerkó in 1949 already emphasized that a certain hormonal regulation of cilium formation should be assumed. In his later work [3] he expressed the opinion that a diencephalic regulation must also be taken into consideration. In animals with an extended sexual cycle, cilium formation displays a certain periodicity. Castration is, after a longer time, followed by considerable changes in the course of which ciliated cells ultimately disappear. The contrary may be observed in pregnancy. *Feyrter* also found a correlation between the cyclic changes of the mucosa and the numerical changes of ciliated cells.

In my examinations of endometrium specimens in which typical cyclic changes occur, the numerical changes observed in various phases were insignificant. The number of pale cells was invariably greater during proliferation than during

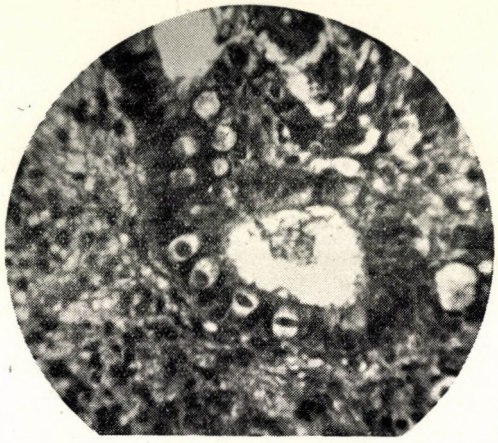

Fig. 2
Chromophobic cells in the endometrium of woman suffering from glandular polypous hyperplasia.

Fig. 3
Strikingly high number of pale cells displaying a tendency to cilium formation in an irregular endometrium. (Histologic opinion, excessive production of follicle hormone.)

the secretory phase. Generally, they occur in the vicinity of dividing cells. From this fact it may be inferred that they appear in the period of re-epithelization. Their number greatly increases in hyperproliferation foci of the mucosa, further on in focal or diffuse adenocystic or polypous hyperplasia (Fig. 2 and 3). The greatest number of pale cells is found in the

proliferative foci associated with irregular bleeding during climacterium or preclimacterium. Polypus-like mucous growths are often covered on the surface

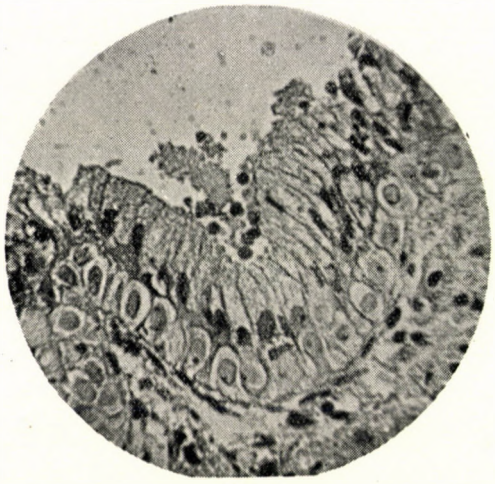

Fig. 4
Double - layered epithelium ; below, pale cells ; above, ciliated cells. Age, 45 years, polypous hyperplasia of the endometrium.

with a double layer, a basal one composed of pale cells and a superficial one consisting of ciliated epithelium (Fig. 4).

Summary

Having examined more than 2000 specimens of curettage material, the author presumes that hormonal function of the chromophobe cells of the endometrium cannot be proved. Nevertheless, the numerical changes of these cells is a morphologic indicator of the functional state of suprauterine hormonal regulations. Their numerical augmentation occurs with an excess of follicle hormone whereas their absence observed in certain periods points to follicle hormone deficiency.

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О ТАК НАЗЫВАЕМЫХ СВЕТЛЫХКЛЕТКАХ

К. Фаркаш

Резюме

На основании исследований более чем 2000 соскобок образовалось то мнение, что гормональная функция светлых-клеток слизистой оболочки матки недоказуемо, однако их количественное изменение является хорошим морфологическим указателем функционального состояния нейрогормональной регулирующей системы, стоящей над маткой. Их размножение указывает на перевес фолликулярных гормонов, их отсутствие же в подходящий период — на дефицит фолликулярных гормонов.