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*V.P. Strekalovsky, S.L. Khankin, L.L. Kapuller*

# Endomicroscopic characterization of the superficial epithelium in patients with colon tumors

Research Institute of Proctology of the Ministry of Health of the RSFSR, Moscow

The use of the technique of coloring the mucous membrane and colonomicroscopy with a large increase (170 times) in 127 patients aged 26 to 75 years with colon tumors and without macroscopic changes made it possible to identify 3 main types of cellular organization of the epithelium. These studies also showed that these types of epithelial structures are located in the form of fields of various areas and configurations. In most observations, their various combinations are noted. A relationship has been established between the types of cellular organization of the epithelium and the morphological structure of the most common neoplasms of the colon.

Keywords: colon, superficial epithelium, endomicroscopy, tumors.

Colonomicroscopy is a new direction in the study of the state of the mucous membrane of the colon. This method, in contrast to generally accepted morphological methods, allows examining the superficial epithelium of the colon, which was not paid enough attention to during histological examination.

Assessing the effectiveness of vital microscopic examination, we came to the conclusion that the object of application of these methods should be areas of the macroscopically unchanged mucous membrane, and not detected during macroscopic examination of the neoplasm. Available relatively few publications in foreign literature [7, 9-11] report the possibility of detecting malignancy in polyps. However, our studies [1, 4, 8] indicate insufficient information content of colonomicroscopy to study the stages of malignancy of polyps and the inexpediency of further studies in this direction.

Based on our previous studies with a 35-fold increase, an endomicroscopic characterization of the normal epithelium, atrophy, its dystrophy, hyperplastic foci and microadenomas was given, as well as facts indicating increased proliferative activity of the mucous membrane.

This work is based on the results of colonomicroscopy at a magnification of 170 times in order to describe in more detail the changes in the mucous membrane of the colon in tumors.

Material and methodology. Studies were conducted in 127 people aged 26 to 75 years (Table 1). In 24 people, no macroscopic changes in the colon were detected, in 22 - single and multiple polyps were found, in 24 - colon cancer was diagnosed. The largest group - 55 people - were patients operated on earlier (in terms of 6 months to 10 years) for colon cancer of various localization; at the time of examination, they had no signs of relapse or generalization of the process. 23 people in this group were diagnosed with polyps.

In all patients, according to the method described earlier [2-4, 8], staining and endomicroscopic examination were performed with an increase in 35 and 170 times of a certain area in the distal third of the sigmoid intestine, which, according to our data, is a zone of increased proliferative activity of the epithelium in the colon. The color zone had approximately the same area of about 60 $^{cm2}$. Analysis of the results was carried out on the basis of photo documentation, and multiple (up to 70) sections of the colored surface were photographed, which clearly reflected the nature of changes in the epithelium of this section of the colon.

To evaluate high-magnification endomicroscopy data, we took into account the following features: 1) the size and shape of cells and their nuclei, 2) color selectivity, 3) color intensity, 4) the quantitative ratio of

cells of different size and color within the crypt. To judge the nature of changes in the mucous membrane along with these signs, we assessed the nature of changes at the crypt level, the presence of microformations and their specific gravity.

TABLE 1. *Distribution of patients by gender, age and depending on changes in the colon*

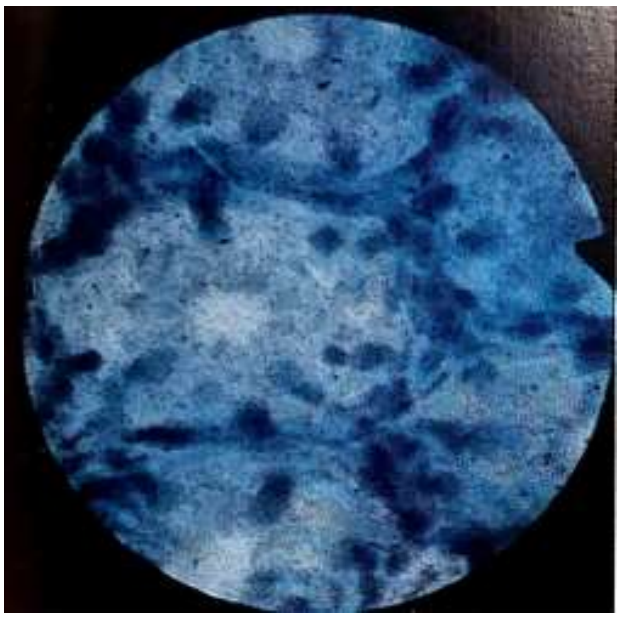
| Changes in the colon | Number of patients | Age, years | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | | up to 29 | | 30–39 | | 40–49 | | 50–59 | | 50 and over | |
| | | M | F | M | F | M | F | M | F | M | F |
| No macroscopic changes | 24 | 2 | – | 2 | 5 | 3 | 4 | 1 | 5 | 1 | 1 |
| Polyps | 22 | – | 1 | 1 | 1 | 2 | 8 | 3 | 3 | 2 | 1 |
| Cancer | 26 | – | – | – | – | 4 | 4 | 5 | 5 | 2 | 6 |
| Condition after radical cancer surgery | 55 | 1 | – | 1 | 2 | 6 | 6 | 8 | 8 | 15 | 8 |
| T o t a l | 127 | 3 | 1 | 4 | 8 | 15 | 22 | 17 | 21 | 20 | 16 |

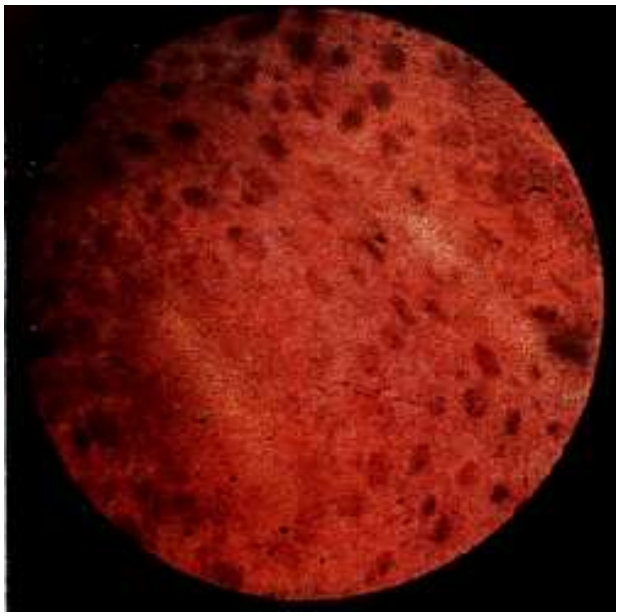
R e s u l t s. The study of the architectonics of the superficial epithelium of the mucous membrane allowed us to identify 3 main types of its structure [5, 6]. Type I is characterized by a clear separation of crypts from each other due to large (15-17 microns) cells intensively staining with methylene blue, while the epithelium located between the borders and the mouth of the crypts is represented by small (4-6 microns) cells staining mainly with toluidine blue. We conventionally call this organization of the surface epithelium "chain mail links" (see figure, a).

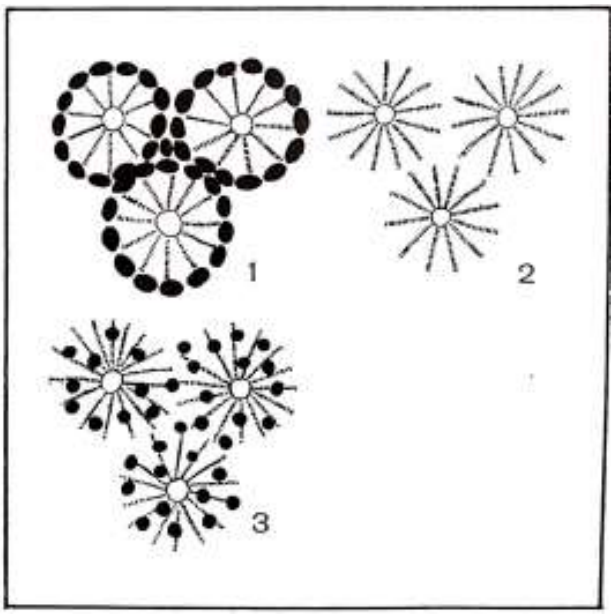
Another type (II) of the structure of the surface epithelium is represented by small cells (4-6 microns), which are stained mainly with toluidine blue. These cells are arranged in the form of chains radially oriented relative to the mouth of the crypt. In most cases, the cells are oval in shape and are located circularly around the mouth of the crypt. Some cells located on the periphery of crypts often have signs of dystrophy. A clear distinction between crypts by means of large cells, as was the case in the previous paragraph, was not revealed in these observations. This type of structure of the surface epithelium is designated by us as "spokes of the wheel" (see Figure, b).

A distinctive feature of the third (III) type of epithelium structure is the presence of large (16-18 microns) cells intensively staining with toluidine blue, which are located quite evenly in the form of a placer against the background of small cells, giving the mucous membrane an external resemblance to the "leopard skin" (see figure, c).

Much less often, other types of epithelial structure were detected, which, due to the small number of observations, we have not yet classified.

a.  b. 

c. 




**Types of colonic mucosal epithelial organization:**
a - type I - "chain mail links"; b - type II - "wheel spokes"; c - type III - "leopard skin."

It can be seen from Table 2 that epithelial organization of the same type is rare in the entire area examined. In the analyzed group, it was observed only in 20 people (15.7%), while in most of the examined there were combinations of different types of cellular organization. Very interesting, from our point of view, is the fact that in the absence of changes in the colon and in patients with polyps, the most frequent types of epithelial organization were I and II, while in patients with colon tumors, the most frequent was type III epithelial organization (having a uniform structure throughout the examined surface or combined with other types). Less commonly, type III epithelial organization occurred in patients who underwent radical cancer surgery. However, when assessing the frequency of detection of type III epithelium structure, it should be noted that in patients who underwent operations for synchronous primary multiple cancer, such changes were detected with a higher frequency than after operations performed for solitary cancer tumors.

TABLE 2. *Qualitative characteristics of surface epithelium structure in patients with benign, malignant tumors and in individuals without macroscopic changes in the colon*

| Nature of changes in the colon | Number of patients | Structures of the same type | | | Mixed structures | | |
|---|---|---|---|---|---|---|---|
| | | Type I - "chain mail links" | Type II - "wheel spokes" | Type III - "leopard skin" | With a predominance of type I. | With a predominance of type II. | With a predominance of type III. |
| No macroscopic changes | 24 | 4 | 2 | – | 11 | 7 | – |
| Polyps | 22 | 4 | – | 1 | 15 | 2 | – |
| Cancer | 26 | 1 | – | 3 | 5 | 2 | 15 |
| Condition after radical cancer surgeries | 55 | 2 | 1 | 2 | 22 | 15 | 13 |
| T o t a l | 127 | 11 | 3 | 6 | 53 | 26 | 28 |
| | | 20 (15,7%) | | | 107 (84,3%) | | |

When analyzing the size of the areas that occupied these types of mucosal organization, it was found that in individuals with no changes and in the presence of polyps in the colon, the largest areas were occupied by types I and II of the epithelium, and in colon cancer and in those operated on for multiple cancer - type III (Table 3).

TABLE 3. *Quantitative correlation of the prevalence of the main types of epithelial organization over the occupied area ($cm^2$) within the stained space of the mucous membrane*

| Changes in the colon | Mucosal area occupied by the main types of epithelial organization ($cm^2$) | | |
|---|---|---|---|
| | I - "chain mail links" (M ± m) | II - "wheel spokes" (M ± m) | III - "leopard skin" (M ± m) |
| No macroscopic changes | 28,7±7,8 | 28,5±8,0 | 3,0±2,6 |
| Polyps | 40,1±6,8 | 14,7±5,72 | 2,72±2,7 |
| Cancer | 15,9±7,4 | 9,9±4,1 | 34,1±8,1 |
| Condition after radical cancer surgeries | 23,4±3,67 | 21,3±3,7 | 14,5±3,9 |

TABLE 4. *Presence of microtubules in patients with various changes in the colon*

| Changes in the colon | Number patients | Hyperplastic formations | Microadenomas | Hyperplastic formations + microadenomas | Total number of patients with microtumors | |
|---|---|---|---|---|---|---|
| | | | | | abs. number | % |
| No macroscopic changes | 24 | 4 | 1 | 3 | 8 | 33,3 |
| Polyps | 22 | 10 | 2 | 3 | 15 | 68,2 |
| Cancer | 26 | 6 | 1 | 2 | 9 | 34,6 |
| Condition after radical cancer surgeries | 55 | 21 | 5 | 12 | 38 | 69,1 |
| T o t a l | 127 | 41 | 9 | 20 | 70 | 55,1 |

Along with various combinations of the main types of structure of the surface epithelium, located in the form of fields having different shapes and areas, various types of micro-tumors are also detected on the surface of the mucous membrane with different

frequencies (Table 4). If, in the absence of macroscopic changes in the colon, microformations were found in 33% of patients, in cancer - in 34.6%, then in patients with polyps and those operated on for cancer, they were determined with approximately the same frequency - in 68.2%-69.1%. The existing differences in the frequency of microneoplasms in patients with malignant tumors can be explained by the fact that during cancer we examined areas of the mucous membrane near the tumor, while the main number of microformation, according to supravital studies, was detected at a certain distance from it. As for the qualitative characteristics of micro-tumors, patients with polyps and those operated on for cancer had a significant predominance of multiple hyperplastic foci combined with microadenomas.

Discussion. Based on the analysis, we can state that all 3 main types of organization of the surface epithelium occur in different age groups, retain their structure quite firmly and can be hereditary. In addition, we have established a certain relationship between the cellular organization of the surface epithelium and the morphological structure of epithelial neoplasms of the colon. So, around hyperplastic polyps, microscopic foci of hyperplasia, the architectonics of the epithelium is represented by type II cell organization ("spokes of the wheel"). Around adenomatous polyps, the mucous membrane has a structure like "chain mail links" - type I. The third (III) type of mucous membrane structure ("leopard skin") is most common near cancerous tumors and in patients who have previously undergone cancer operations.

Characterizing the condition of the entire colored area of the mucous membrane, taking into account the nature of microneoplasms, we can argue that the highest frequency of detection of multiple microadenomas in combination with type I organization of the epithelium occurs in a group of patients with adenomatous polyps, which, apparently, indicates a certain predisposition of the mucous membrane of this type to the occurrence of adenomas. In multiple foci of hyperplasia and hyperplastic polyps, type II organization of the superficial epithelium is detected with high frequency. The third (III) type of epithelial structure, according to our data, is most often the background on which cancerous tumors are determined. We cannot currently establish causal relationships between these facts. However, it is noteworthy that foci of hyperplasia and microadenoma do not occur within fields organized by this type.

These data give us reason to believe that types I and II of the organization of the superficial epithelium should be more likely to be regarded as variants of the norm, while type III should seem to be considered potentially less favorable in terms of the possibility of cancer.

We believe that the results obtained allow us to outline a new direction in the study of the structure of the mucous membrane of the colon, which, apparently, makes it possible to obtain new information about the morphogenesis of benign and malignant neoplasms of the colon.

## LITERATURE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