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Microendoscopic Features of the Surface Epithelium in Patients with Colonic Tumors

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Summary

Vital studies of the colonic mucosa in 127 patients using the method of colonomicroscopy have allowed us to establish that the surface epithelium has a heterogeneous structure. It was possible to single out three main types of cell organization. Correlation has also been detected between types of cell organization of surface epithelium and morphological structure of the most common neoplasms of the colon.

Key words

Colon – Tumor – Surface epithelium – Endomicroscopy

Microcolonoscopy at different magnifications is a new trend in the study of the colonic mucosa. This method, as distinct from commonly applied morphologic methods, permits the investigation of the surface columnar epithelium of the colon, usually neglected on biopsy.

We have concluded that this method should be applied when the mucosa has a normal aspect, rather than for the study of macroscopic lesions. Relatively few papers (6, 9, 10, 11) describe possible findings of malignancy in polyps. However, our investigations (2, 5, 8) show that microcolonoscopy is insufficiently informative for the study of stages of malignant transformation in polyps. Hence, microcolonoscopy is unsuitable for this purpose.

On the basis of our studies at a magnification of × 35 magnification, we have defined the normal state, atrophy and dystrophy of the colonic epithelium. We have also identified hyperplastic foci and microadenomas, and determined the features of an increase in the proliferative activity of the colonic mucosa. However, the evaluation of the results of colonomicroscopic studies at a magnification of × 170 made it possible to obtain supplementary data which permitted a more detailed interpretation of previously obtained results at a lower magnification.

Materials and methods

We have examined 127 patients aged between 26 and 75 years. Data on the distribution of these patients with regard to sex and age, as well as to clinical diagnosis are presented in Table 1. It is necessary to note that these groups were singled out on the basis of the mucosal changes found during a total colonoscopy. In 24 patients no macroscopic changes in the colon were seen; in 22 patients single and multiple polyps were diagnosed; in 24 patients colonic cancer was identified at different sites. The largest group of patients (55) had been operated on for colonic cancer six months to 10 years earlier. There were no signs of recurrence or generalization of the process at the time of endoscopic observations. In 23 patients of this group polyps were diagnosed.

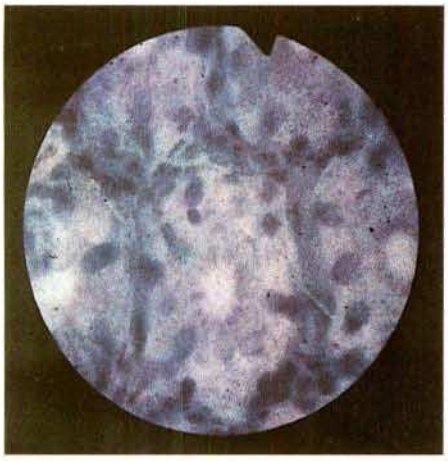
Microendoscopy by our methods (1, 2, 3, 4, 7) at magnifications of × 35 and × 170 was performed at a certain site in the distal sigmoid colon, which is, as our data show, an area of increased proliferative activity in the colon. The surface area of the stained mucosa was about 60 cm^2. The analysis of the results was based on photography. It is important that many sites (up to 70) of the stained surface were photographed. Such photography reflected with adequate ac-

Table 1 Distribution of patients according to sex, age and changes seen in the colon

Changes in the colon	Number of patients	29 years and younger		30–39		40–49		50–59		60 and over	
		male	female	male	female	male	female	male	female	male	female
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 surgery for cancer	55	1	–	1	2	6	6	8	8	15	8
Total	127	3	1	4	8	15	22	17	21	20	16

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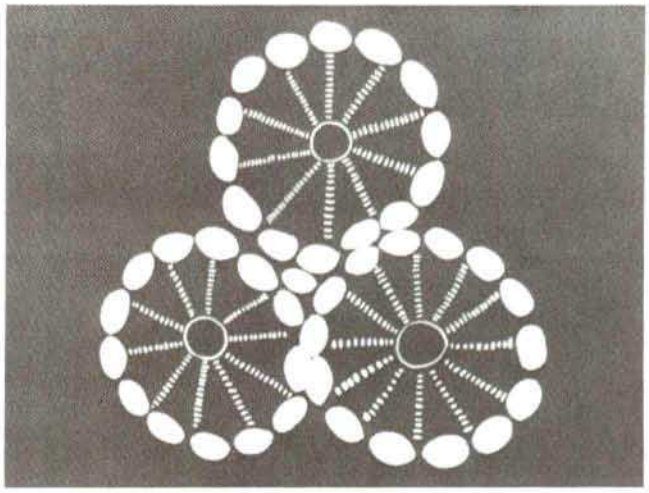
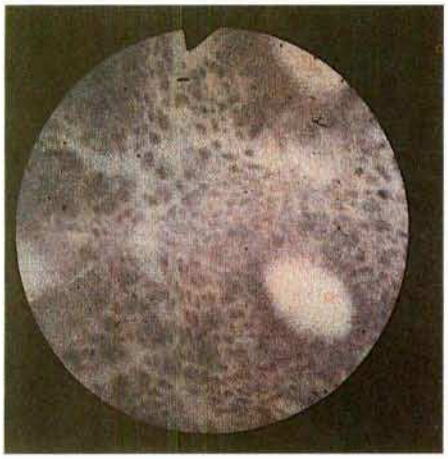


Fig. 1 Type I epithelial organization – "chain-mail links" (Endophoto with a magnification of × 170, and a schematic image).



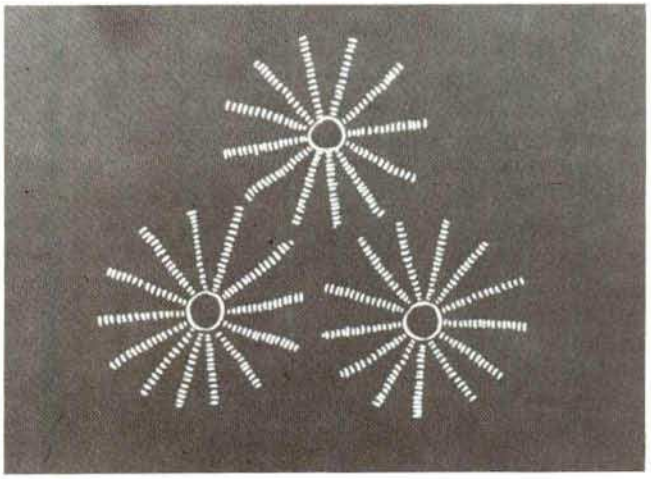
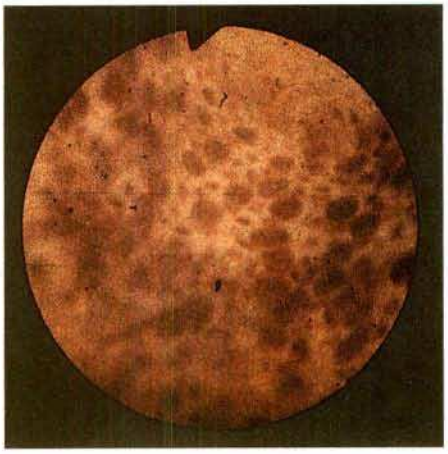


Fig. 2 Type II epithelial organization – "wheel spokes" (Endophoto with a magnification of × 170, and a schematic image).



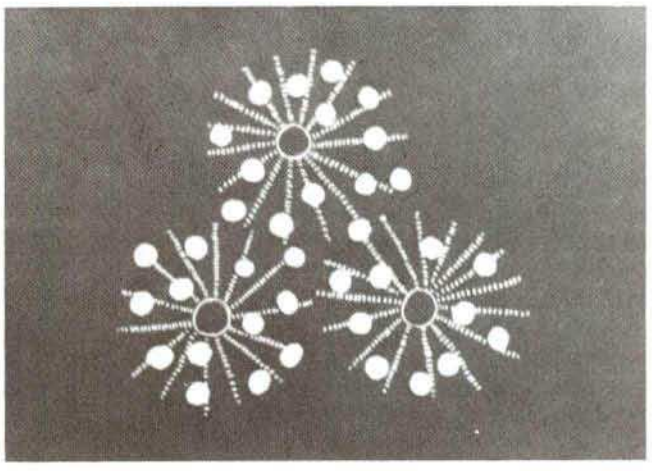


Fig. 3 Type III epithelial organization – "leopard skin" (Endophoto with a magnification of × 170, and a schematic image). Endomicroscopy was performed with an Olympus "CF-UHM".

curacy the real character of the epithelial changes that had taken place within the limits of the stained mucosal area. We suppose that this analysis is valid enough to draw conclusions as to the character of the epithelial changes.

Our evaluation of the endomicroscopic data at a large magnification was based on the following criteria:
1) dimensions and form of the cells and their nuclei;
2) selectivity of the staining of different groups of cells with methylene blue and toluidine blue;
3) staining intensity
4) quantitative correlation of the cells which differ in their dimensions and staining within the limits of the crypt.

Assessing the character of the changes within the whole of the area examined, we also took into account the changes in the crypts as well as the presence of microadenomas and microhyperplastic foci and their specific density.

Results

A study of the mucosal surface epithelial cell structure has allowed us to establish three major types. The first type, resembling chain-mail, is characterized by clear-cut delineation of the crypts from each other due to the presence of cells of large size (15–17 microns), which are intensely stained

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Table 2 Qualitative features of the surface epithelium in patients with benign and malignant tumors, and in those with normal endoscopic findings

Nature of the changes in the colon	Number of patients	Structure of one type			Mixed structures		
		Type I "chain-mail links"	Type II "wheel spokes"	Type III "leopard skin"	with prevalence of type I	with prevalence of type II	with prevalence of type III
Normal endoscopic findings	24	4	2	–	11	7	–
Colonic cancer	26	1	–	3	5	2	15
Condition after radical surgery for cancer	55	2	1	2	22	15	13
Total	127 (100%)	11	3	6	53	26	28
		20 (15.7%)			107 (84.3%)		

Table 3 Quantitative distribution of the main types of epithelial organization according to the occupied area (in cm^2) within the limits of the stained space of the mucosa in the sigmoid colon

Nature of the changes in the colon	Area of the mucosa occupied by the main types of epithelial organization (in cm^2)		
	Type I "chain-mail links" (M ± m)	Type II "wheel spokes" (M ± m)	Type III "leopard skin" (M ± m)
Absence of macroscopic changes in the colon	28.7 ± 7.8	28.5 ± 8.0	3.0 ± 2.6
Colonic polyps	40.1 ± 6.8	14.7 ± 5.72	2.72 ± 2.7
Colonic cancer	15.9 ± 7.4	9.9 ± 4.1	34.1 ± 8.1
Condition after radical surgery for cancer	23.4 ± 3.67	21.3 ± 3.7	14.5 ± 3.9

Table 4 Presence of microtumors in patients with different changes in the colon

Nature of the microtumors / Nature of the changes in the colon	Number of patients	Hyperplastic tumors	Microadenomas	Hyperplastic microtumors + microadenomas	Total number of patients with microtumors absolute number	
Absence of macroscopic changes in the colon	24	4	1	3	8	33.3
Polyps of the colon	22	10	2	2	15	68.2
Cancer of the colon	26	6	1	2	9	34.6
Patients radically operated on for cancer	55	21	5	12	38	69.1
Total	127	41	9	20	70	55.1

by methylene blue, while the epithelium, situated between the borders and orifices of the crypts is represented by small cellular structures (5–6 microns), (Fig. 1). The second type of surface epithelium which includes small cellular structures, resembles the spokes of a wheel. This variety is characterized by the absence of large cellular formations between the crypts, (Fig. 2). The third type is represented by large cells (up to 18 microns) intensely stained by toluidine blue and scattered in a relatively even pattern against the background of small cells. This type we termed "leopard skin", (Fig. 3).

Other types of epithelial structure occurred considerably less often. Owing to the small number of cases observed, we have not been able to classify them so far. Table 2 shows that the structure of columnar epithelium of the same type all over the area investigated is seldom found. In our series it was noted only in 20 patients (15.7%), whereas in most patients combinations of different types of cell organization were observed. We find it very interesting that type I and type II epithelial structure occurred most often both in the colon with normal mucosa and in the colon affected by polyps,

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whereas patients with colonic carcinomas most often had type III epithelial organization, which is of uniform structure all over the area observed, and is seen in combination with other types of mucosal structure. Type III epithelial organization was less often found in patients who had undergone radical surgery for cancer. However, it should be borne in mind that type III had a higher occurrence in those who were operated on for synchronous primary multiple carcinomas than in those who had surgery for solitary tumors.

An analysis of the surface areas occupied by these types of mucosal structure has shown (Table 3) that the largest areas were occupied by types I and II in those persons who had either normal colonic mucosa or colonic polyps, while type III occupied the largest areas in patients with colonic cancer or who had been operated on for multiple cancer.

Apart from different combinations of main types of surface epithelial structure having the aspect of fields of various form and area, the mucosal surface presents different kinds of microtumors with varying incidence (Table 4). Microneoplasms were noted in 33% of patients with normal-appearing mucosa. In those with carcinomas they were detected in 34.6%. In patients with polyps and those operated on for cancer, the incidence of microneoplasms was similar, i.e. 68.2% and 69.1%, respectively. The difference in the observed incidence of microneoplasms in patients with malignant tumors can be explained by the fact that in patients with cancer we investigated parts of the mucosa near the tumor, but according to the results of supravital studies, microneoplasms predominate at a certain distance from the tumor. As for the qualitative aspect of microtumors, a considerable prevalence of multiple hyperplastic foci, associated with microadenomas, was detected in patients with polyps and those operated on for cancer.

Discussion

Our findings show that all three main types of surface epithelial organization occur in different age groups with a rather stable preservation of structure, which does not preclude their hereditary nature. In addition, we have established a certain correlation between the cell organization of superficial epithelium and the morphological structure of the epithelial neoplasms of the colon. Thus, for example, around the hyperplastic polyps, which are microscopic foci of hyperplasia, the epitheli architecture features type II cell organization ("wheel spokes"). The mucosa around adenomatous polyps has type I structure ("chain-mail links"). Type III mucosal structure ("leopard skin") occurs most frequently near malignant tumors and in patients who for the most part have undergone surgery for cancer.

When describing the state of the entire stained area of the mucosa, with attention paid to the nature of microneoplasms, we can assert that the high incidence of multiple microadenomas in association with type I epithelial organization is seen in the group of patients with adenomatous polyps. This seems to indicate a certain predisposition of this type of mucosa to develop adenomas. Type II epithelial structure is most often seen in multiple foci of hyperplasia and hyperplastic polyps. According to our data, type III epi-thelium structure more often than not serves as a background against which carcinomas are detected. At present, we cannot yet establish any causal relationship between these facts and the specific structure of the epithelium. However, it is worth noting that foci of hyperplasia and microadenomas do not occur within areas with this type of structure.

These findings allow us to admit that types I and II surface epithelial organization should in all likelihood be regarded as normal variants, whereas type III potentially seems to have a greater predisposition for the development of malignancy in the colon.

Conclusion

Thus, an analysis of findings of the endomicroscopic study show that in the superficial layer of the columnar epithelium there are various types of structure that appear to be characteristic of various morphological forms of epithelial tumors. There are also good reasons why these changes can serve as a background for epithelial neoplasms of the colon. The surface areas of these fields can vary, but their limits and distribution through all the colonic segments cannot yet be established by endoscopic microscopy alone. At the same time, we are of the opinion that these findings can help to outline a new trend in the study of the structure of the colonic mucosa. This new trend will probably contribute to a better understanding of the morphogenesis of both benign and malignant neoplasms of the colon.

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