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Endoscopic Microscopy of the Colon

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Summary

The authors analyse the results of endoscopic colonomicroscopy at various magnifications in 250 patients.

A study of dye absorption in different histological types of colonic tumor made it possible to establish that chromocolonoscopy is an effective method in diagnosing and differentiating some types of tumors and hyperplastic changes in the mucosa of the colon. Adenomas with severe dysplasia of the glandular epithelium, and tumors with a structure of an adenocarcinoma do not readily accept vital staining.

Key-Words: Colon, Tumors, Endomicroscopy, Chromocolonoscopy, Vital staining

Modern endoscopic facilities permit an examination of any section of the colon and an assessment of the nature of macroscopic changes. However the desire to widen the endoscopic diagnostic possibilities has led to the creation of equipment permitting an examination of the mucous membrane under various magnifications so as to detect the earliest signs of disease.

In the early, seventies lens-type rigid rectomicroscopes were developed (*Barski* et al. 1976, *Drozdova, Strekalovski* 1976, and others) which permitted a x150–200 magnification. However these devices failed to find application in clinics, due to their design. In 1978, *Tada* reported on the use of a fibromicroscope with a variable focal distance and a x10 magnification. In 1979, the same authors reported on the successful use of a colonoscope with a x35 magnification, and in 1981 – with a x170 magnification. *Nishizawa* et al. (1980) used the method of endoscopic microscopy to assess the degree of activity of the process involved in non-specific ulcerative colitis. The same authors believed it possible to use the method to study small polyps of the colon, with the aim of identifying points of malignancy in them. Assessing the data in the literature, it should be noted that there is a tendency toward using endomicroscopy, instead of the histological investigation of biopsy specimens. However, no clear answers to the questions posed have been obtained. This is why we undertook the task of comparing the data of endomicroscopy with the results of histological examination, to assess the effectiveness of endomicroscopy in identifying the points of malignancy.

In the Research Institute for Proctology of the Ministry of Health of the Russian Federation we have gained experience with more than 250 endomicroscopic investigations of the colon, using the flexible x35 and x170 magnification microscopes made available by the firm "Olympus."

Notwithstanding the reports on the successful staining of mucous membrane of the colon with methylene blue (*Tada* et al.), we ran into a number of difficulties. To master the method of vital staining, we employed the method of supravital staining, to this end studying 30 non-fixed surgical specimens of the colon. It proved rather difficult to obtain satisfactory staining of the tissues. When a solution of methylene blue is applied to the mucosa during colonoscopic examination, most of the dye is washed off together with the mucus. When the mucous membrane of the colon is stained with the aid of an enema (*Sinvey* et al. 1981) the surface of the colon in the left sections acquires a dark blue or sky-blue colouring. In the right section of the colon the mucosa frequently fails to stain the methylene blue is quickly evacuated from the caecum and ascending colon. In 5–10 minutes the staining of the colon surface becomes non-uniform owing to the separation of the protective mucus from it, and when the mucus is washed off through a catheter the mucous membrane can be cleaned of the pink colour. Thus, the presence of mucus on the surface prevents staining of the cells of the epithelium. All this means that when the dye is applied to the wall of the colon that has not previously been cleaned of mucus it is possible to obtain definite information only on the characteristic features of the surface of the mucous membrane of the colon.

This is why we have employed the following method of vital staining.

Method

After the selected section of the colon has been examined, the mucosa is mechanically cleaned of its mucus by introducing a jet of a 20–40 ml of an isotonic solution through a catheter. To ensure dissolution and final removal of the mucus we used the fermental emulsion "EndoParactol" or "Mucosolvin," a 50% solution of which is introduced through the same catheter. 15 20 ml of the preparation cleans 5–7 cm^2 of the colonic mucosa. Following the cleaning of the mucosa and aspiration of excess liquid, 5–10 ml of a mixture of a 1% solution of toluidine blue and a solution of methylene blue is sprayed on this segment of the colon, and excess dye is also removed by aspiration. Qualitative staining requires that the dye should remain on the walls of the colon for not less than 3 4 minutes, when a thorough washing of the mucosa with the isotonic solution is undertaken and excess liquid is aspirated from the lumen of the colon. Observing these conditions, it is possible to achieve satisfactory staining of the mucosa, but the staining is nevertheless not uniform and staining

Endoscopic pictures were obtained with Olympus Instruments

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intensity differs even in a group of patients with a similar endoscopic picture. The use of dyes permits us not only to contrast the formations identified by colonoscopy, but also to identify invisible changes.

The data of endomicroscopy are interpreted by analysing slides and prints.

Results

A visibly normal mucous membrane appears under the microscope as a rather smooth surface. On stained sections a x35 magnification permits good identification of crypts, mostly polygonal in shape. Each of these crypts is formed by the blue-stained colonocytes, the number of which varies over a rather wide range. A calculation of the number of crypts has shown them to vary in number within a rather wide range, from 35 to 80 per 1.13 mm^2, with the crypt diameter varying from 0.15 to 0.21 mm. In addition to the crypts, vessels are also identified. Contact microscopy with a x170 magnification permits identification of 2–5 crypts of polygonal or oval shape with a round opening. The cells forming the crypts are light blue in colour, with more intensely stained nuclei (Fig. 1).

The described normal microscopic picture is of great importance for assessing the changes that originate during various pathological processes.

Taking into account the data reported by *Sinvey* et al. (1980), indicating that malignant tumors and points of malignancy are stained more intensely than benign tumors, we have specially stained malignant tumors of the rectum and colon. When a solution of methylene blue is applied to a tumor there appear on its surface points of intense staining. However, after the mucus and fibrin films are washed off its surface the tissue of the tumor reverts to its initial appearance. After these tumors have been treated by the method described above and then stained, in 7 out of 65 observations small slightly blue-stained section were identified on the surface of the tumor. The endomicroscopic picture is then characterized by the chaotic arrangement of individual stained cells seen against the background of the main mass of non-stained structures of the tumor.

With respect to the histological structure all these tumors were adenocarcinomas of varying degrees of differentiation. These data permit us to state that adenocarcinoma – which is the predominant morphologic type of tumor in the colon – does not readily undergo vital staining.

In 37 patients various anatomical types of villous and glandular-villous adenomas of the rectum and colon were stained with a methylene blue and toluidine blue solution. These tumors failed to stain. Endomicroscopy revealed a slight degree of staining of individual epithelial cells covering the villi. In 34 patients these tumors were removed through a colonoscope. Three patients were operated on to remove large creeping tumors. In 32 observations, a histological investigation of specimens of tumors indicated the presence of tubular or tubular-villous adenomas with a varying degree of cellular atypia. In three observations sections with infiltrated growth of cancer in villous adenomas were identified, and in 2 patients polyp-like carcinomas. Endomicroscopic investigations failed to identify sections of malignancy, since these sections had not stained, in common with the surrounding adenomas and adenovillous tissue.



Fig. 2 Endomicroscopic view of a proliferate with x35 magnification (colonomicroscope – model CF-HM "Olympus")

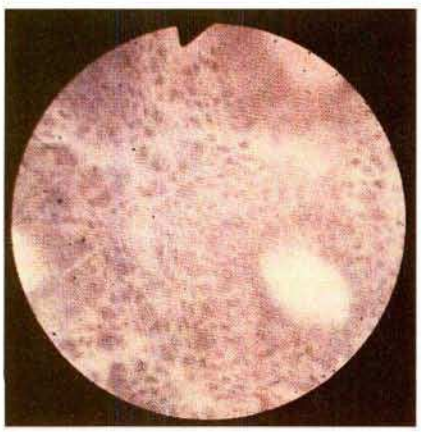


Fig. 1 Normal colonic mucosa at x170 magnification (colonomicroscope – model CF-UHM "Olympus")

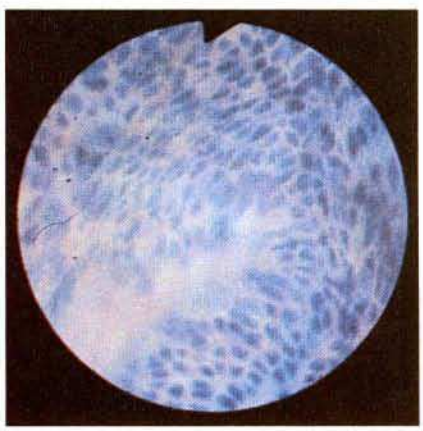


Fig. 3 x170 magnification of a proliferate (colonomicroscope – model CF-UHM "Olympus")

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A study of small polyp-like tumors of the colon (up to 0.6 cm) revealed several types, depending on the intensity of dye absorption:

1) Polyps 0.2–0.5 cm in size that stained more intensely than the surrounding mucosa, appear in endomicroscopy as crypts, whose size is increased 1.5–2.0-fold as compared with normal crypts. Of importance is the increase in the number and staining intensity of colonocytes. A histological investigation has identified these tumors as hyperplastic polyps.

2) Polyps 0.2–0.6 cm in size with a wide base which do not accept the stain, appear at colonoscopy as groups of crypts whose size is increased 3–6-fold as compared with normal. The intercryptal spaces remain virtually unenlarged. Histologically, these neoplasms are usually tubular adenomas.

3) Polyp-like formations whose size does not exceed 0.3 cm that stain less intensely than the surrounding mucosa. Endomicroscopy identifies crypts of small size and round shape with wide intercryptal spaces. A histological investigation identifies such polyp-like formations as hyperplastic lymph follicles.

In addition to polyp-like formations that are well seen in a common endoscopic investigation, there are also lesions in the mucous membrane that do not protrude beyond its surface. They are poorly discernible at usual magnification, since their size does not exceed 0.5 mm. A x35 endomicroscopic investigation identifies them as a group of more intensely stained crypts (Fig. 2). The diameter of these crypts is slightly enhanced. They are distinguished by the great number of intensely stained colonocytes. A x170 magnification permits identification of the varied size and polychromia of the nuclei (Fig. 3). Allowing for these features, such changes have been assessed as proliferates. A histological investigation identifies all these formations as the initial formation stage of hyperplastic polyps.

Another type of rarely detected formations that do not stain, are sections up to 0.4 cm in size that are identified only by staining. Their surface practically does not project beyond the mucous membrane. A histological investigation of these sections identifies groups of crypts with sharply pronounced dysplasia of the glandular epithelium.

Thus, the cited data indicate that sections of hyperplasia of glandular epithelium and the hyperplastic polyps stain intensely irrespective of their size. Tubular and villous adenomas, especially adenomas with pronounced dysplasia of the epithelium do not readily undergo staining. Tumors with a structure of an adenocarcinoma fail to undergo staining. In view of these data, it is hardly expedient to interpret the greater absorption of the dyestuff as indicative of malignancy.

Endomicroscopic investigations permit a sufficiently reliable assessment of the morphological structure of polyps, but the possible identification of the malignant sections of polyps, and even more the degree of invasion into underlying layers, is disputable. This is why it is hardly expedient to use endomicroscopy to this end, all the more so since the data obtained by endomicroscopy are little comparable with the results of histological investigation, owing to the different spatial orientation of the object investigated.

We believe endomicroscopic investigation to be a new trend in microscopy – plane microscopy. This is why the most important task of the given section is the assessment of the microendoscopic changes in various states and the establishment of objective criteria for various diseases, and also their assessment from the point of view of prognosis and the possible development of tumors.

Conclusions

1. A higher absorption of the dyestuff is characteristic of hyperplastic polyps and sections of hyperplasia of the glandular epithelium, irrespective of their size, but higher absorption is far from being a criterion of malignancy.

2. At the given stage of microendoscopic investigation it is hardly advisable to use this research tool to identify malignant sections in polyps, since the endomicroscopic picture is not identical with the data of histological investigation, owing to the different spatial orientation of the object studied when the two methods of investigation are employed.

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