TABLE 18. Predictive value of the morphology of LST of neoplastic lesions for Ca in the submucosa: results of 699 lesions from the Yokohama Hospital during the period April 2001 through July 2007*

			No. lesion (% submucosal)		
	Subtype of LST	Total no.	10-19 mm	20-29 mm	≥30 mm
Granular type	Homogenous	251	0/120 (0)	1/65 (1.5)	0/66 (0)
	Nodular mixed	81	2/16 (12.5)	4/24 (16.7)	13/41 (31.7)
Nongranular type	Elevated	298	13/203 (6.4)	7/67 (10. 4)	8/28 (28.6)
	Pseudodepressed	69	10/36 (27.8)	12/29 (41.4)	4/4 (100)

Ca, Cancer.
*Ca with submucosal invasion occurs rarely in the granular homogenous type and is frequent in the nongranular pseudodepressed type.

TABLE 19. Predictive value of the pit pattern for Ca in the submucosa—exploration conducted in magnification with chromoscopy or NBI: no. Ca with submucosal invasion in relation to pit pattern of 7749 colorectal lesions in the series at the Yokohama Northern Hospital during the period between April 2001 and July 2007*

		No. adenoma		
Pit pattern	No. total	Low-grade IEN	High-grade IEN	No. Ca sm
IIIL	5519	5228	291	0
IIIs	73	56	15	2
IV	1577	1190	343	44
Vi (irregular)	463	109	198	156
VN (amorphous)	117	0	10	107

Ca, Cancer; *IEN*, intraepithelial neoplasia.
*Adenoma is classified in low-grade IEN and high-grade IEN (of the Vienna classification); mucosal Ca is included in high-grade IEN; high-grade adenoma includes intramucosal Ca. Most adenomas show a pit pattern type III or IV, most Ca show a pit pattern type V.

These criteria[57] include a persisting serrated growth pattern, pools of mucin, cytoplasmic eosinophilia, and an absence of necrosis.[57] Serrated adenocarcinoma accounts for about 7.5% of all colorectal cancers and up to 17.5% of the most proximal cancers.[57] The proportion of serrated cancer is higher in the proximal portion of the colon and lower in the rectum.

MAGNIFYING ENDOSCOPY IN MALIGNANT NONPOLYPOID LESIONS WITH SUBMUCOSAL INVASION

Evaluation of submucosal invasion from the superficial pit pattern

The pit pattern of the colonic mucosa can be assessed by using magnifying endoscopy in conjunction with chromoscopy or NBI. The studies conducted by various endoscopy groups in Japan, with histologic controls, confirmed that some categories of the pit pattern are predictive of cancer extension into the submucosa. In 7740 neoplastic colorectal lesions analyzed at the Northern Yokohama Hospital (Table 19), submucosal cancer was confirmed by histology in 33.7% of lesions that showed a category V "irregular" pit pattern and in 91% of the lesions that showed an "amorphous" category V pit pattern, whereas the proportion in lesions that showed pit patterns III or IV was extremely low (0.64%). Furthermore, the "irregular" or "amorphous" subtypes of the pit pattern in category V showed a predictive value for the slight or massive invasion in the submucosa, as shown in Table 20. The slight or massive submucosal invasion is classified in reference to 3 successive levels (sm1, sm2, and sm3) in vertical extension and to 3 successive degrees of transversal extension of the cancer, estimated just below the level of the muscularis mucosae (sm1a, sm1b, and sm1c). Slight invasion of submucosa corresponds to sm1a or sm1b. Massive invasion corresponds to sm1c, sm2, and sm3. The pit pattern V "amorphous" always corresponds to a massive invasion of the submucosa in the experience at the Northern Yokohama Hospital.

Evaluation of submucosal invasion from the superficial vascular pattern

The vascular pattern of the colonic mucosa can be assessed by using magnifying endoscopy with NBI and has a predictive value for the detection of cancer. The vascular pattern at the surface of 843 superficial neoplastic lesions of the colon was analyzed in the endoscopy unit at the Yokohama Northern Hospital. The "irregular" or "sparse" patterns were found in only 1 of 639 adenomas or serrated adenomas, in 22 of 133 intramucosal cancers, and in 59 of 71 cancers with submucosal invasion (Table 21). The reliability of the vascular pattern in predicting the depth of invasion of the submucosa was explored by the same group during the period from January 2006 to September 2007 (S. Kudo, H. Kashida, unpublished observations, 2008)

TABLE 20. Predictive value of the pit pattern for the depth of submucosal invasion in superficial Ca: depth of invasion in 178 colorectal lesions that showed a surface pit pattern Vi or VN in the series from the Akita and Yokohama Northern Hospitals during the period April 1992 through July 2007

		Ca with submucosal invasion	
Pit pattern V	Total no.	Slight	Massive*
Pattern type Vi irregular histology (low-grade IEN)†	35	29	6 (17%)
Pattern type Vi irregular histology (high-grade IEN)†	80	12	68 (85%)
Pattern type VN (amorphous)	63	0	63 (100%)

Ca, Cancer; *IEN,* intraepithelial neoplasia.
*Massive invasion shows either a pit pattern VN or Vi.
†Pit pattern type Vi is highly suggestive of a superficial invasion of the submucosa.

TABLE 21. Predictive value of the vascular pattern for Ca in the submucosa, with exploration conducted in magnification with NBI: distribution of the categories of vascular pattern in relation to histology of 843 lesions in the series of the Yokohama Northern Hospital, in the period January 2006 through September 2007

		No. carcinoma	
Vascular pattern	No. adenoma + adenoma serrated	Intramucosal	Submucosal invasion
Faint	15	0	0
Network*	484	60	7
Dense	139	51	5
Irregular†	1	17	27
Sparse†	0	5	32
Total	639	133	71

*Suggests adenoma.
†Suggests carcinoma with submucosal invasion.

in 204 superficial neoplastic lesions with histologic controls. The invasion was classified as slight or massive, with the criteria already used for the evaluation of the pit pattern. The patterns "network" or "dense" were observed in 123 lesions, of which 120 had a slight invasion of the submucosa and 3 had massive invasion. The patterns "irregular" or "sparse" were observed in 81 lesions, of which 28 had slight invasion and 53 had massive invasion. The sensitivity and specificity of "irregular + sparse" patterns for massive submucosal invasion were 94.6% and 81.1%, respectively. It was concluded that the pit pattern has a high predictive value for a massive invasion of the submucosa.

PROTECTION AFFORDED BY COLONOSCOPY AGAINST COLORECTAL CANCER

The role of colonoscopy in the prevention of colorectal cancer depends on its double function: first, in the diagnosis of cancer at an early curable stage and for the diagnosis of the precursors of cancer—this occurs in opportunistic screening of asymptomatic patients and in organized screening after a positive fecal occult blood test; second, as a therapeutic procedure that allows the endoscopic resection of precursors of cancer and of superficial cancers without massive invasion of the submucosa. The degree of protection afforded by colonoscopy can be explored in patients in whom the initial colonoscopy was negative or in patients in whom the index procedure detected and removed neoplastic lesions. This raises the question of the interval to be proposed for surveillance colonoscopy.

Protection after a negative colonoscopy

Evaluation of the miss rate in back-to-back colonoscopy. Neoplastic lesions detected a few years after a negative colonoscopy may result from a missed diagnosis, ie, false negative for neoplasia. The magnitude of such a miss rate has been determined in Western countries when a second procedure is performed on the same day (back-to-back colonoscopy) by another observer. In a demonstrative study conducted by Rex et al[140] in the United States, the tandem procedure detected adenomas in 24% of 183 patients who had a negative colonoscopy at the initial procedure. The rate varied with the size of the missed adenomas and the figures were 27% for adenomas up to 5 mm, 13% for adenomas between 6 and 9 mm, and 6% for adenomas 10 mm or larger. One may think that this proportion should decrease with the use of recent high-resolution endoscopes. However, in a recent study of back-to-back colonoscopies in 286 patients conducted in France by Heresbach et al,[141] the global miss rate was still high (20%), with proportions of 26% for adenomas up to 5 mm and 9% for adenomas larger than 5 mm. Regardless, when the colorectal mucosa was systematically scrutinized with a high-resolution colonoscope, the prevalence of diminutive adenomas was so high (in the range of 30% to 50%) that some degree of miss rate was unavoidable.

Neoplastic lesions found after a negative colonoscopy. Despite the absence of neoplastic lesions at the initial colonoscopy, benign or malignant metachronous neoplastic lesions can develop in the interval before a second procedure. Interval neoplasia results either from an

TABLE 22. Risk of finding neoplastic lesions in the years after a negative colonoscopy: a retrospective case-control study conducted in patients affiliated with the Medicaid Program for California and having continuous eligibility since at least 60 months preceding the index examination*

	No. cases (Ca)	No. controls (no Ca)	RR†
All Ca; both sexes			
Had no screening	3746	37,155	1.00
Had negative colonoscopy‡	151	2426	0.55
Had negative sigmoidoscopy‡	68	750	0.82
All Ca, men			
Had no screening	1448	14,209	1.00
Had negative colonoscopy	33	837	0.35
All Ca, women			
Had no screening	2298	22,946	1.00
Had negative colonoscopy	118	1589	0.66
Right-sided Ca, men			
Had no screening	442	3802	1.00
Had negative colonoscopy	11	228	0.38
Right-sided Ca, women			
Had no screening	861	7796	1.00
Had negative colonoscopy	50	523	0.81

Ca, Cancer; *RR*, relative risk; *Right-sided Ca*, cancer in the proximal colon.
*Colorectal Ca detected up to 5 years after a negative colonoscopy or sigmoidoscopy in a retrospective case-control study conducted in patients affiliated to the Medicaid Program for California and having continuous eligibility since at least 60 months preceding index (G. Triadafilopoulos, unpublished data, 2008).
†Estimation of the RR after a negative procedure.
‡Colonoscopy offers better protection against Ca than sigmoidoscopy but is less effective in prevention in women than in men; the difference is because of poor effectiveness in prevention of right-sided cancer.

initial miss rate or from the development of metachronous evolutive lesions. Interval cancer found shortly after a complete colonoscopy is often a metachronous tumor with rapid growth rather than a lesion missed at the first examination. This particularly applies to flat and depressed nonpolypoid lesions, which are often classified as de novo cancers. The proportion of MIS-positive tumors was analyzed by Sawhney et al[142] in 51 patients, with interval cancers that occurred within 5 years after a colonoscopy and in 112 noninterval colorectal cancers, and a 3.7-fold higher frequency of MIS-positive tumors occurred in the group of interval cancers. Many studies on interval cancers have been conducted in the United States. Squillace et al[143] examined 29 patients after an average interval of 5.7 years of a negative colonoscopy: adenomas were detected in 12 (41.4%). Neugut et al[144] repeated colonoscopy in 99 patients after an average interval of 3 years after the negative first procedure and detected adenomas in 24 patients (24%). Rex et al[145] examined 154 patients after an average interval of 5.5 years after the negative colonoscopy and found adenomas in 41 patients (27%). The Lilly multicenter study (D. Ransohoff, unpublished data, 2008), with 1256 subjects evaluated after an average interval of 5.3 years after a negative colonoscopy, detected adenomas in 201 (16%) and advanced neoplasia in 16 subjects (1.2%).

Evaluation of neoplasia protection after a negative colonoscopy. Despite its limitations, a negative colonoscopy offers an appreciable protection against the risk of developing colorectal cancer.[146] The degree of protection was assessed in a large retrospective case-control study conducted in the United States by using the California MediCal database (Table 22). The occurrence of a negative colonoscopy or sigmoidoscopy in the recent years was explored in patients with (cases) or without cancer (controls). It was concluded that colonoscopy offers better protection than sigmoidoscopy and that such protection was more effective in men than in women, the latter difference being a consequence of a less efficient assessment of the proximal portion of the colon in women. In Japan, the protection afforded against incident neoplastic lesions by a negative colonoscopy was assessed in a retrospective cohort study conducted by 6 distinct centers: the relative risk of finding a incident lesion was very low at 1 year (0.1) and higher at 3 years (0.8) (Table 23).

Neoplasia protection after a colonoscopy with polypectomy. Neoplastic lesions of the colorectal mucosa detected a few years after a colonoscopy with complete resection of all superficial neoplastic lesions may result from 3 possible scenarios: (1) the lesions were missed at the first procedure, (2) new lesions developed during the interval, and (3) lesions were incompletely treated during the first procedure. The proportion of neoplastic lesions detected during the second procedure was explored in Western countries[147-153] and, as shown in Table 24, this figure varies between 32% and 60%. In the United States, the National Polyp Study showed that the percentage of patients with incident adenomas 3 years after the inclusion colonoscopy was 32.0%.[152] In Denmark, in the Funen adenoma follow-up study, the figure was 35% after 4 years, and 60.1% after 8 years.[153] A lower proportion occurs when counting is restricted to metachronous lesions with advanced neoplasia.

The detection of lesions upon surveillance colonoscopy confirms a persistent increased risk in patients with positive findings at the first procedure; however, the risk of recurrence is modulated in relation to the initial findings. In the United States, in the Veterans Affairs cooperative study (Table 25), which was conducted in 13 distinct centers, the relative risk for interval lesions

TABLE 23. Relative risk of recurrent neoplasia in relation to findings at first colonoscopy: retrospective cohort study from the Japan Polyp Study Working Group

Colonoscopy at inclusion	No. cases	No. index lesions detected after follow-up of mean 5.1 y†	Relative risk for finding a index lesion‡ At 1 y	At 3 y
Negative	2006	52	0.1	0.8
Adenoma, up to 5 mm	1655	111	1.0	2.9
Adenoma, more than 5 mm	1123	150	2.5	5.4
Intramucosal cancer	525	66	2.9	5.7

*From the Retrospective Cohort Study from the Japan Polyp Study Working group (T. Matsuda, unpublished data, 2008).
†Index (recurrent) lesions detected during follow-up (mean 5.1 y) after colonoscopy were defined as adenoma > 10 mm, intramucosal cancer, invasive cancer (submucosa or deeper); after 5 years, the number of index lesions was higher after polypectomy than after a negative colonoscopy and increased with the severity of initial findings.
‡In relation to the relative risk of finding an index lesion, colonoscopy should be performed after 3 years for patients without polyps or with polyps <5 mm and after 1 year for patients with large polyps or intramucosal cancer.

detected after a negative colonoscopy varied in relation to the increased severity of the index lesions, from 1.92 to 13.56. A similar study has been conducted in 6 centers by the Japan Polyp Working Group (Table 23). The relative risk of recurrent lesions, compared with patients who had a negative colonoscopy at inclusion, varied at 3 years, from 0.8 to 5.7, according to the severity of the index lesions.

STRATEGY OF ENDOSCOPIC DIAGNOSIS

Superficial neoplastic lesions of the colorectal mucosa were first described by using rigid rectosigmoidoscopes, then with fiber-colonoscopes. Since then, there has been a considerable technical evolution, and the most recent electronic video colonoscopes offer high resolution, magnification, and image processing, including the NBI technique. Because of this, the proportion of patients with abnormal findings at colonoscopy is higher than in previous reports; yet seeing more does not mean more clinically relevant abnormalities. High-resolution endoscopy is not a substitute to the careful exploration of the mucosa during endoscopy and expert discriminative analysis.

The 4-steps strategy

Good practice in endoscopic diagnosis requires a step-by-step methodology as the only protection against overdetection and overtreatment.[154]

1. A complete intestinal preparation is an essential first step, because any solid and liquid matter that persists at the surface of the mucosa can mask small nonpolypoid lesions.
2. Detection of an abnormal area is the second step that is performed in a standard visualization, without image processing or chromoscopy. Here, nonpolypoid lesions may easily be missed if the operator lacks the cognitive training to detect a slight change in the color of the mucosa and the deviation of the subepithelial capillaries at the demarcation.
3. Characterization of the lesion is the third step. The routine practice of chromoscopy with indigo carmine (0.1%-0.5% solution) is required to assess the lesion margins and identify elevations or depressions of the lesion's surface. The morphology of the lesion is then identified according to the categories of the Paris classification. Chromoscopy with cresyl violet (0.2% solution) or crystal violet (0.05% solution), achieves a more durable staining, but the use of these stains is reserved for very small areas observed in magnification. The microarchitecture of the epithelial surface is then explored in magnification combined either with chromoscopy or with NBI, and the categories of the pit pattern bring forth a predictive value for histology. The microvascular network is also explored in "transparency," without chromoscopy and with some magnification. NBI is now the criterion standard technique for the classification of the capillary pattern in nonneoplastic and neoplastic lesions.
4. The fourth step is classification and treatment decision and takes into account the lesion's morphology and

TABLE 24. Interval cancer in the years after polypectomy: proportion of recurrent neoplastic lesions found in the endoscopic surveillance after a colonoscopy with complete resection of the index lesions*

Investigator/country	Study	No. patients	Interval (years of follow-up)	% Patients with neoplasia	% Patients with advanced neoplasia†
Winawer et al,[152] U.S.	Surveillance National Polyp Study	766	3	32	3.3
Jørgensen et al,[153] Denmark	Surveillance Funen trial	1056 at inclusion	4	35.5	8.6
Alberts et al,[147] U.S.	Controls of fiber trial	584	3	51.2	31.4
Schatzkin et al,[151] U.S.	Controls of celecoxib trial	947	4	39.5	7
Arber et al,[148] Israel	Controls of fiber trial	557	3	49.3	10.4
Baron et al,[150] U.S.	Controls of rofecoxib trial	1218	3	55	17.4
Bertagnolli et al,[149] U.S.	Controls of celecoxib trial	613	3	60.7	17.2

*Recurrent lesions result either from incomplete polypectomy, from missed detection during the first procedure, or from fast-developing incident lesions.
†Advanced neoplasia, defined as tubular adenoma, at least 10-mm villous adenoma, high-grade atypia, or Ca.

TABLE 25. Relative risk of recurrent neoplasia in relation to findings at first colonoscopy: estimation of the relative risk of finding an advanced neoplasia during a 5-year surveillance after screening colonoscopy in relation to the baseline findings*

Baseline finding at colonoscopy	Advanced neoplasia, no. (%)†	Relative risk
No neoplasia (n = 298)	7 (2.4)	1.00
Neoplasia (n = 895)		
Tubular adenoma: 1 or 2, less 10 mm	23 (4.6)	1.92
Tubular adenoma: 3 and more, less 10 mm	15 (11.9)	5.01
Tubular adenoma: over 10 mm	19 (15.5)	6.40
Villous adenoma	13 (16.1)	6.05
Adenoma with high-grade atypia	8 (17.4)	6.87
Cancer	8 (34.8)	13.56

*Results of the Veterans Affairs Cooperative Study no. 380 (D. Lieberman, unpublished data, 2008) in 2007. There is a strong association between the occurrence of advanced neoplasia and the results of the baseline screening colonoscopy.
†Advanced neoplasia is defined as tubular adenoma at least 10-mm, villous adenoma, adenoma with high-grade atypia or cancer.

location. The treatment decision offers the choice between abstention, endoscopic resection, or surgery. The en bloc endoscopic resection of nonpolypoid lesions may require the complex technique of endoscopic submucosal dissection.

A pragmatic choice for treatment

1. Superficial lesions in the proximal portion of the colon are often more advanced or evolutive than those in the distal portion of the colon; most small HP lesions are nonneoplastic; large HP lesions in the proximal portion of the colon often host high-grade neoplasia.
2. Large polypoid or nonpolypoid lesions are more at risk of malignancy; most small lesions that show a 0-IIa or 0-IIb morphology host low-grade neoplasia; lesions that show a 0-IIc depressed morphology often host high-grade neoplasia with frequent submucosal invasion.

Quality control in colonoscopy

Major requirements in quality control include the use of a new-generation high-resolution video colonoscope, the routine application of chromoscopy with indigo carmine as a first step in the characterization of each lesion that, in turn, should be attributed to a subtype according to the Paris classification. This subtyping must be mentioned in the endoscopy report (as well as in the pathology report if the lesion is resected). When there is a suspicion of high-grade neoplasia, magnifying endoscopy, combined with image processing, has the capacity to evaluate, with more precision, the severity of neoplasia and its possible invasion of the submucosa.

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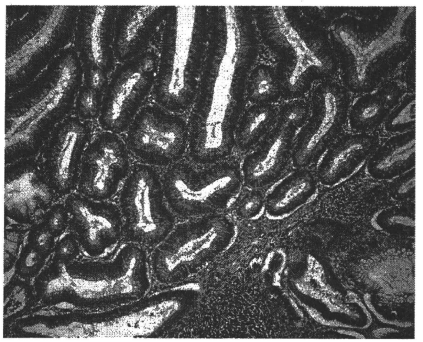
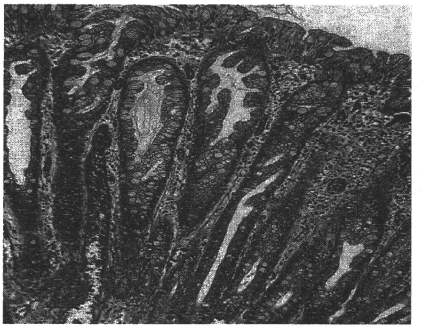
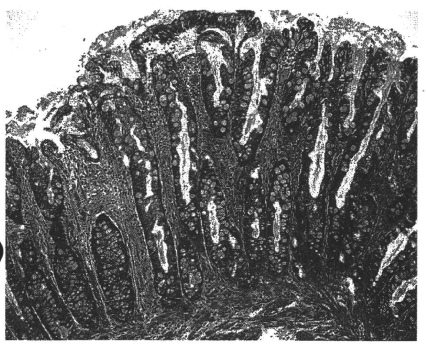
IMAGE ATLAS



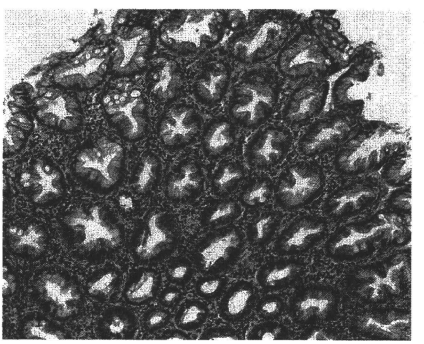
A1. Histopathology of tubular adenoma. Hyperchromatic palisading elongated nuclei in highly prismatic columnar epithelium (H&E, orig. mag. × 100).



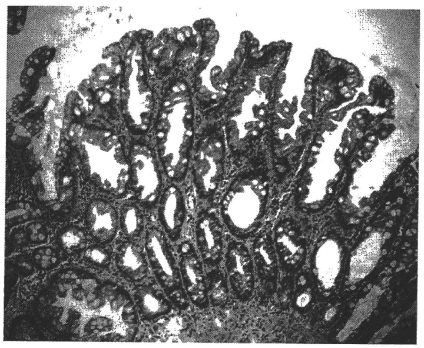
A3. Histopathology of HP lesion. Serration in upper half of crypts (H&E, orig. mag. × 150).



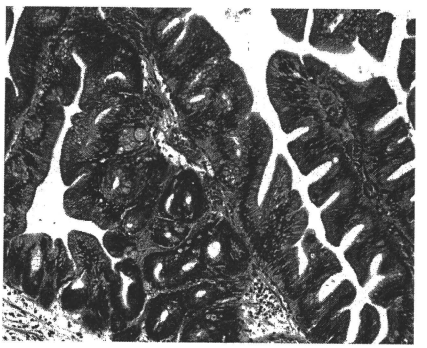
A2. Histopathology of HP lesion. Serration in upper half of crypts. Normal proliferation in basal half: small, regular, basal orientated nuclei (H&E, orig. mag. × 100).



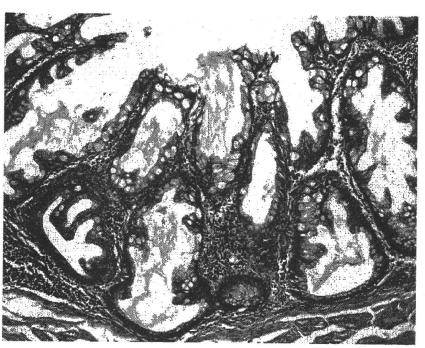
A4. Histopathology of HP lesion. Transverse section of the serrated crypts (H&E, orig. mag. × 100).



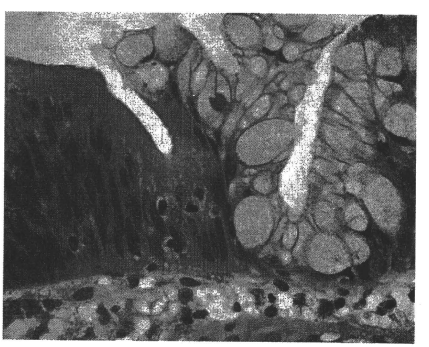
A5. Histopathology of sessile serrated lesion. Dilated crypts in basal area. No cell atypia (H&E, orig. mag. × 100).



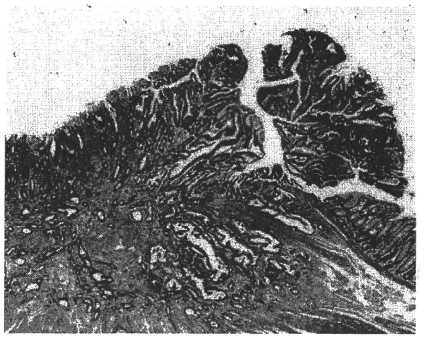
A7. Histopathology of serrated adenoma. Intraepithelial microacini in upper half. Low-grade intraepithelial neoplasia, eosinophilic cytoplasm, elongated nuclei (H&E, orig. mag. × 150).



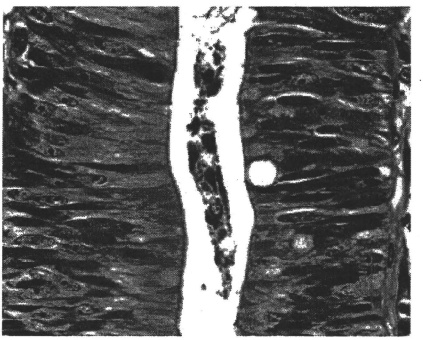
A6. Histopathology of sessile serrated lesion. Proliferation, architectural distortion: serration in basal half of crypts, enlarged with horizontal growth; abundant mucus (H&E, orig. mag. × 120).



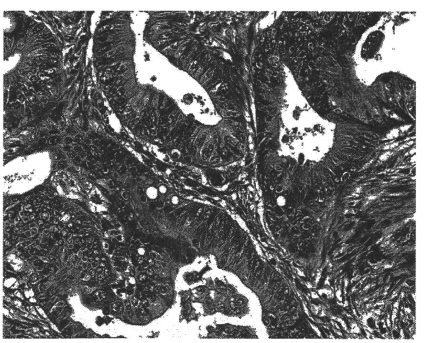
A8. Histopathology of mixed polyp: adenoma (*left*), with elongated hyperchromatic nuclei; sessile hyperplastic polyp with goblet cells (*right*) (H&E, orig. mag. × 300).



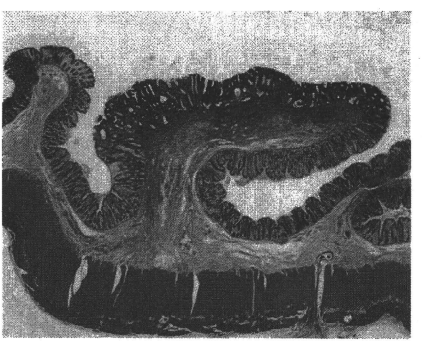
A9. Histopathology of neoplastic lesion, 8 mm, 0-IIa, panoramic view (H&E, orig. mag. × 50).



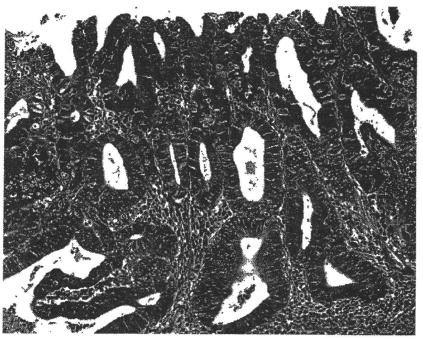
A11. Histopathology of neoplastic lesion, low-grade cell atypia, well-differentiated intramucosal adenocarcinoma; hyperchromatic elongated nuclei in basal arrangement (H&E, orig. mag. × 300).



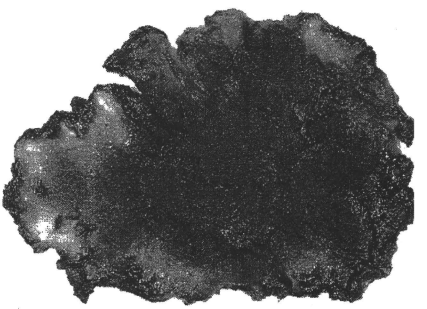
A10. Same case as in image no. 9. Low-grade cell atypia, well-differentiated adenocarcinoma, no residual adenoma; submucosal invasion (H&E, orig. mag. × 150).



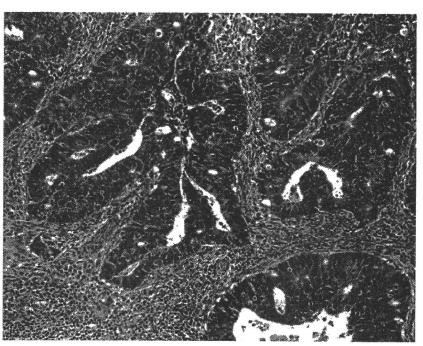
A12. Histopathology of neoplastic lesion, 7 mm, 0-IIa, panoramic view (H&E, orig. mag. × 40).



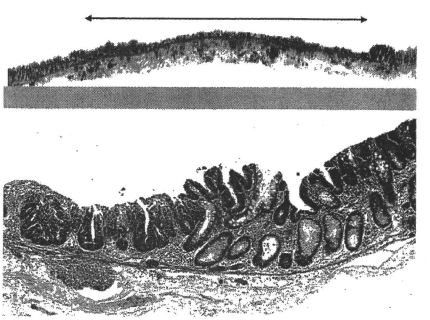
A13. Same case as in image no. 12. High-grade cell atypia, well-differentiated intramucosal adenocarcinoma, no residual adenoma; nuclei up to apical pole of cells (H&E, orig. mag. × 100).



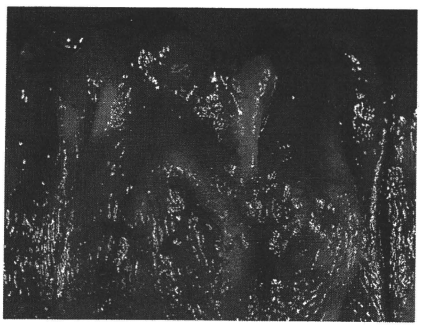
A15. Operative specimen after fixation, mucosectomy; neoplastic lesion 20 mm, 0-IIc.



A14. Histopathology of neoplastic lesion, 5 mm, 0-IIa + 0-IIc; high-grade cell atypia, well-differentiated adenocarcinoma, submucosal invasion; no residual adenoma; nuclei up to apical pole of cells (H&E, orig. mag. × 150).

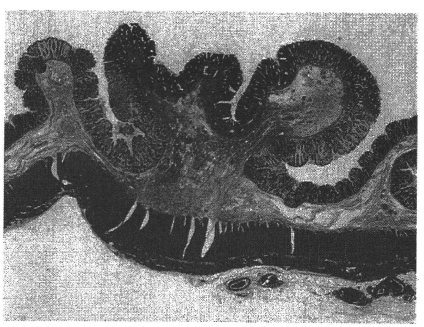


A16. Same case as in image no. 15. Panoramic view, showing a large flat depression (*upper*) (H&E, orig. mag. × 20); well-differentiated intramucosal adenocarcinoma, no residual adenoma (*lower*) (H&E, orig. mag. × 50).

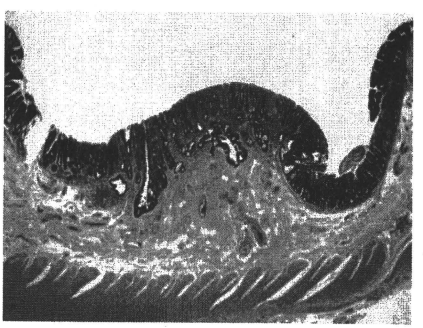


A17. Operative specimen, fresh, neoplastic lesion 7 mm, 0-IIc.

A19. Operative specimen after fixation. Neoplastic lesion, 20 mm, 0-IIc, deep mucosal depression, fold convergence suggestive of invasive cancer.

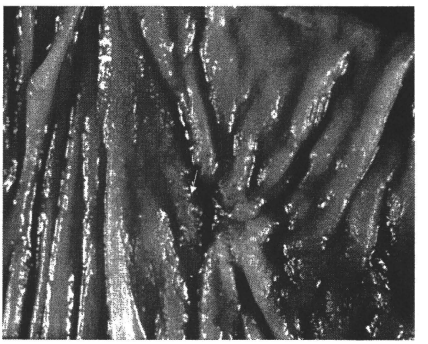


A18. Same case as in image no. 17. Well-differentiated intramucosal adenocarcinoma, no residual adenoma (H&E, orig. mag. × 40).

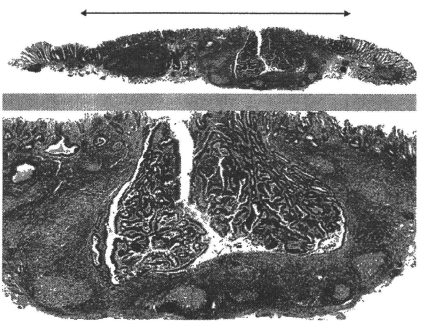


A20. Same case as in image no. 19. Well-differentiated adenocarcinoma, submucosal invasion, no residual adenoma (H&E, orig. mag. × 60).

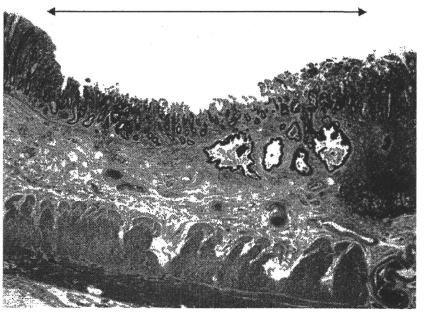
A21. Operative specimen after fixation, mucosectomy, neoplastic lesion, 20 × 13 mm, 0-IIc.



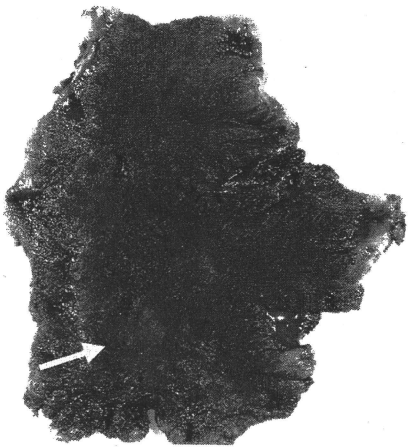
A23. Operative specimen after fixation, neoplastic lesion, 8 mm, 0-IIc, deep depression; convergence of fold suggestive of invasive cancer.



A22. Same case as in image no. 21. Panoramic view, central elevation in a shallow depression (*upper*) (H&E, orig. mag. × 20); well-differentiated adenocarcinoma, submucosal invasion, 1500 μm in depth, no residual adenoma (*lower*) (H&E, orig. mag. × 50).

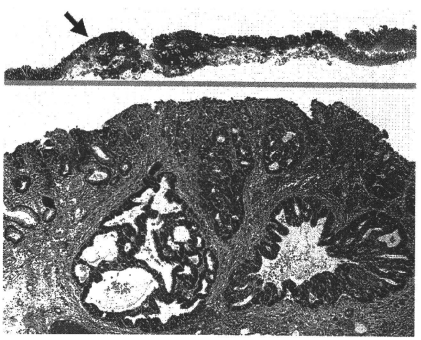


A24. Same case as in image no. 23. Well-differentiated adenocarcinoma, submucosal invasion at the level of the depression, no residual adenoma (H&E, orig. mag. × 60).

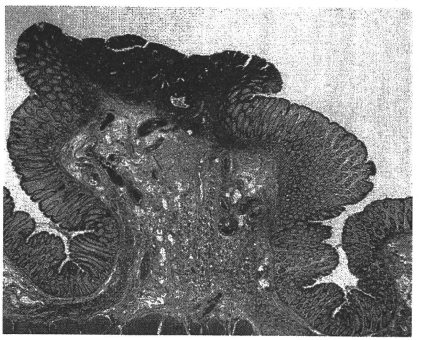


A25. Operative specimen after fixation, mucosectomy, neoplastic lesion, 39 × 33 mm, 0-IIc + IIa, depressed area with a small elevated nodule (*arrow*).

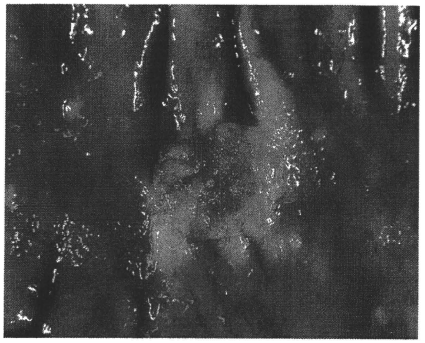
A27. Operative specimen after fixation, neoplastic lesion 5 mm, 0-IIa + IIc.



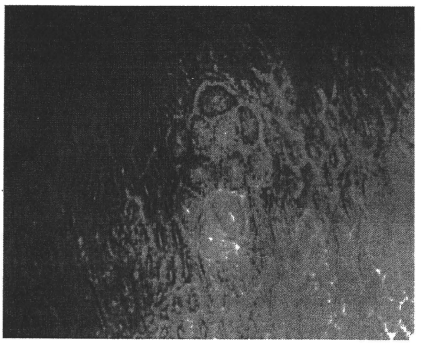
A26. Same case as in image no. 25. Panoramic view of lesion (*upper*) (H&E, orig. mag. × 20); moderately differentiated adenocarcinoma, submucosal invasion, no residual adenoma (*lower*) (H&E, orig. mag. × 50).



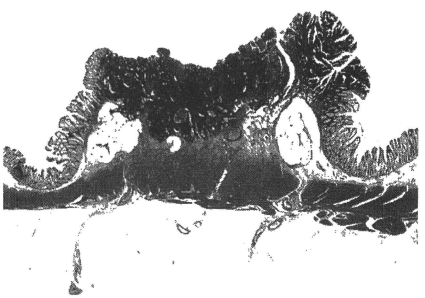
A28. Same case as in image no. 27. Panoramic view of depressed surface of the lesion; well-differentiated adenocarcinoma, submucosal invasion, no residual adenoma (H&E, orig. mag. × 60).



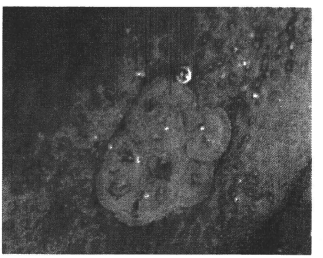
A29. Operative specimen, fresh, neoplastic lesion, 13 mm, 0-IIa + IIc, slightly elevated tumor, with irregular central depression.



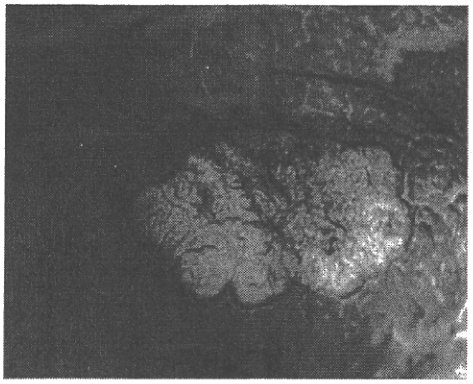
A31. Endoscopy (magnification ×100), chromoscopy with methylene blue 0.01%; ACF nonneoplastic in the rectum; cluster of enlarged crypts.



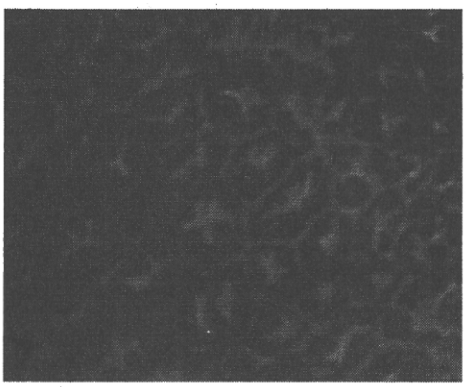
A30. Same case as in image no. 29. Moderately differentiated advanced adenocarcinoma, massive submucosal invasion that involved muscularis propria, no residual adenoma (H&E, orig. mag. × 40).



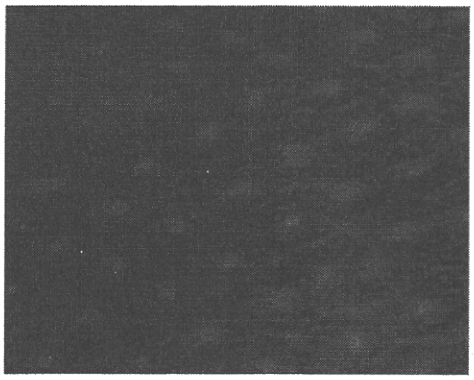
A32. Endoscopy (magnification ×100) and NBI; ACF, nonneoplastic; cluster of enlarged crypts; no pericryptic vascular change.



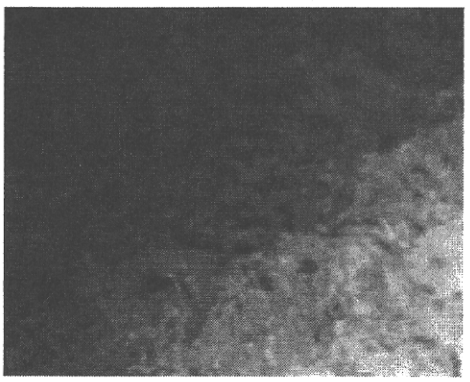
A33. Endoscopy (magnification ×100), chromoscopy with methylene blue 0.01%; ACF, neoplastic; cluster of enlarged, disordered crypts.



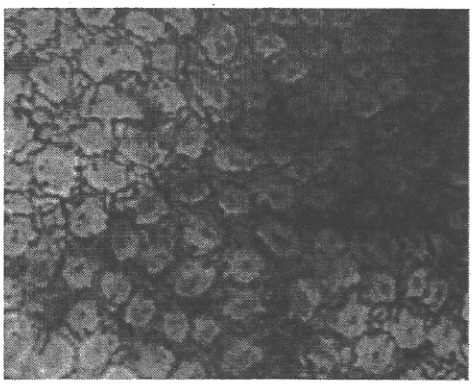
A36. Endoscopy (magnification), chromoscopy with cresyl violet; HP lesion; pit pattern II, star-like crypt openings.



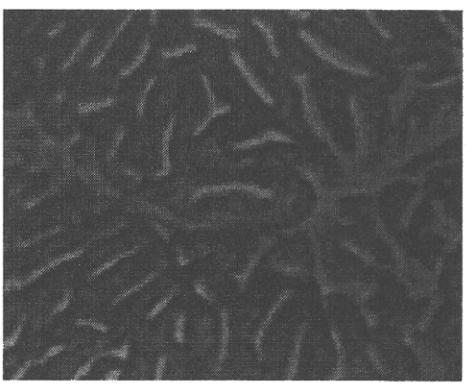
A34. Endoscopy (magnification), chromoscopy with cresyl violet; normal colonic mucosa. Pit pattern I.



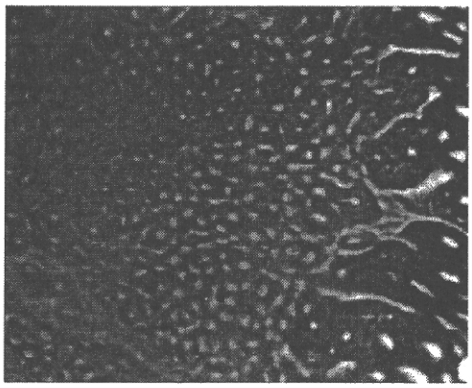
A37. Endoscopy (magnification), NBI; HP lesion; vascular pattern "faint."



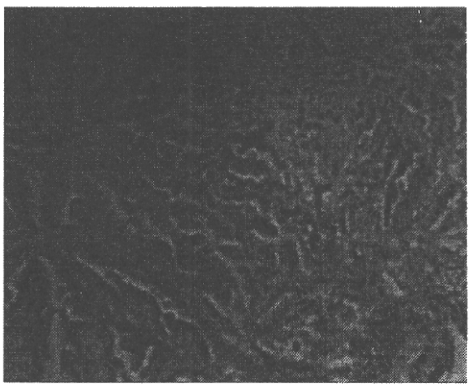
A35. Endoscopy(magnification), NBI; normal colonic mucosa; vascular pattern "normal."



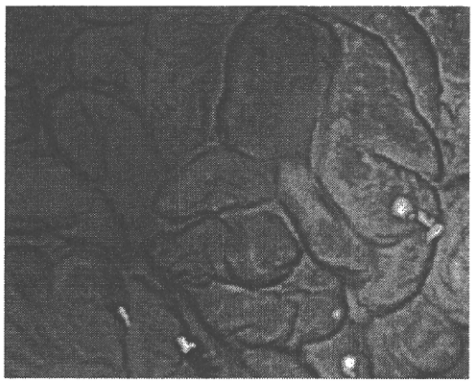
A38. Endoscopy (magnification), chromoscopy with cresyl violet, neoplastic lesion, premalignant; pit pattern IIIL, large crests.



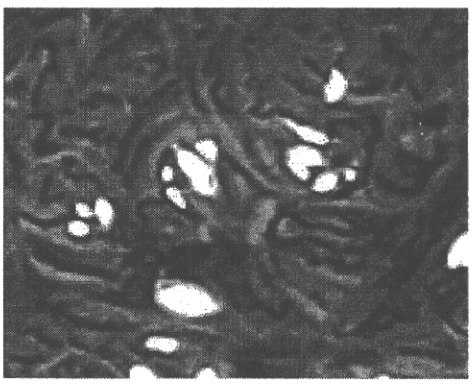
A39. Endoscopy (magnification), chromoscopy with cresyl violet; neoplastic lesion, premalignant; pit pattern IIIS, narrow crypt openings.



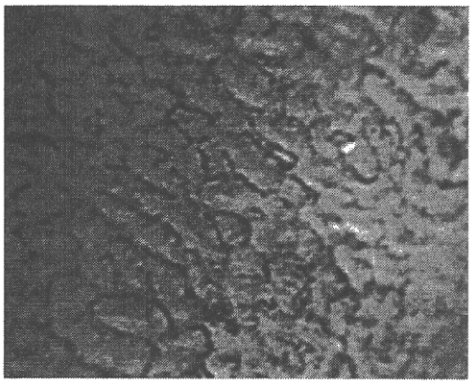
A42. Endoscopy (magnification), chromoscopy with cresyl violet carcinoma; pit pattern Vi, irregular.



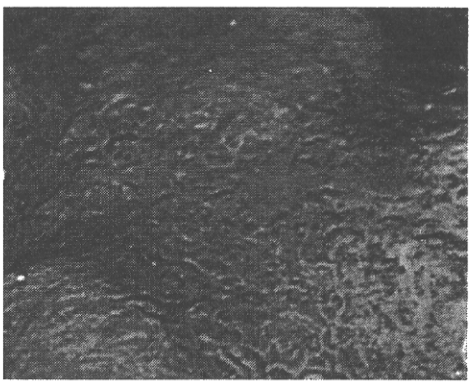
A40. Endoscopy (magnification), chromoscopy with cresyl violet, neoplastic lesion, premalignant; pit pattern IV, branched crests.



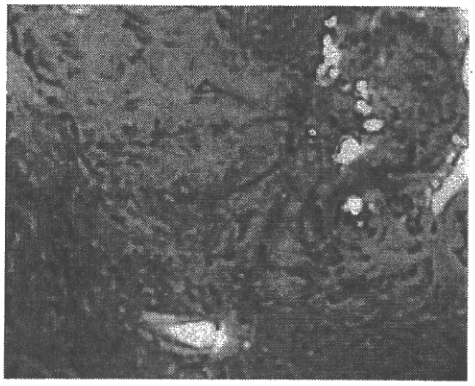
A43. Endoscopy (magnification), NBI; carcinoma; vascular pattern "irregular."



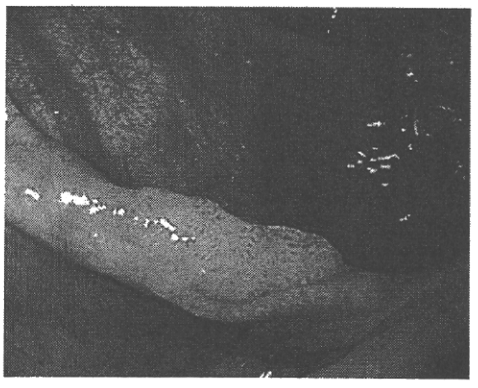
A41. Endoscopy (magnification), NBI; neoplastic lesion, premalignant; vascular pattern "network."



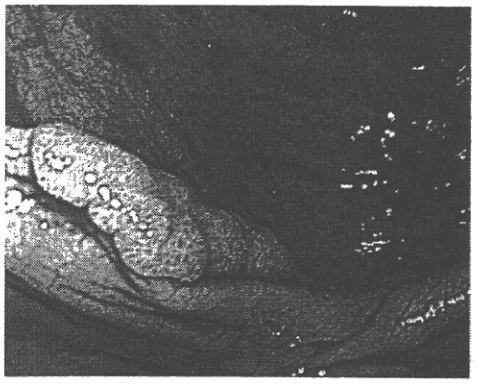
A44. Endoscopy (magnification), chromoscopy with cresyl violet; carcinoma; pit pattern VN, nonstructural.



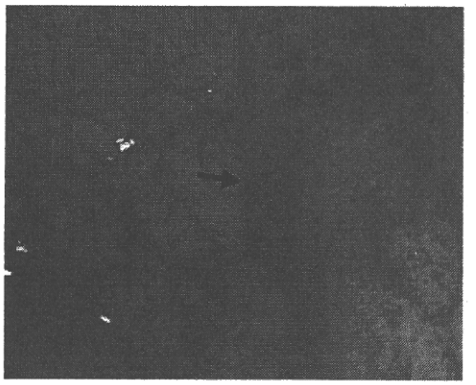
A45. Endoscopy (magnification), NBI; carcinoma; vascular pattern "sparse."



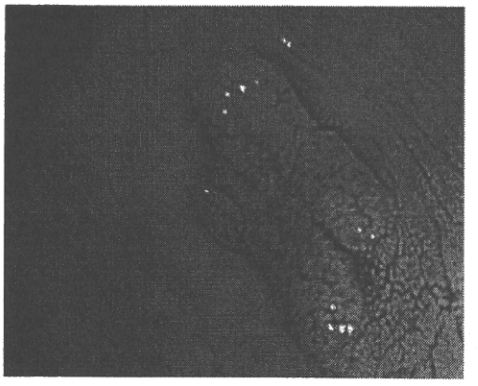
A46. Endoscopy, slightly elevated neoplastic lesion, 0-IIa.



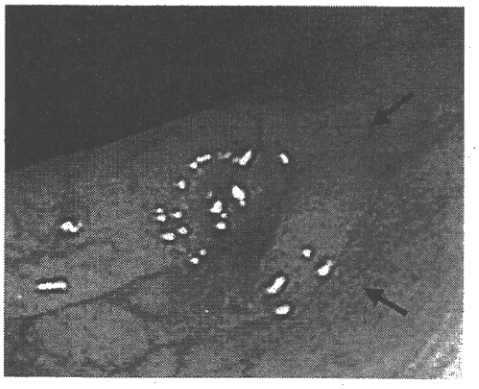
A47. Same case as in image no. 46, chromoscopy with indigo carmine.



A48. Endoscopy, slightly elevated neoplastic lesion (*arrow*), 0-IIa.



A49. Same case as in image no. 48, chromoscopy with indigo carmine.



A50. Endoscopy, depressed neoplastic lesion (*arrows*), 0-IIc.