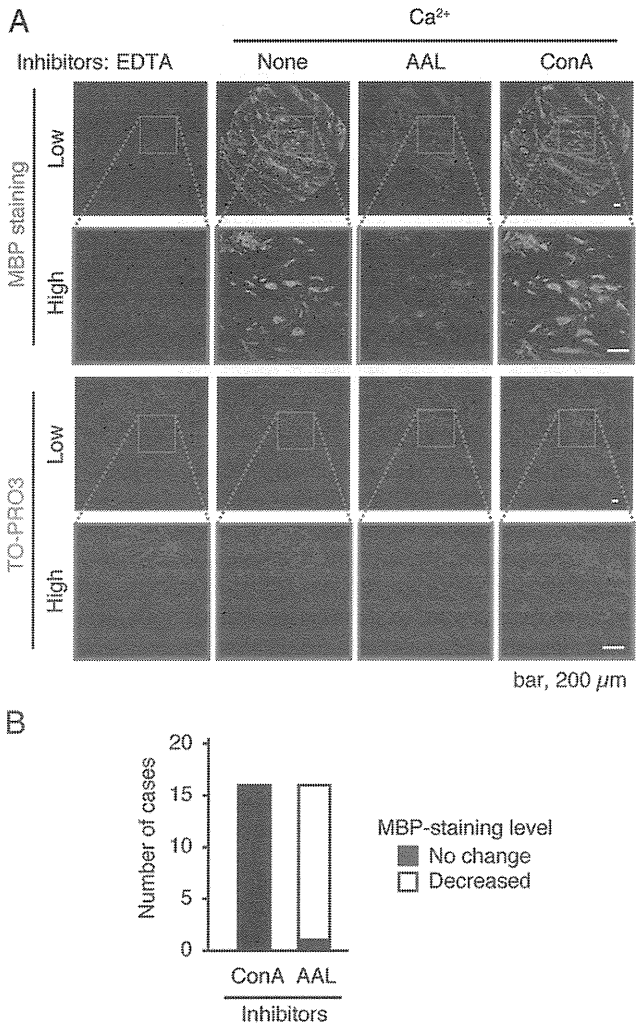

FIGURE 3. MBP recognizes fucose residues expressed on colorectal carcinoma cells. (**A**) Competitive-staining assay with plant lectins. MBP staining with the indicated inhibitor—EDTA, None, AAL, or Con A—was performed in the presence of 5 mM EDTA, 5 mM $CaCl_2$ only, 5 mM $CaCl_2$ plus 100 μM AAL, or 5 mM $CaCl_2$ plus 100 μM Con A, respectively. An MBP-staining image (green) is shown at low magnification (*top row*) and high magnification (*second row*). (**B**) Comparison of the numbers of cases in which the MBP-staining level decreased between Con A–treated and AAL-treated tissues.

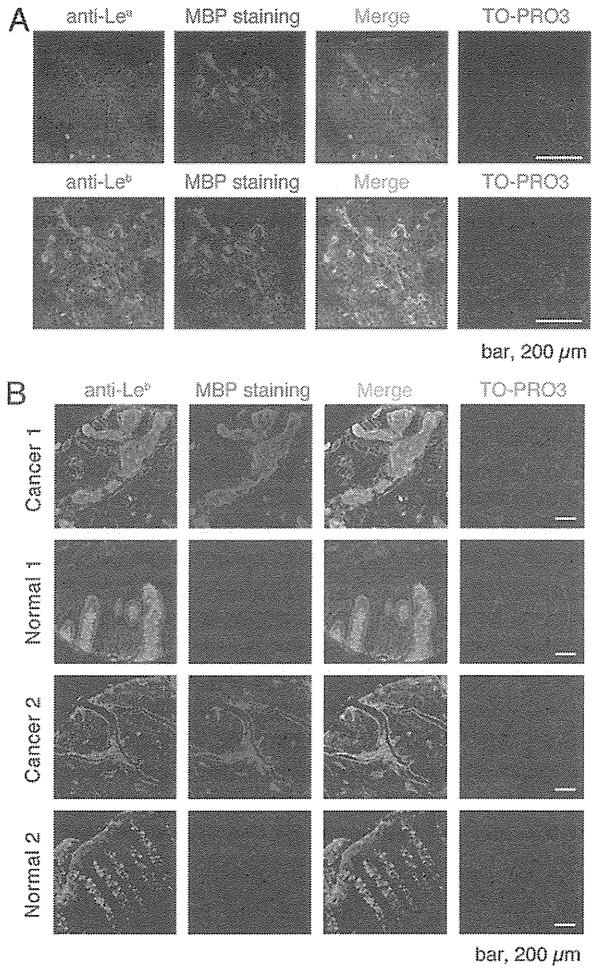

FIGURE 4. MBP recognizes tumor-derived Le^b glycans in colorectal carcinoma cells. (**A**) Double-stained MBP (red) and Le^a/Le^b glycans (green) in colorectal carcinoma tissues. MBP staining was performed in the presence of anti-Le^a mAb or anti-Le^b mAb, as described in *Materials and Methods*. The images were obtained with a confocal laser microscope. (**B**) MBP ligands (red) and Le^b (green) in cancer and noncancerous tissues. Double staining with MBP and anti-Le^b Abs was conducted for the cancer tissue and adjacent noncancerous tissue derived from the same patients. The images were obtained with a confocal laser microscope.

proposed structure of the MBP ligands isolated from SW1116 cells) (15, 26, 27).

MBP ligands are expressed in patients with CA19-9$^-$ colorectal carcinomas

MBP binds preferably to α1,2-fucosylated Le^a epitopes (Le^b tetrasaccharide epitope), but the binding is largely abolished when the terminal fucose residue of a Le^b epitope is replaced by α2,3-sialylation (15). CA19-9 (α2,3-sialyl-Le^a) is the frequently applied biomarker that provides prognostic information on pancreatic and gastrointestinal cancers. We investigated the expression profiles on MBP ligands in comparison with those of CA19-9. Interestingly, as shown in Fig. 5, the expression profile of CA19-9 correlated inversely with that of MBP ligands for some cancer patients. Table I summarizes the results of 54 cases. CA19-9 was expressed in 29 of the total 54 cases (53.7%), and predominant portions of the MBP$^+$ tissues (78.6%) were not stained by anti–CA19-9; instead, large portions of the MBP$^-$ tumor tissues (65%) were CA19-9$^+$. In contrast, the expression pattern of CEA did not show significant statistical correlation with that of MBP ligands (Table I).

Clinicopathological analysis of expression of MBP ligands in human colorectal carcinomas

Differences in expression patterns between CA19-9 and MBP prompted us to investigate the clinicopathological backgrounds of the patients. We analyzed 196 patients: 77 cases were MBP ligand$^+$, and 119 patients were negative. Table II shows the statistical analyses of the clinicopathological features of colorectal carcinomas. We found a significant correlation between MBP ligand expression and age ($^{**}p = 0.002$). The ratio of MBP ligand$^+$ patients among people aged ≥60 y (61.0%; 47 of 92) was significantly higher than that for people aged <60 y (39.0%; 30 of 104). The ratio of MBP ligand$^+$ patients became significantly lower as the tumor differentiation diminished ($^*p = 0.0118$): 51.2% (22 of 43) in well differentiated, 41.1% (51 of 124) in moderately differentiated, and 0% (0 of 9) in poorly differentiated. Moreover, MBP ligand expression was detected more frequently in transverse, descending, and sigmoid colon (52.4%; 53 of 101)

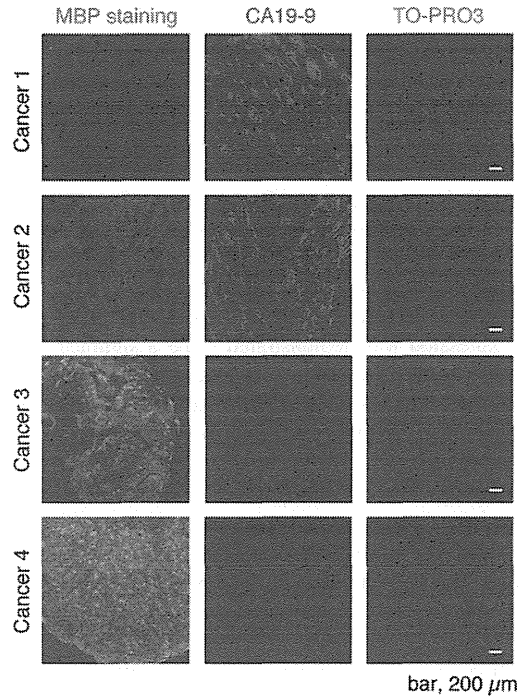

FIGURE 5. Comparison of the staining patterns for MBP and anti–CA19-9 Abs in colorectal cancer tissues. Colorectal carcinoma tissues were double stained with MBP (green) and anti–CA19-9 Abs (red), as described in *Materials and Methods*. The images were obtained with a confocal laser microscope. The data shown are representative of 54 cancer tissues.

than in cecum and ascending colon (25.0%; 15 of 60) or in rectum (25.7%; 9 of 35) (***$p < 0.001$).

Correlation between expression of MBP ligands and presence of tumor-infiltrating CD3/HLA-DR$^+$ immune cells

Colorectal tumor often contains nonmalignant immune cells. It was demonstrated that the immune cells that are positive for HLA class II protein HLA-DR frequently infiltrate colorectal tumor and that the HLA-DR expression is associated with lower tumor stages and with a better prognosis (28–30). HLA-DR is expressed broadly on B cells, activated T cells, monocytes/macrophages, dendritic cells, and other nonprofessional APCs. In this study, to determine whether MBP ligand expression correlated with immune infiltration, we performed immunohistochemistry by anti–HLA-DR mAb in combination with MBP staining for 136 cases of cancer tissue (Table III). The percentage of tumor tissues positive for both MBP ligand expression and HLA-DR cells (35 of 136; 25.7%) was significantly higher compared with tissue positive for MBP ligand only (12 of 136; 8.8%) or HLA-DR only (12 of 136; 8.8%) ($p < 0.001$). HLA-DR$^+$ cells were mostly irregular in shape with surface protrusions, which was reminiscent of monocytic cell lineages distinct from round-shaped T or B lymphocytes. Indeed, most HLA-DR$^+$ cells in MBP ligand$^+$ tissues were substantially costained by anti-CD83 and anti-CD163 Abs but not MBP (Fig. 6),

Table II. Clinicopathological features of the study population according to MBP staining in cancer mucosae

Parameters	Negative (n = 119) No. of Cases (%)	Positive (n = 77) No. of Cases (%)	p Value[a]
Age (y)			
≥60	45 (37.8)	47 (61.0)	0.0020**
<60	74 (62.2)	30 (39.0)	
Gender			
Male	76 (63.9)	56 (72.7)	0.2151
Female	43 (36.1)	21 (27.3)	
Tumor size[b]			
T_2	4 (3.6)	8 (10.4)	0.0526
T_3	107 (89.7)	60 (77.9)	
T_4	8 (6.7)	9 (11.7)	
Nodal status[b]			
N_0	60 (50.4)	39 (50.6)	0.9946
N_1	32 (26.9)	21 (27.3)	
N_2	27 (22.7)	17 (22.1)	
Metastasis[b]			
M_0	104 (87.4)	64 (83.1)	0.4113
M_1	15 (12.6)	13 (16.9)	
Tumor stage[b]			
≤II	54 (45.3)	35 (45.4)	0.6640
III	50 (42.0)	29 (37.7)	
IV	15 (12.7)	13 (16.9)	
Histological differentiation			
Well	21 (17.6)	22 (28.6)	0.0118*[c]
Moderate	73 (61.3)	51 (66.2)	
Poor	9 (7.6)	0 (0.0)	
Mucinous	16 (13.5)	4 (5.2)	
Tumor localization			
Cecum	11 (9.2)	3 (3.9)	<0.001***[d]
Ascending	34 (28.6)	12 (15.6)	
Transverse	12 (10.1)	10 (13.0)	
Descending	7 (5.9)	5 (6.5)	
Sigmoid	29 (24.4)	38 (49.4)	
Rectum	26 (21.8)	9 (11.6)	

[a]Analyzed using χ^2 test or Fisher exact test.
[b]American Joint Committee on Cancer's Cancer Staging Manual (6th edition).
[c]The p value was calculated by comparison among three groups of varied differentiation stages without the mucinous adenocarcinoma group.
[d]The p value was calculated by comparison among three groups: Cecum + Ascending, Transverse + Descending + Sigmoid, and Rectum.
*$p < 0.05$, **$p < 0.01$, ***$p < 0.001$.

Table I. Tissue expression correlation between CEA/CA19-9 and MBP ligands in cancer mucosae

Tissue Staining	MBP Staining: Negative (n = 40) No. of Cases (%)	MBP Staining: Positive (n = 14) No. of Cases (%)	p Value[a]
Anti–CA19-9			
Negative	14 (35.0)	11 (78.6)	0.0111*
Positive	26 (65.0)	3 (21.4)	
Anti-CEA			
Negative	23 (57.5)	4 (28.6)	0.1188
Positive	17 (42.5)	10 (71.4)	

[a]Analyzed using Fisher exact test.
*$p < 0.05$.

Table III. Tissue expression correlation between CD3/HLA-DR and MBP ligands in cancer mucosae

Tissue Staining	MBP Staining: Negative (n = 89) No. of Cases (%)	MBP Staining: Positive (n = 47) No. of Cases (%)	p Value[a]
Anti–HLA-DR			
Negative	77 (86.5)	12 (25.5)	<0.001***
Positive	12 (13.5)	35 (74.5)	
Anti-CD3			
Negative	76 (85.3)	34 (72.3)	0.0719
Positive	13 (14.7)	13 (27.7)	

[a]Analyzed using Fisher exact test.
***$p < 0.001$.

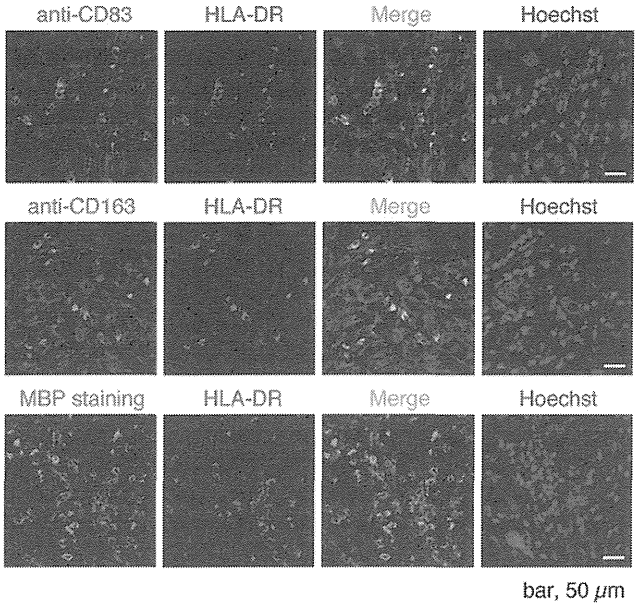

FIGURE 6. HLA-DR$^+$ macrophages and activated dendritic cells infiltrating into MBP ligand$^+$ tumor tissues. HLA-DR$^+$ cells (red) in MBP ligand$^+$ colorectal carcinoma tissues were stained with anti-CD83 mAb, anti-CD163 mAb, or MBP, as described in *Materials and Methods*. The images were obtained with a confocal laser microscope.

indicating that the majority of HLA-DR$^+$ cells are macrophages or activated dendritic cells but not tumor cells.

It also was reported that patients whose tumors are highly infiltrated by CD3$^+$ T cells have longer survival compared with those with poorly infiltrated tumors (31). However, in our immunohistochemical study using anti-CD3 Ab, we did not detect a statistically significant correlation between MBP ligand expression and tumor-infiltrating CD3 T cells ($p = 0.0719$). Taken together, these results indicated that MBP ligand expression correlates with immune infiltration of HLA-DR$^+$ cells but not CD3$^+$ cells.

Expression of MBP ligands in metastatic tumors

To examine whether MBP ligand expression is limited to primary tumor sites, we analyzed 20 primary and corresponding metastatic colorectal cancer tissues (Table IV). We found that 13 of 20 metastatic tumor tissues were negative for MBP ligand, and 7 tissues were positive. Moreover, among 11 patients with MBP ligand$^-$ primary tumor tissues, only 1 patient (9.1%) exhibited MBP ligand expression in the metastatic tumor. In contrast, three of nine patients (33%) lost MBP ligand expression in the metastatic tumors. These results indicate that MBP ligand is expressed in metastatic sites, as well as in primary tumor sites, and the expression may change after metastasis.

Table IV. Expression changes in MBP ligand between primary and metastatic tumor

MBP Staining of Primary Tumor	MBP Staining of Metastatic Tumor: Negative ($n = 13$) No. of Cases (%)	MBP Staining of Metastatic Tumor: Positive ($n = 7$) No. of Cases (%)	p Value[a]
Negative	10 (76.9)	1 (14.3)	0.3711
Positive	3 (23.1)	6 (85.7)	

[a]Analyzed using McNemar test.

Expression of MBP ligands is associated with a favorable survival for the patients

We next evaluated the difference in survival rates between patients with MBP ligand$^-$ and MBP ligand$^+$ carcinomas. Multivariate survival analysis was carried out for 186 patients for 186 patients of which 76 cases (40.9%) had MBP ligand$^+$ tumor, using the Cox proportional hazard models with a stepwise backward procedure (Table V). We found that lymph node status (hazard ratio, 5.105; 95% confidence interval [CI], 3.043–8.565; $p < 0.001$) and distant metastasis (hazard ratio, 1.671; 95% CI, 1.239–2.254; $p < 0.001$) were independent predictors of shorter survival. In contrast, MBP ligand expression was demonstrated to be a significant independent factor, with a hazard ratio < 1.0 (hazard ratio, 0.580; 95% CI, 0.353–0.954; $p = 0.032$), indicating that MBP ligand expression correlates independently with a prolonged survival of colorectal cancer patients.

Discussion

Because glycan biosynthesis is a nontemplate-driven process in the endoplasmic reticulum and Golgi body, epigenetic regulation of glycosyltransferase expression during carcinogenesis causes drastic changes in cell surface carbohydrate structures, which may further affect immune functions by creating or masking ligands for endogenous lectins (32). During oncogenic transformation in the gastrointestinal epithelium, changes in the expression patterns of glycosyltransferase genes frequently result in aberrant synthesis of ABH and Lewis (Le)-related carbohydrate Ags (33). The advent of mAb technology has enabled precise definition of such alterations, including upregulation of fucosylated or sialylated lactoseries type 1 or type 2 chain structures (e.g., H/Lewis y/Le^b, Le^a, Lewis x, sialyl-Le^a, and sialyl-Lewis x) (33–38). The CA19-9 (sialyl-Le^a) epitope is, above all, a well-known tumor marker that is useful for cancer prognosis or monitoring of the colon, pancreas, and other organs (39, 40). However, accumulating evidence revealed that colorectal tumor–associated Le Ags consist of more complex structures than previously believed. In fact, several years ago, we isolated MBP ligand oligosaccharides from an oligosaccharide mixture prepared by hydrazinolysis of a pronase digest of SW1116 cells. They are large, multiantennary *N*-glycans with highly fucosylated polylactosamine-type structures having Le^b–Le^a or tandem repeats of the Le^a structure at their nonreducing ends (15). A little later, we isolated a major MBP ligand glycoprotein from SW1116 cell lysates using an MBP column and identified them as CD26/dipeptidylpeptidase IV (110 kDa). MALDI mass spectrometry of the *N*-glycans released from CD26 by PNGase F suggested that complex-type *N*-glycans carrying a minimum of four Le^a/Le^b epitopes, arranged either as multimeric tandem repeats or terminal epitopes on multiantennary structures, are critically important for the high-affinity binding to MBP. On the basis of these observations, a hypothetical three-dimensional model of the MBP–Le oligosaccharide complex was presented (26, 27). In this study, we demonstrated that MBP recognizes human primary and metastatic colorectal carcinoma

Table V. Survival analysis by multivariate Cox proportional-hazards model

Prognostic Factor	Hazard Ratio	95% CI	p Value
Nodal status	5.105	3.043–8.565	<0.001***
Metastasis	1.671	1.239–2.254	<0.001***
MBP ligand	0.580	0.353–0.954	0.032*

*$p < 0.05$, ***$p < 0.001$.

cells. MBP binding was inhibited completely by EDTA chelation, which indicates that the binding occurs in a Ca^{2+}-dependent manner and, thus, is mediated through its CRD. In addition, MBP staining was blocked by a fucose-specific lectin, AAL, and partially overlapped with Le^b expression in carcinoma tissues. It may be reasonable to assume that the same type of high-affinity interaction between a multimeric protein and multimeric ligands plays an important role in the specific recognition of cancer cells by MBP in human tissues. We also showed that, following metastasis, three tissues changed from MBP ligand$^+$ to MBP ligand$^-$, and one tissue changed from MBP ligand$^-$ to MBP ligand$^+$. Although there was no statistical difference in the expression changes ($p = 0.3711$), it is tempting to speculate that MBP ligand expression may decrease during metastasis.

CA19-9 is one of the most widely used markers for colorectal cancer in clinical practice. The antigenic determinant of CA19-9 recognized by mAb 116NS-19.9 is sialyl-Le^a. Because MBP did not bind to sialylated oligosaccharides, it makes sense that the MBP-staining pattern did not overlap with CA19-9 expression in cancer tissues. Our histochemical study revealed that MBP stained 11 of 25 (44%) CA19-9$^-$ colorectal carcinoma tissue samples, and that the percentage of patients who exhibited positive staining with either MBP or anti–CA19-9 Abs was markedly increased (40 of 54; 74%) compared with anti–CA19-9 staining only (53%), suggesting that MBP may be a useful marker for CA19-9$^-$ carcinomas. Furthermore, the expression of MBP ligands in the basolateral, as well as the apical, area of cancer mucosae suggests that MBP ligands on the basolateral surface may enter the blood stream through a neovessel. Accordingly, the establishment of a detection system for MBP ligands in situ may have a clinical benefit.

We demonstrated the good prognosis of MBP ligand$^+$ patients compared with MBP ligand$^-$ patients in the multivariate survival analysis. The positivity of MBP staining is entirely independent of nodal status ($p = 0.9946$), metastasis ($p = 0.4113$) (Table II), and anti-CD3 staining ($p = 0.0719$) (Table III), indicating that MBP stains colorectal carcinoma tissues, regardless of those factors. Therefore, the N_0, M_0, or CD3$^-$ cohort can be divided into subgroups that do or do not stain positive for MBP, which provides new prognostic information that would not be predicted simply by nodal status, metastasis, or anti-CD3 staining. In addition, this prolonged survival suggests that the expression of MBP ligands may contribute to inhibition of tumor growth or metastasis. We reported previously that SW1116 cell growth in nude mice mostly regressed within several days after intratumoral and s.c. inoculation of vaccinia virus carrying the MBP gene, and we designated this process as MDCC (14). Therefore, the finding of good survival in MBP ligand$^+$ patients may reflect the antitumor effect of MBP in humans. We showed in this study that immune infiltration by HLA-DR$^+$ cells correlated with MBP ligand expression in the tumor, and most of the HLA-DR$^+$ cells were CD83$^+$ and/or CD163$^+$ monocytic-lineage cells. This result supports our previous hypothesis that activated immune cells, but not complement activation, induce MDCC. In addition, the finding that MBP ligand expression was observed more frequently as the tumor-differentiation levels increased suggests that MDCC driven by MBP may be effective at an early stage of cancer.

Finally, we found tumor-specific carbohydrate-mediated interaction between endogenous lectin MBP and human primary colorectal carcinoma tissues. The ligand on the tumor cells may be identical or similar to MBP ligand oligosaccharides, which we isolated previously from SW1116 cells. They are highly fucosylated polylactosamine-type structures having Le^b–Le^a or tandem repeats of the Le^a structure at their nonreducing ends, and they have a high-affinity interaction with MBP. Our results suggest a possible role for endogenous MBP, as well as its potential usefulness as a novel diagnostic marker or an indicator of better prognoses for colorectal carcinomas. The fact that there was no false positive staining by MBP in noncancerous tissues may stimulate its use in the in situ diagnosis of colorectal cancer tissues and selective removal of cancer cells by endoscopic surgery in the near future.

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Disclosures

The authors have no financial conflicts of interest.

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Ⅷ.　研究成果の刊行物

潰瘍性大腸炎・クローン病
診断基準・治療指針

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潰瘍性大腸炎

クローン病

1 潰瘍性大腸炎診断基準

1. 定義

主として粘膜を侵し、しばしばびらんや潰瘍を形成する大腸の原因不明のびまん性非特異性炎症である。WHOのCouncil for International Organization of Medical Science (CIOMS)医科学国際組織委員会で定められた名称と概念は、つぎの通りである。(1973)

特発性大腸炎　idiopathic proctocolitis

An idiopathic, non-specific inflammatory disorder involving primarily the mucosa and submucosa of the colon, especially the rectum. It appears mainly in adults under the age of 30, but may affect children and adults over the age of 50. Its aetiology remains unknown, but immunopathological mechanisms and predisposing psychological factors are believed to be involved. It usually produces a bloody diarrhoea and various degrees of systemic involvement, liability to malignant degeneration, if of long duration and affecting the entire colon.

(訳) 主として粘膜と粘膜下層をおかす、大腸とくに直腸の特発性、非特異性の炎症性疾患。30歳以下の成人に多いが、小児や50歳以上の年齢層にもみられる。原因は不明で、免疫病理学的機序や心理学的要因の関与が考えられている。通常血性下痢と種々の程度の全身症状を示す。長期にわたり、かつ大腸全体をおかす場合には悪性化の傾向がある。

2. 診断の手順

慢性の粘血・血便などがあり本症が疑われるときには、放射線照射歴、抗生剤服用歴、海外渡航歴などを聴取するとともに、細菌学的・寄生虫学的検査を行って感染性腸炎を除外する。次に直腸あるいはS状結腸内視鏡検査を行って本症に特徴的な腸病変を確認する。このさい、生検を併用する。これだけの検査で多くは診断が可能であるが、必要に応じて注腸X線検査や全大腸内視鏡検査などを行って、腸病変の性状や程度、罹患範囲などを検査し、同時に他の疾患を除外する。

3. 診断基準

次のa) のほか、b) のうちの1項目、およびc) を満たし、下記の疾患が除外できれば、確診となる。

a) 臨床症状：持続性または反復性の粘血・血便、あるいはその既往がある。

b) ①内視鏡検査：ⅰ) 粘膜はびまん性におかされ、血管透見像は消失し、粗ぞうまたは細顆粒状を呈する。さらに、もろくて易出血性(接触出血) を伴い、粘血膿性の分泌物が付着しているか、ⅱ) 多発性のびらん、潰瘍あるいは偽ポリポーシスを認める。
②注腸X線検査：ⅰ) 粗ぞうまたは細顆粒状の粘膜表面のびまん性変化、ⅱ) 多発性のびらん、潰瘍、ⅲ) 偽ポリポーシスを認める。その他、ハウストラの消失(鉛管像) や腸管の狭小・短縮が認められる。

c) 生検組織学的検査：活動期では粘膜全層にびまん性炎症性細胞浸潤、陰窩膿瘍、高度な杯細胞減少が認められる。いずれも非特異的所見であるので、総合的に判断する。寛解期では腺の配列異常(蛇行・分岐)、萎縮が残存する。上記変化は通常直腸から連続性に口側にみられる。

b) c) の検査が不十分、あるいは施行できなくとも切除手術または剖検により、肉眼的および組織学的に本症に特徴的な所見を認める場合は、下記の疾患が除外できれば、確診とする。

除外すべき疾患は、細菌性赤痢、アメーバ性大腸炎、サルモネラ腸炎、キャンピロバクタ腸炎、大腸結核、クラミジア腸炎などの感染性腸炎が主体で、その他にクローン病、放射線照射性大腸炎、薬剤性大腸炎、リンパ濾胞増殖症、虚血性大腸炎、腸型ベーチェットなどがある。

〈注1〉まれに血便に気付いていない場合や、血便に気付いてすぐに来院する(病悩期間が短い) 場合もあるので注意を要する。

〈注2〉所見が軽度で診断が確実でないものは「疑診」として取り扱い、後日再燃時などに明確な所見が得られた時に本症と「確診」する。

〈注3〉Indeterminate colitis
クローン病と潰瘍性大腸炎の両疾患の臨床的、病理学的特徴を合わせ持つ、鑑別困難例。経過観察により、いずれかの疾患のより特徴的な所見が出現する場合がある。

4. 病態（病型・病期・重症度）

A. 病変の拡がりによる病型分類

全大腸炎	total colitis
左側大腸炎	left-sided colitis
直腸炎	proctitis
右側あるいは区域性大腸炎	right-sided or segmental colitis

〈注4〉左側大腸炎は、病変の範囲が脾彎曲部を越えていないもの。

〈注5〉直腸炎は、前述の診断基準を満たしているが、内視鏡検査により直腸S状部（RS）の口側に正常粘膜を認めるもの。

〈注6〉右側あるいは区域性大腸炎は、クローン病や大腸結核との鑑別が困難で、診断は経過観察や切除手術または剖検の結果を待たねばならないこともある。

〈注7〉胃十二指腸にびまん性炎症が出現することがある。

B. 病期の分類

活動期	active stage
寛解期	remission stage

〈注8〉活動期は血便を訴え、内視鏡的に血管透見像の消失、易出血性、びらん、または潰瘍などを認める状態。

〈注9〉寛解期は血便が消失し、内視鏡的には活動期の所見が消失し、血管透見像が出現した状態。

C. 臨床的重症度による分類

軽　症	mild
中等症	moderate
重　症	severe

診断基準は下記の如くである。

	重　症	中等症	軽　症
1）排便回数	6回以上	重症と軽症との中間	4回以下
2）顕血便	(+++)		(+)～(−)
3）発熱	37.5℃以上		(−)
4）頻脈	90/分以上		(−)
5）貧血	Hb10g/dL以下		(−)
6）赤沈	30mm/h以上		正常

〈注10〉軽症の3）、4）、5）の（−）とは37.5℃以上の発熱がない。90/分以上の頻脈がない。Hb10g/dL以下の貧血がない、ことを示す。

〈注11〉重症とは1）および2）の他に全身症状である3）または4）のいずれかを満たし、かつ6項目のうち4項目以上を満たすものとする。軽症は6項目すべて満たすものとする。

〈注12〉左記の重症と軽症との中間にあたるものを中等症とする。

〈注13〉重症の中でも特に症状が激しく重篤なものを劇症とし、発症の経過により、急性劇症型と再燃劇症型に分ける。劇症の診断基準は以下の5項目をすべて満たすものとする。
①重症基準を満たしている。
②15回/日以上の血性下痢が続いている。
③38℃以上の持続する高熱がある。
④10,000/mm^{3}以上の白血球増多がある。
⑤強い腹痛がある。

D. 活動期内視鏡所見による分類

軽　度	mild
中等度	moderate
強　度	severe

診断基準は下表の如くである。

炎　症	内視鏡所見
軽　度	血管透見像消失 粘膜細顆粒状 発赤、アフタ、小黄色点
中等度	粘膜粗ぞう、びらん、小潰瘍 易出血性（接触出血） 粘血膿性分泌物付着 その他の活動性炎症所見
強　度	広汎な潰瘍 著明な自然出血

〈注14〉内視鏡的に観察した範囲で最も所見の強いところで診断する。内視鏡検査は前処置なしで短時間に施行し、必ずしも全大腸を観察する必要はない。

E. 臨床経過による分類

再燃寛解型	relapse-remitting type
慢性持続型	chronic continuous type
急性劇症型（急性電撃型）	acute fulminating type
初回発作型	first attack type