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Editors

Endoscopy in the Diagnosis of Small Intestine Diseases

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Preface

This volume was about one year in the planning, and was inspired by the realization that capsule endoscopy and double-balloon endoscopy frequently reveal findings that nevertheless do not result in diagnosis. Another reason was our recognition of the difficulty in distinguishing findings of ulcerative colitis from those of Crohn's disease and other disorders in small intestinal endoscopy. Of course, we have seen numerous case presentations at academic conferences and have also read several books on small intestinal endoscopy. However, these frequently do nothing more than list a large number of disorders without providing a detailed analysis of findings. European and American reference works also seem to fail to address issues such as radiographic comparisons. When endoscopic findings were discussed at an international conference on double-balloon endoscopy held in Japan a few years ago, a leading Western researcher was unaware of such basic observations as the fact that ulcers of the small intestine present on the side of mesenteric attachment in Crohn's disease and on the opposite side in tuberculosis. Probably this lack of awareness was mainly because the researcher had never seen an accurate macroscopic depiction of a resected specimen. Although the United States and European nations are advanced in terms of capsule endoscopy, Americans and Europeans still face many problems in diagnostic imaging for this very reason. We therefore decided to put together a large number of carefully selected Japanese examples of small intestinal lesions, in an effort to compare and contrast small intestinal lesions that exhibit consistent findings and morphologies.

The basic premise of this book is differential diagnosis on the basis of endoscopic findings, and readers should start by taking a close look at the individual endoscopic findings illustrated on the left side of each full-page spread. We have then added an explanation of each finding on the right side, together with radiographic images and macroscopic depictions of resected specimens for comparison. This layout was designed with everyday clinical practice in mind, and we hope that readers will interpret the elements that compose each of these endoscopic findings with the aim of understanding the pathology and distinguishing features of each condition. Radiographic comparisons comprise another important element of the findings. There are limitations to endoscopic observations when it comes to long or large lesions of the small intestine, with its many curves. Therefore, we have also emphasized radiographic findings in this volume. In Japan, many institutions still practice double-contrast imaging, providing beautiful results, and we believe this point will resonate with many readers. Since a single disorder may exhibit great variety, this volume includes multiple depictions of the same disorders. We have also included lesions in both active and inactive phases. This is because both appearances are highly likely to be encountered simultaneously in actual clinical practice. Presenting a good overall balance of these cases would require a huge page area. We therefore decided to limit the number of findings depicted and to put together only carefully selected cases. In producing a work such as this, we thought it important to reflect the underlying concept in the title. After consulting among all the editors, we decided on *Endoscopy in the Diagnosis of Small Intestine Diseases*.

Because we wanted this book to be published before the Japan Digestive Disease Week (JDDW) held in Fukuoka in the fall of 2011, we had only about six months to spend on production. The editors were in communication with one another on a daily basis and brought in colleagues to share diagnostic knowledge. The cases presented in this volume were assembled jointly from three institutions: the Department of Gastroenterology at Kyushu University, the Department of Gastroenterology at Fukuoka University, and the Department of Gastroenterology at Fukuoka University Chikushi Hospital. A number of cases were requested from leading researchers at external institutions in the event that no suitable case was available from any of these three institutions. Within our group, we regularly hold joint seminars and undertake joint clinical trials. As we were already using the same methods for diagnosing small intestinal disease and applying radiographic procedures and treatment methods, we could assemble cases at the same pace. This meant that each institution ultimately held responsibility for a very similar number of cases.

As members of our group have some predecessors in common, we have a long history of joint research into disorders of the small intestine, such as Crohn's disease. We have also treated and accumulated a large number of cases. *Shōchō shikkan no rinshō* (Clinical Treatment of Small Intestinal Disease), edited by Tsuneyoshi Yao and Mitsuo Iida, was a major compilation of a large number of disorders published by Igaku Shoin in 2004. Since then, dramatic advances have been made in the field of small intestinal endoscopy. The simplicity of diagnostic operations has also meant that an increased number of images are now shared among multiple institutions. However, the inadequacy of a number of aspects has also become evident, including comparisons with radiography, pathological diagnosis, and handling of cases. We therefore regarded as a matter of great importance the publication of this volume focusing on accurate diagnosis and procedures for differentiating between conditions on the basis of endoscopic findings.

We are grateful for the assistance of Mr. Shingo Ano from the Medical Publications Department of Igaku Shoin in the production of this book. He established the original plan, provided swift editing, and overcame numerous problems in assembling the manuscript. We would also like to express our warm thanks to the pathologists who provide everyday diagnostic support for our clinical work. We are profoundly grateful to Dr. Akinori Iwashita (Department of Pathology, Fukuoka University Chikushi Hospital), Dr. Minako Hirahashi (Department of Anatomic Pathology, Graduate School of Medical Sciences, Kyushu University), Dr. Satoshi Nimura (Department of Pathology, Fukuoka University Faculty of Medicine), and Dr. Takashi Yao (Department of Human Pathology, Juntendo University School of Medicine; formerly of the Department of Anatomic Pathology, Graduate School of Medical Sciences, Kyushu University), who not only were involved in diagnosing the cases presented in this volume, but also have been passionately dedicated to the macroscopic and histological diagnosis of small intestinal disease for many years. It is thanks to their efforts that we were able to compile this volume. If our purpose in proposing this book is widely understood and arouses interest in the interpretation of findings rather than being viewed solely as a collection of rare cases, we will have succeeded beyond our expectations.

Chikushino, Japan

Toshiyuki Matsui
On behalf of the editors

Preface to the English Edition

The original Japanese edition of this book was prepared in October 2011. It has subsequently been published as an English atlas, and its content remains extremely valuable. In this preface to the English edition, we would like to emphasize several points.

We are currently in the era of small intestinal diagnostic endoscopy. Since 2000, the advent of double-balloon endoscopy and capsule endoscopy has shed new light on small intestine diseases. Thanks to the results of substantial research, a large number of small intestine diseases can now be diagnosed. In particular, the pathology of obscure gastrointestinal bleeding (OGIB) has now been almost completely explained. However, for many small intestine diseases, the diagnostic sensitivity and specificity of endoscopy remains low. This may be due to the poor resolution of the endoscopic images obtained, or the inability, for a variety of reasons, to depict small intestinal lesions accurately. The small intestine is extremely long; therefore, inserting the endoscope and completing the examination can be difficult. Both skill and creativity are required to overcome these problems. In addition, although small intestine diseases themselves are relatively few in number, they may display wide variations in morphology, which may also contribute to the difficulty of endoscopic diagnosis. For this reason, it is important to study in advance endoscopic images of key diseases in an atlas. Here, we should learn from the study of diagnostics in other fields. Endoscopic diagnosis of the severity of ulcerative colitis is surprisingly difficult, and determinations of the Mayo score frequently differ greatly between observers. This is because the definitions in the documents are inconsistent with the decisions made during actual diagnostic endoscopy. Production of an endoscopy atlas with an emphasis on severity has been shown to improve inter-observer consistency. Such subtle inter-observer variability also occurs in diagnostic image-enhanced endoscopy (IEE). This is because completely new diagnostic imaging criteria are used, and shared awareness of how to use them is currently lacking. In this situation, too, the production of an atlas is regarded as useful for establishing common perspectives. Atlases are thus used in many new fields of diagnostics.

Diseases of the small intestine may display many morphological variations, even if they share the same diagnosis. Simply providing a catalog of numerous endoscopic images for each diagnosis is not an efficient method to facilitate learning. Therefore, this atlas has adopted the format of categorizing lesions by morphology and providing a catalog of the corresponding diseases, both for the reason mentioned above and for consistency with the actual diagnostic process. Although this is a novel format, we consider it a highly effective approach to learning. This atlas has also been designed with problems set out on the left-hand page and their answers and explanations on the right, in the hope of cultivating an inquiring mind on the part of readers. Several major problems with the diagnosis of small intestine disease remain, and it is not a perfect form of diagnostics. If this book eventually becomes known as a milestone on the journey toward effective diagnostics, it would far exceed even the greatest hopes of the editors.

Here we would like to give a simple description of the characteristics of diagnostic endoscopy in Japan. The Japanese tend to emphasize comparisons either with macroscopic images or with macroscopic and histological images of resected specimens as the basis of diagnostic

endoscopy. They are thus constantly aware of the rationalization and interpretation of endoscopic images, and for this reason, they pay special attention to resected materials. They also frequently bear the findings of endoscopic observation in mind when immobilizing or resecting specimens. Their detailed expertise in the endoscopic diagnosis of both early gastric cancer and early colorectal cancer has been cultivated in this way. We believe it is appropriate to apply this concept to small intestine diseases. Therefore, macroscopic images of resected specimens also appear in this atlas for comparison, as the morphological characteristics should help improve the interpretation of endoscopic images. Comparisons of radiographic and endoscopic images are also fundamental to Japanese diagnostics, for the same reason. Here we would like to mention some examples from other fields. For example, colitis-associated cancer is difficult to diagnose. It has been previously regarded as beyond the diagnostic capability of modern endoscopy, with diagnosis possible only by means of blind biopsy. If it had not been for the Japanese style of diagnostics, which involves painstakingly cutting out resected colorectal materials and comparing them with findings from diagnostic endoscopy (such as the extent of redness, as well as detailed patterns and differences in level), endoscopic diagnosis of this condition would have remained a pipe dream. However, endoscopic diagnosis of various small intestine diseases, driven by improvements to procedures and the development of new devices, is gradually becoming a reality.

The morphology of small intestine diseases may be difficult to accurately imagine in two dimensions for many reasons, including whether a lesion is in the active phase, whether it is hemorrhaging, its orientation, and its relationship with the long axis. Observations may often be inadequate due to the lumen being immobilized by adhesions, fistula formation, and so on. Of course, endoscopic observation is often impossible if stenosis is present. To overcome these problems, it may be necessary to combine endoscopy with procedures such as barium contrast, computed tomography, and magnetic resonance imaging. We regard diagnostic radiography of the small intestine as preferable from the perspectives of panoramic imaging of small intestinal disease and visualization of the mucosal surface, and have endeavored to master diagnostic radiography for many years. However, the impact of diagnostic endoscopy normally far outweighs diagnostic radiography, and endoscopy is gradually becoming the main method of diagnosis.

Histopathological diagnosis also had limitations in the small intestine. Little biopsy material is typically available, and histological diagnosis may end unsatisfactorily for reasons such as unresectability. When producing this atlas, we requested numerous diagnoses from pathologists. From among those diagnoses, we have concentrated on cases with adequate diagnostic results. For rare diseases, this frequently involved a large amount of work from the diagnostic perspective. Therefore, we would like to express our profound gratitude to those pathologists here. Of course, we requested individuals with ideas similar to our own to author the clinical side. Due to the large number of items, we asked young doctors from the departments of gastroenterology at Kyushu University, Fukuoka University, and Fukuoka University Chikushi Hospital to provide case descriptions. These three universities have grown from a shared foundation and are constantly holding joint case conferences and study groups. On this point, a shared perspective on endoscopy has already been established. The pathologists of these universities have also developed from a shared foundation, meaning that differing viewpoints are not an issue.

Some of the problems we encountered in the production of this atlas were that images were somewhat small and their resolution was not fully utilized, and it was not possible to provide adequate space to other images. However, the compact design of the atlas was chosen because our priority was to include as many images as possible. We hope that readers will understand the purpose of this atlas and will utilize it to train young endoscopy practitioners.

Chikushino, Japan
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Part III Basic Knowledge and Classification

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Part I

General Considerations

Diagnostic Process for Small Intestinal Disease

1

Takayuki Matsumoto

1.1 Symptomatology of Small Intestinal Disease

The small intestine is the longest organ of the digestive tract, with main functions of digestion, absorption, and maintenance of innate immunity. Accordingly, symptoms of small intestinal disease comprise impaired digestion and absorption due to widespread damage to the intestinal mucosa, as well as diarrhea, abdominal pain, and malnutrition caused by immune abnormalities. The development and widespread adoption of small intestinal endoscopic techniques has increased the frequency with which small intestinal lesions are diagnosed following hemorrhage from a small lesion. Symptoms of small intestinal disease must therefore be categorized into two types: gastrointestinal hemorrhage; and other symptoms. The latter are suggestive of more widespread small intestinal disease.

1.1.1 Gastrointestinal Hemorrhage

Hemorrhagic lesions may occur at any point along the gastrointestinal tract, from the oral cavity to the anus. If the apparent source of bleeding cannot be identified on upper gastrointestinal endoscopy or colonoscopy, this is known as "obscure gastrointestinal bleeding" (OGIB). OGIB is categorized as overt OGIB, in which red blood or black excretions comprising the metabolic products of hemoglobin are visible, or occult OGIB, which can only be confirmed by recurrent or persistent iron-deficiency anemia or a positive result on testing for fecal occult blood [1].

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With overt OGIB in small intestinal disease, blood is excreted via the anus. The color of this blood is affected by the location and amount of hemorrhage, with stool being black or tarry for a small hemorrhage occurring *on the proximal side of GI tract*, and tinged with red in the case of a large hemorrhage or one occurring on the distal side.

1.1.2 Other Symptoms

1.1.2.1 Diarrhea

In healthy adults, around 9 L of orally ingested liquid and intestinal fluid flow into the small intestine each day, but the majority is reabsorbed, with only around 100–200 mL of liquid excreted in feces. Diarrhea is a condition comprising the repeated excretion of feces with increased liquid content, although there is no clear definition of the frequency or amount of liquid involved. The mechanisms whereby diarrhea occurs can be categorized as hyperosmosis of intestinal contents, increased exudation and hypersecretion by the intestinal mucosa due to small intestinal disease, and intestinal dysmotility (Table 1.1).

1.1.2.2 Edema, Pleural Effusion, and Ascites

Malabsorption syndrome or protein-losing enteropathy due to widespread damage to the small intestinal mucosa can cause hypoproteinemia. As a result, the colloidal osmotic pressure of serum drops, and edema, pleural effusion, and ascites occur. Normally, edema appears systemically and symmetrically as pitting edema. Improvement and exacerbation appear in accordance with changes in total serum protein levels. Serum protein levels are low, but serum lipid levels are normal. In many cases, the condition is accompanied by other signs of malnutrition, including weight loss, weakness, diarrhea, tetany, and osteomalacia. If lymphangiectasis is present, pleural effusion and ascites are milky.

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Table 1.1 Mechanisms of diarrhea and associated disorders

	Osmotic diarrhea	Exudative diarrhea	Secretory diarrhea	Intestinal dysmotility
Mechanism	Increased liquid content due to rise in osmotic pressure within the intestine	Increased exudation by inflammatory lesions	Hypersecretion by the intestinal mucosa	Reduced transit time due to hyperperistalsis Intestinal bacterial proliferation due to hypoperistalsis
Features	Worsens with eating, improves with fasting	Worsens with eating, does not resolve completely even after fasting	Does not improve with fasting	Infrequently woken at night by diarrhea
	Steatorrhea, watery diarrhea	Bloody diarrhea, mucous and bloody stool present	Watery diarrhea, sometimes steatorrhea	Watery diarrhea
Main underlying disorders: acute	Oral saline laxatives	Infectious enteritis (infectious type)	Infectious enteritis (toxin production type)	
	Ingestion of non-absorbable sugars	Drug-induced enteropathy	Abuse of laxatives	
	Overeating	Ischemic enteritis		
Main underlying disorders: chronic	Malabsorption syndrome Short bowel syndrome	Chronic inflammatory bowel disease	Zollinger-Ellison syndrome WDHA syndrome	Irritable bowel syndrome Hyperthyroidism Scleroderma Amyloidosis Neurological disorders

1.1.2.3 Abdominal Distension and Flatulence

These are symptoms caused by the accumulation of excess gas or liquid in the small intestinal lumen or abdominal cavity, or the development of a massive tumor, with gas frequently accumulating due to intestinal stenosis. Under physiological conditions, the volume of gas in the intestines is maintained at around 100 mL. This volume increases, however, as a result of stenotic lesions of the intestinal tract or reduced intestinal motility, leading to abdominal distension and flatulence. In particular, nausea and vomiting are evident in cases of gastrointestinal stenosis, and may lead to alkalosis or hypochloremia if severe.

1.1.2.4 Abdominal Pain

This is the most common symptom of gastrointestinal disorders, and is non-specific. Depending on the mechanism involved, abdominal pain may be visceral, somatic or referred.

Visceral abdominal pain occurs when a stimulus to the intraluminal sensory nerve is transmitted through the intraluminal nerve plexus via sympathetic nerve afferent fibers to the brain. Transmission speed is slow, and an aching pain is felt that is not clearly localized. Somatic abdominal pain is a sharp, localized pain transmitted from receptors located in the peritoneum and mesenterium via the encephalomyeloneuropathic sensory conduction route, and is associated with symptoms of peritoneal irritation. Referred pain occurs when a strong stimulus from visceral abdominal pain spills over into somatic afferent nerves that run through the dorsal spinal root, resulting in the pain being perceived as somatic abdominal pain. The majority of abdominal pain in small intestinal disease is visceral abdominal pain in the periumbilical area. If caused by severe transmural inflammation and perforation, somatic abdominal pain becomes pronounced. Symptoms of peritoneal irritation may not be present during the acute phase of widespread ischemic small intestinal lesions, however, and caution is therefore required.

1.2 Diagnostic Procedure for Small Intestinal Disease

1.2.1 Patient Interview and Current Symptoms

As for other conditions, conducting the patient interview is often central to the diagnosis of small intestinal disease. This applies not just at the point when a lesion is suspected; reconfirmation of clinical information after a lesion has been confirmed must never be neglected. The small intestine is a common site for the occurrence of lesions as localized symptoms of systemic disorders, and it is important to ask about family history, including place of birth, and previous medical history (particularly tuberculosis infection, previous oral medication, foreign travel, autoimmune disorders, allergic disorders, radiation exposure, inflammatory bowel disease, and polyposis of the digestive tract). In terms of current symptoms, particular attention should be paid to the presence and nature of lesions of the skin, lips and oral cavity, and anal area, and a specialist should be consulted proactively for cases in which such findings are present.

1.2.2 Clinical Test Results

In addition to general testing such as blood and biochemical tests, Sudan III should be used to test for steatorrhea, and blood vitamin levels (vitamin K, vitamin B_{12}, and folic acid) can be measured using simple absorption tests. The α-1 antitrypsin clearance test is an appropriate technique for quantifying small intestinal protein exudate, and offers a valuable objective testing method if protein-losing enteropathy is strongly suspected or when strict indications such as response evaluation apply.

A wide range of testing methods have been developed for testing the absorption of sugars, protein, and lipids, but from the perspectives of reliability and clinical necessity, there is little opportunity to utilize these at present. Tests such as intestinal mucosa permeability tests using orally administered sugars as markers and fecal calprotectin can also be used as indirect indicators of small intestine inflammatory cell infiltration, but are not yet in wide use.

1.2.3 Imaging Techniques Other Than Small Intestinal Radiography and Endoscopy

The least invasive of these is abdominal ultrasonography, which can also be used to screen for a thickened bowel wall. In recent years, visualization of the small intestine by multidetector row computed tomography (MDCT) and magnetic resonance imaging (MRI) has improved, and in the United States and Europe the use of CT-enterography and MR-enterography is becoming more widespread. These techniques can also be expected to replace small intestinal radiography in Japan in the future. Nuclear medical techniques such as hemorrhagic scintigraphy and protein-losing scintigraphy have already been in use for some time, and today offer comparatively good diagnostic performance.

1.3 Diagnostic Algorithm for Small Intestinal Disease

1.3.1 OGIB

Small intestinal endoscopy has been shown in prospective studies to have a high rate of positive findings in OGIB compared with other diagnostic methods. This fact means that two approaches incorporating either capsule endoscopy or balloon endoscopy are recommended for OGIB [2, 3].

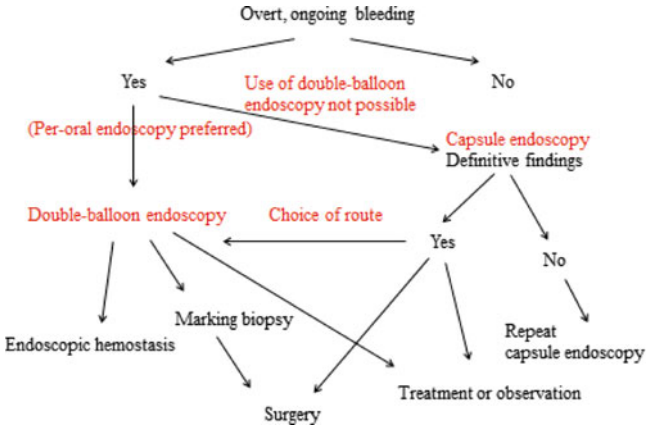

Fig. 1.1 Diagnostic process for OGIB (recommendations of the first international workshop on double-balloon endoscopy consensus meeting)

Figure 1.1 shows an algorithm centering on double-balloon endoscopy that was devised with the participation of Japanese small intestinal endoscopists [3]. Per-oral double-balloon endoscopy, which does not require any pretreatment, is used for overt OGIB, whereas capsule endoscopy is the first choice in cases of occult OGIB or when double-balloon endoscopy is difficult to perform. When using either of these diagnostic methods, the performance of endoscopic hemostasis and histological diagnosis by double-balloon endoscopy in cases with positive findings is assumed. This approach thus takes efficient treatment into account.

Figure 1.2 shows the algorithm proposed by the American Gastroenterology Association, which focuses on capsule endoscopy as the diagnostic method [2]. Capsule endoscopy is the first choice in cases of both overt and occult OGIB, and angiography is given as an option in cases of overt OGIB. Dealing with cases in which results of capsule endoscopy are negative is also referred to, with laparoscopic investigation and intraoperative endoscopy given as options.

In Japan, balloon endoscopy is widely used, and the diagnostic and treatment frameworks in use emphasize the first approach. Diagnosis and treatment of cases of overt OGIB are also performed with contrast CT as the first choice and interventional radiography as an additional treatment option. Given the fact that hemorrhagic lesions may have been missed by previous upper and lower gastrointestinal endoscopy, however, there should be no hesitation in performing repeated tests. If capsule endoscopy is preferred, the possibility of retention due to unexpected stenosis must be kept in mind.

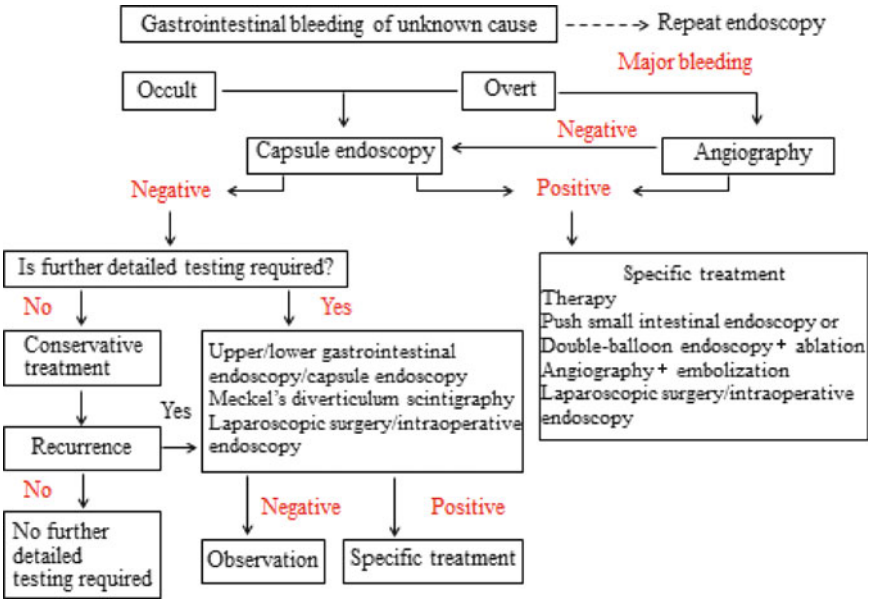

Fig. 1.2 Diagnostic process for OGIB (recommendations of the American Gastroenterological Association)

1.3.2 Small Intestinal Disease Other Than OGIB (Fig. 1.3)

For conditions other than OGIB, it is important to suspect small intestinal disease on the basis of the patient interview, physical findings, and general test results. In this process, it should be remembered that diffuse lesions and multisystem disorders are common. This means that information that is conclusive for diagnosis can frequently be obtained from diagnostic imaging, such as upper and lower gastrointestinal endoscopy, abdominal ultrasonography, and abdominal CT.

Decisions on whether to use radiography or endoscopy should also be made with care. Endoscopy is better suited to the diagnosis of small lesions and localized disease, whereas radiography is more useful for evaluating the extent of the affected area and the distribution of lesions. Radiography is particularly valuable for stenotic lesions and lesions located principally within the intestinal wall [4].

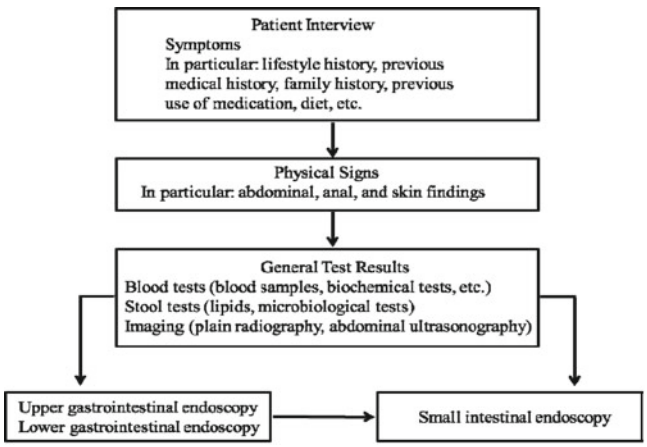

Fig. 1.3 Diagnostic process for small intestinal disease other than OGIB

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Small Intestinal Radiography

2

Fumihito Hirai

2.1 Practical Importance of Radiographic Diagnosis

The advent of capsule endoscopy (CE) and balloon-assisted endoscopy (BAE) is revolutionizing the diagnosis of small intestinal disease, which has hitherto relied on radiographic methods. Endoscopic examination offers a range of advantages, and its future development and widespread adoption are expected. Conversely, the use of radiography can be anticipated to decline still further. However, it is unlikely that it will ever be possible to diagnose small intestinal disease using endoscopy alone, without any need for radiography. The small intestine is bordered on the proximal end by the esophagus, stomach, and duodenum, and on the distal end by the large intestine, and is the longest organ in the human body. These anatomical characteristics mean that it is no easy task to observe the small intestine in its entirety, even with the help of capsule and balloon endoscopy. Endoscopy may also encounter problems due to stenosis, adhesions, or unusual dispositions following surgery. From the disease perspective, although malignant conditions are less frequent compared with other parts of the gastrointestinal tract, chronic inflammatory disorders such as Crohn's disease and lesions associated with systemic disorders are common. In such disorders, grasping the entire picture and describing responses to treatment and the natural course objectively is more important than observing localized areas in detail. Radiography is clearly superior to endoscopy in terms of grasping the entire picture and objectively describing areas or lesions. If imaging is performed properly and interpreted by a competent practitioner, radiography will still have an important role to play in the diagnosis of small intestinal disease. Mechanical advances have also improved visualization by CT and MRI, and these modalities have recently been used for procedures such as enterography and enteroclysis. Unlike regular radiography, these methods also provide information external to the lumen, and have the advantages of being performable even if intestinal tract obstruction is present as well as minimal invasiveness, meaning they will continue to hold important places in diagnostic imaging of the small intestine.

2.2 Radiography of the Small Intestine [1–3]

Small intestinal radiography may be broadly divided into the per-oral method, in which contrast agent is administered by mouth, and the per-tube method, in which it is administered via a probe placed deep into the duodenum (in the neighborhood of the ligament of Treitz) or otherwise injected. Another special method is selective contrast administration following endoscopy of the large or small intestine. In actual clinical practice, the condition of the patient, suspected disease, and pathology of existing disorders are taken into account, and a method is selected in accordance with the objectives of radiography. Table 2.1 shows the contrast agents used in different methods, and the associated advantages and disadvantages [1–3]. Radiography is indicated in most types of small intestinal disease, but the use of barium in radiography is contraindicated in patients with obvious intestinal obstruction or generalized peritonitis.

2.2.1 Per-Oral Method

This can be performed simply to look for small intestinal lesions following gastric fluoroscopy, or with the small intestine as the sole target. In the former case, the objective of radiography is to identify gastric lesions and undertake detailed investigation, with the small intestine as the subject

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Table 2.1 Comparison of methods of small intestinal radiography

	Contrast agent, etc.	Advantages	Disadvantages
1. Per-oral method	50–100 w/v %	Simple, minimally invasive	Poor visualization of small lesions
	200–300 mL	Can be used for screening	Easily affected by conditions
2. Per-tube method	50–100 w/v %	Capable of visualizing extensive lesions	Invasive (probe insertion)
(a) Double-contrast method (b) Herlinger's method	250–400 mL + 600–800 mL air	Good visualization of small lesions	Accuracy depends on operator
	70–90 w/v %	Short radiography time	Poor visualization of small lesions
	250–300 mL + 1.5-2.0 L 0.5 % methyl cellulose	Easy separation of loops of small intestine	Inferior visualization of lower ileum
3. Retrograde ileography	50–100 w/v %	Capable of visualizing intrapelvic lesions	Pain (due to insertion of endoscope into small intestine or large intestine), invasiveness
	100–250 mL + 200–500 mL air	Enables evaluation of proximal side of stenoses through which an endoscope is unable to pass	Complex procedure

Modified from Nakamura et al. [1], Yao [2]

of secondary observation. This discussion focuses on the latter case.

For barium, 200–250 mL of a 50–100 w/v % suspension is used. In our department, we normally administer 250 mL of 100 w/v % barium by mouth. Because of individual differences in transit time through the small intestine and the area to be investigated, however, this must be adjusted for each patient. A basic principle common to all small intestinal radiography is to separate the loops of small intestine as far as possible and eliminate overlap, to improve radiographic accuracy. In particular, as barium-filled and compression images are the main types of image with this technique, it is important for the small intestine to be completely filled with barium and for the loops of small intestine to be carefully compressed when searching. Different procedures are required for different areas to avoid overlapping of the small intestine. For the upper small intestine, a shallow left anterior oblique position is adopted, and observation and imaging are performed while the patient takes a deep breath. For the central small intestine, frontal imaging and a right anterior oblique position are adopted, and imaging is normally performed while the patient breathes in. In both cases, a small quilt may be used as necessary to apply an appropriate level of compression. The ileum within the small pelvic cavity and the terminal ileum are frequent sites of lesions, but are often difficult to separate. The use of sedatives and compression with a quilt are both effective, and clear separation can be achieved in many cases by putting the patient in the prone position and placing the quilt over the lower abdomen (Fig. 2.1a–c). Transanal air insufflation may also prove effective.

During fluoroscopy, or when interpreting images, it is important to focus on whether abnormal disposition edema, deformity, or stenosis is present. In particular, deformity is an important key to the identification of small intestinal disease. If a deformity is observed under fluoroscopy, applying pressure may permit some type of cause to be recognized in the surrounding area (Fig. 2.2a, b). It is vital to be well acquainted with the characteristic images seen in each different disorder in order to interpret radiographic images. For example, the presence of the widespread spoke-like lesions seen in systemic lupus erythematosus (SLE) (Fig. 2.3), or the longitudinal aphthae evident in Crohn's disease (Fig. 2.4) in themselves comes close to a confirmed diagnosis. Detailed descriptions of the various disorders are given in Part II, "Specific Findings of Small Intestinal Lesions," and are therefore omitted here, but it is important to carry out any additional tests required for diagnosis in an efficient manner based on the results obtained by this method.

2.2.2 Per-Tube Method

Two different methods are used: the double-contrast method [1, 2] utilizing air; and Herlinger's method [3] in which barium transit is enhanced by the use of methyl cellulose. In both cases, a 12- to 16-Fr probe is used, which is normally inserted per-nasally as far as the neighborhood of the ligament of Treitz under fluoroscopy. This technique is unaffected by gastric juices or transit time through stomach, unlike the per-oral method, and has the advantage that the

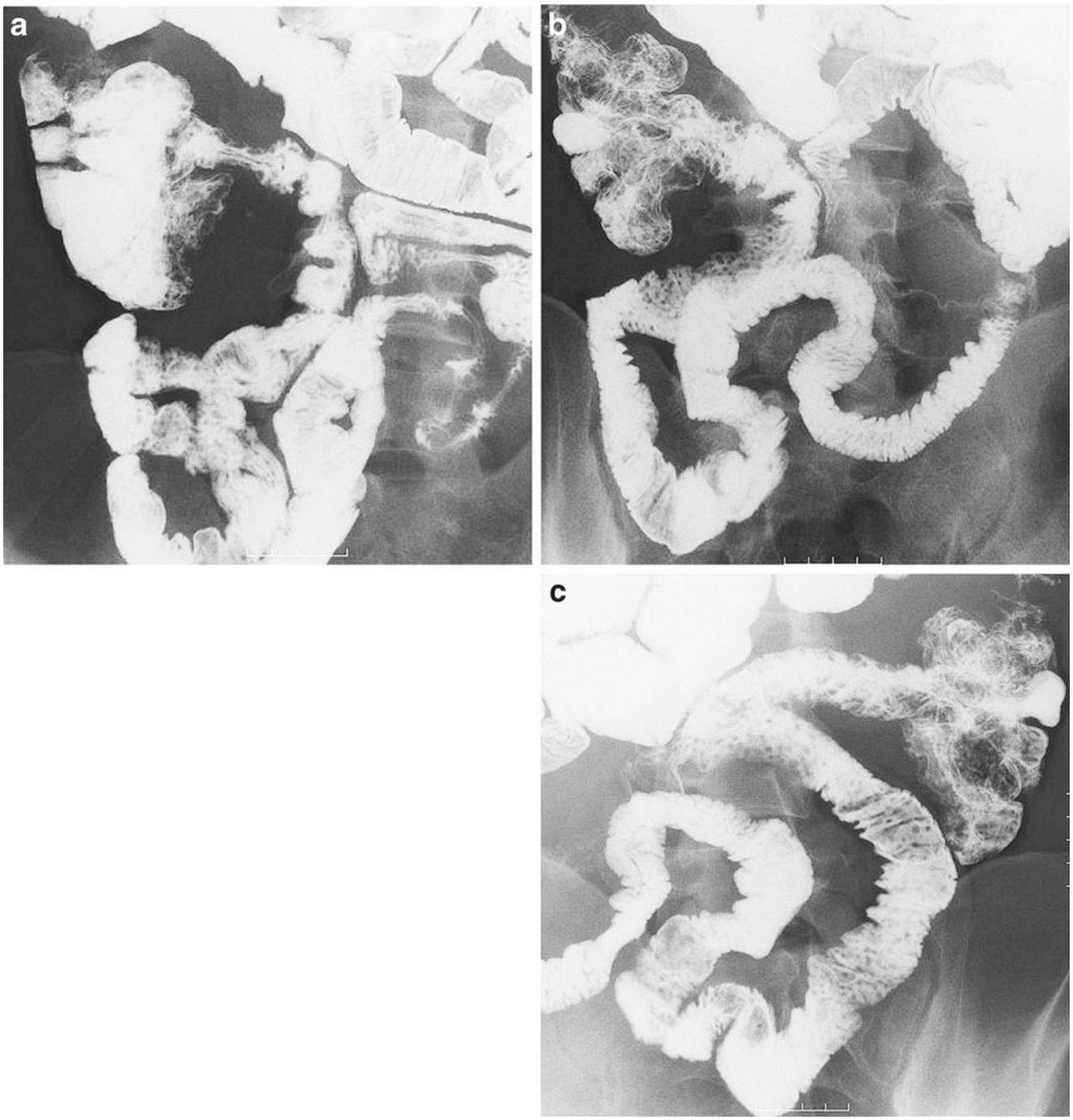

Fig. 2.1 Performance of per-oral small intestine contrast imaging. (**a**) X-ray image focusing on the lower ileum once the contrast agent has reached the terminal ileum. The intrapelvic small intestine is not separated. Peristalsis is present, making evaluation of the mucosal surface difficult. (**b**) Image obtained after intramuscular sedative injection and application of pressure with a quilt. The small intestine within the pelvis is almost completely separated, and lymph follicles are visualized in the terminal ileum. (**c**) When imaging is performed with the patient in the prone position and a quilt placed on the abdomen, the small intestine within the pelvis is completely separated. This image can be interpreted as showing the presence of multiple lymph follicles, restricted to the terminal ileum

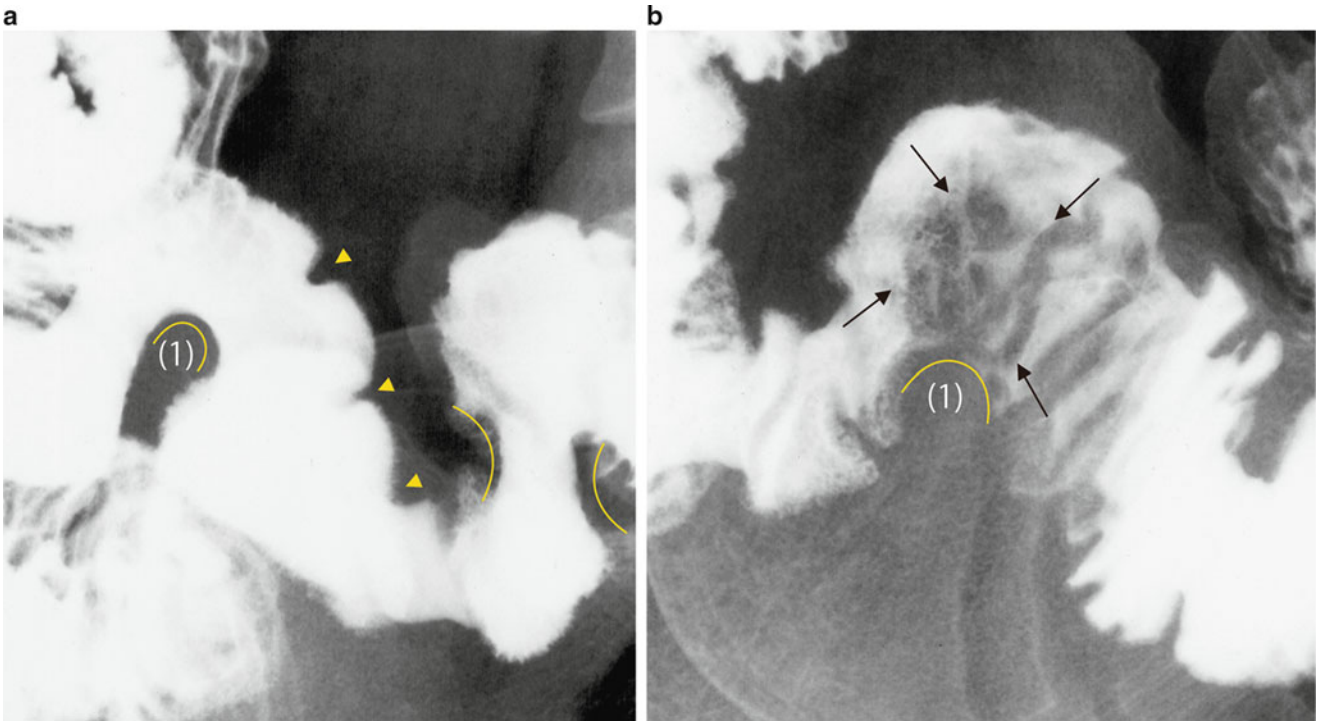

Fig. 2.2 Use of compression to visualize findings of deformity. (**a**) Multiple deformities of the ileum seen in chronic non-specific multiple ulcers of the small intestine (CNSU). The barium-filled image shows indentations of different sizes within a small area of the ileum (the area marked (*1*) is a comparatively severe indentation). (**b**) When the severe indentation marked (*1*) on the barium-filled image was carefully compressed, ulcerative lesions with mild activity and slight protrusion were visualized in the surrounding area (*arrows*)

Fig. 2.3 Small intestinal lesions in SLE. Diffuse, spoke-shaped lesions are evident across a wide area from the jejunum to the ileum. This finding is characteristic of the enteritis seen in SLE

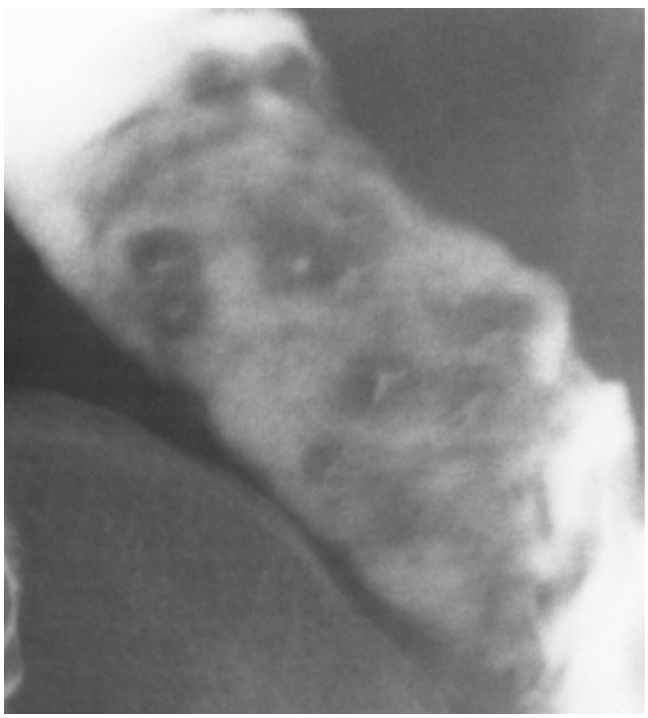

Fig. 2.4 Visualization of small aphthae by compression. Multiple aphthae of the ileum seen in Crohn's disease. Aphthae with a prominent pattern of protrusions are visualized in this compression image

Fig. 2.5 Double-contrast image of longitudinal ulceration. Longitudinal ulceration of the ileum seen in Crohn's disease. Double-contrast images have been obtained over a wide area from the lower ileum to the terminus of the ileum, and the lesions are clearly visualized

volume of barium can be adjusted while its passage through the small intestine is observed.

2.2.2.1 Double-Contrast Method

The double-contrast method is capable of visualizing tiny lesions in the small intestinal mucosa over a wide area, and is therefore suited to detailed investigations (Fig. 2.5). The barium concentration is varied as appropriate, but in general is around 50–100 wv %, with 250–300 mL often used. In our department, we place the patient in the left lateral decubitus position or a steep right anterior oblique position, and normally start with an initial introduction of 100–150 mL of 80 wv % barium. We then move the patient to a position from supine to left anterior oblique and observe the passage of the barium, adding a further 100–200 mL. As increasing the amount of barium makes it more difficult to obtain double-contrast images over a wide area, it is preferable that the terminus of ileum be reached with a volume of around 300 mL if possible. We perform the procedure while massaging the barium manually toward the distal end, but as barium degrades if this takes too long, we also administer water or inject metoclopramide (Primperan®) if necessary to speed the process along. Air insufflation is initiated after barium has reached the terminal ileum. To start with, 200–300 mL is injected, and movement of the air toward the distal end is monitored. A further 100–200 mL is then injected while the position of the patient is repeatedly varied, until the air reaches the terminal ileum. Under favorable conditions, double-contrast images can be obtained across a wide area of the small intestine, but there are always at least a few points at which the barium pools and continues to fill the intestine, or where it has been preceded by air and barium adhesion is insufficient. It is therefore necessary to adjust the procedure to enable clear visualization by double-contrast imaging of the location where visualization is most desired (Fig. 2.6a, b). Once the air has reached the terminal ileum and the target location contains sufficient air, a sedative is administered (normally an intravenous injection of 1-2A hyoscine butylbromide (Buscopan®) and imaging is performed. It is no exaggeration to state that the quality of radiographic films is determined by the timing of sedation, and this therefore requires care.

Interpretation of double-contrast images is basically the same as for the per-oral method, but there is a greater possibility of obtaining information on matters such as tiny bumps and patterns on the mucosal surface (Fig. 2.7), abnormal disposition of Kerckring's folds (Fig. 2.8), and the degree of deformity (when extended). Because lesions that go unnoticed during screening may be picked up during image interpretation, imaging should be performed for areas in which lesions frequently occur for the suspected disease while varying body positions and angles.

2.2.2.2 Herlinger's Method [3]

The greatest advantage of this method is that radiography can be completed during a short space of time. Methyl cellulose is used to speed up passage of the barium, which is effective in reducing the time required and preventing loops of small intestine from overlapping. Around 250–300 mL of barium of around 50–100 wv % concentration is used. When 1.5–2.0 L of 0.5 % methyl cellulose is introduced immediately after barium introduction, sequential double-contrast images can be obtained from the proximal end of the small intestine. Visualization of lesions, however, is poor compared with both good compression images obtained by the per-oral method and double-contrast images obtained by utilization of air (Fig. 2.9). The barium also degrades the closer it approaches the distal end of the ileum, and this method is therefore not generally used.

2.2.3 Retrograde Ileography

One disadvantage of double-contrast imaging is the difficulty of visualizing the intrapelvic small intestine and the terminal ileum. Barium frequently fails to reach these locations even after some time has passed, or becomes denatured, reducing the quality of radiography. Barium may also fail to flow smoothly, making double-contrast images difficult to

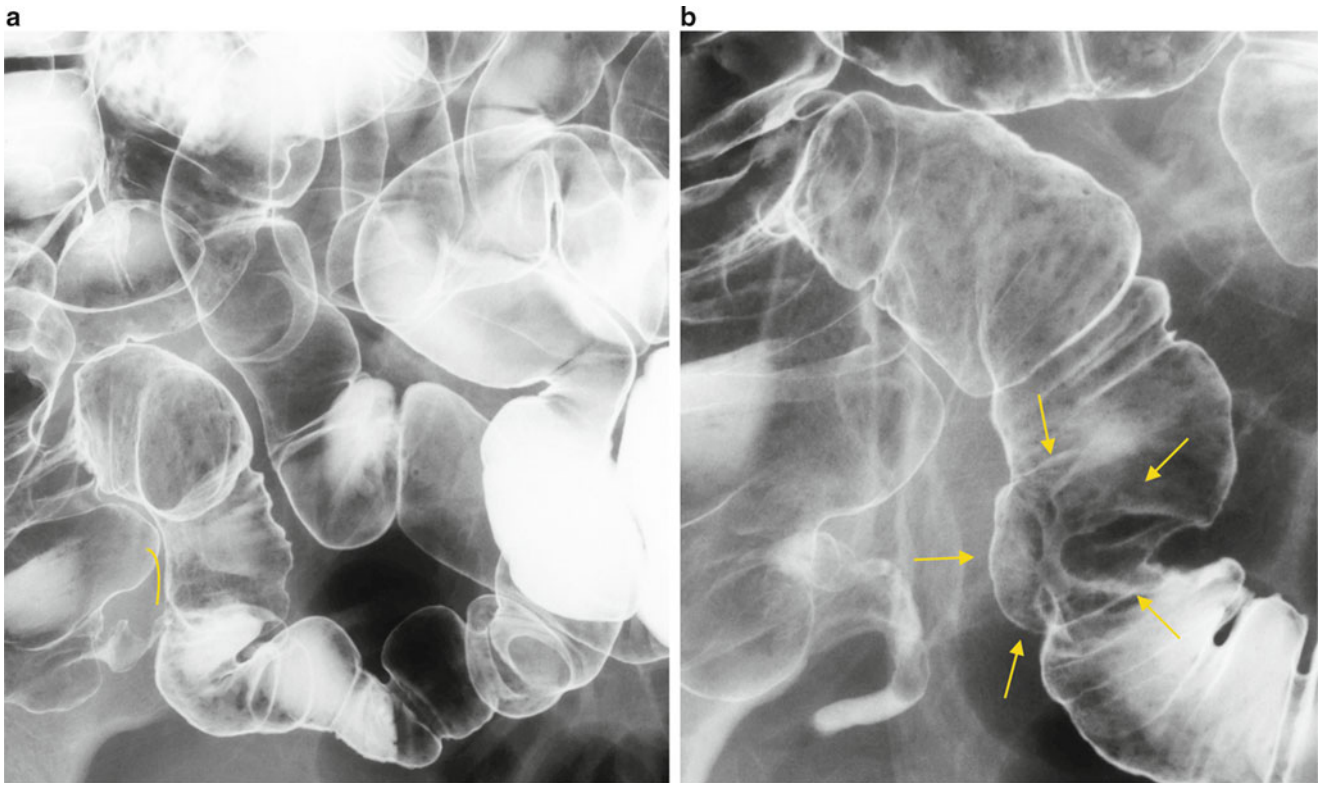

Fig. 2.6 Double-contrast imaging in practice. (**a**) Double-contrast imaging focusing on the lower ileum. Barium is pooled in some areas, and there are overlapping loops of bowel. A lesion of the terminus of the ileum was originally suspected in this case, so radiography focused on that area, and a sclerotic area was noticed during scanning. (**b**) When imaging was performed from a different angle, a somewhat bumpy concave lesion was visualized (*arrows*). Non-steroidal anti-inflammatory drug (NSAID)-induced enteropathy was diagnosed on the basis of the patient's history of NSAID use, biopsy results, and the fact that improvement was observed after medication was discontinued

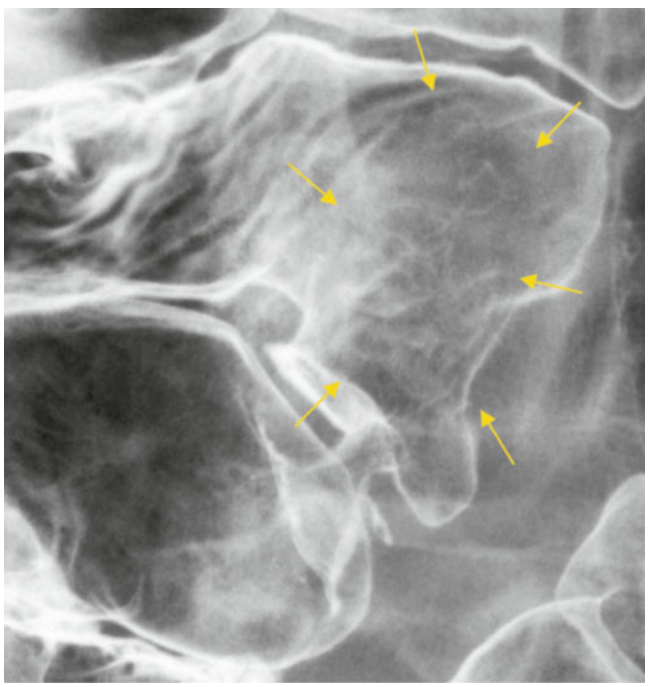

Fig. 2.7 Double-contrast image of small intestinal tuberculosis. Ileal stenosis seen in intestinal tuberculosis. Kerckring's folds have disappeared on the proximal side of the stenotic area, and the mucosal surface is roughened (areas of atrophic scarring). Shallow depressions can be seen in the same area (*arrows*)

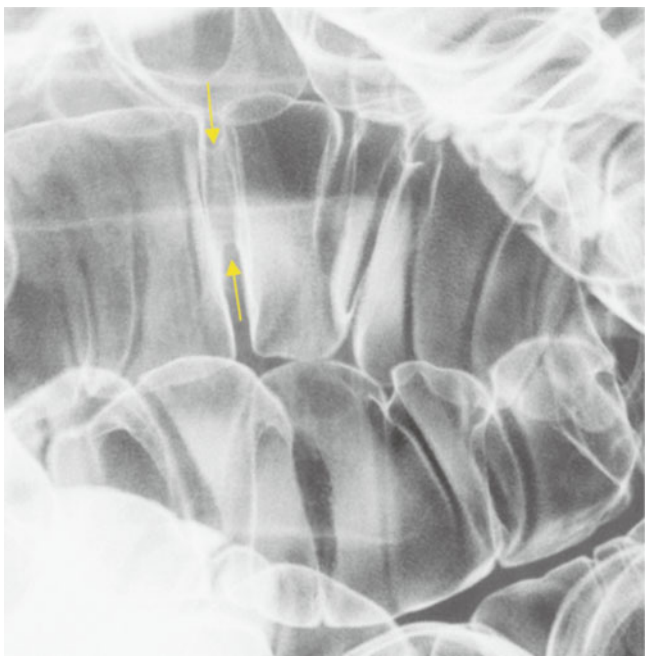

Fig. 2.8 Annular stenosis seen in NSAID-induced enteropathy. Abnormal Kerckring's folds seen in NSAID-induced enteropathy. The disposition of folds is inconsistent, with uneven spacing and width. Mild membranoid stenosis is also evident (*arrows*)

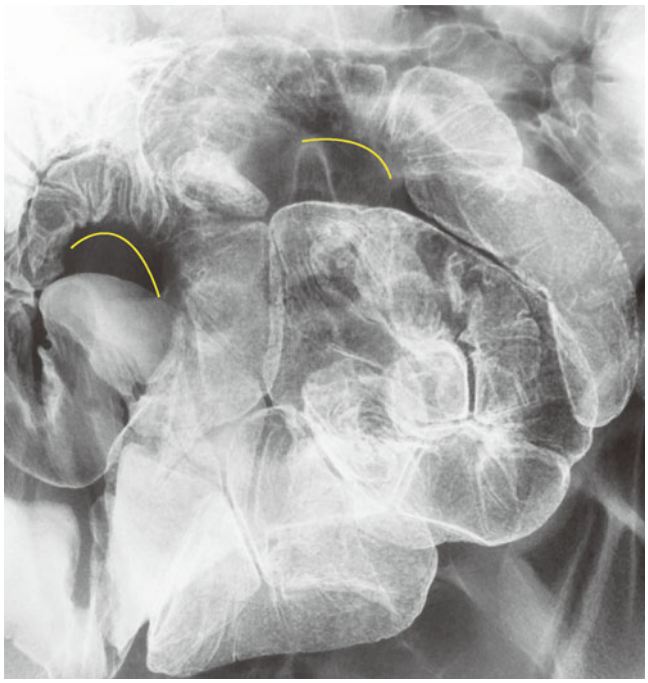

Fig. 2.9 Herlinger's method. Small intestine contrast image obtained by using Herlinger's method from a patient with Crohn's disease during remission (after total parenteral nutrition therapy). Longitudinal ulcerative scarring and lateral deformity can be seen, but dilution and degradation of the barium mean that the properties of the mucosal surface cannot be determined

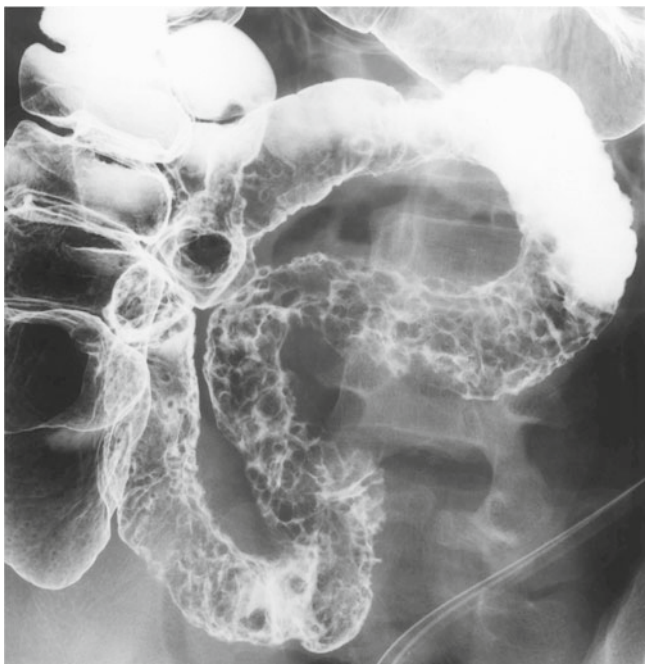

Fig. 2.10 Cobblestone appearance of the ileum visualized by retrograde ileography. Retrograde ileography image taken following on from colonoscopy. The typical cobblestone appearance of Crohn's disease is evident mainly from the terminal ileum to the intrapelvic ileum, together with lateral deformity

obtain, and an inability to separate loops of small intestine despite changing positions, applying pressure, and taking other measures is also common. Retrograde ileography has been devised as a selective contrast method to compensate for these disadvantages of double-contrast imaging. The method was formerly performed following colonoscopy [4], and involved: (1) inserting a lower gastrointestinal endoscopy scope as far as the terminus of the ileum via a sliding tube, and placing a guidewire via the forceps port; (2) withdrawing the scope, and inserting a contrast tube along the guidewire left inside the sliding tube; (3) after the contrast tube had been placed in the terminus of the ileum, inflating the balloon at its tip; and (4) using barium and air from the tip of the tube for selective contrast of the ileum. This method enables high-quality double-contrast images to be obtained using comparatively small volumes of barium and air even for the intrapelvic small intestine, which is difficult to separate (Fig. 2.10). The complexity of using a sliding tube, however, as well as the difficulty of inserting and placing the contrast tube, mean that this method frequently ends unsatisfactorily. In recent years, the use of balloon-assisted endoscopy (BAE) has become widespread, facilitating endoscopic observation of the small intestine and resulting in something of a decline in the significance of conventional retrograde ileography. BAE, however, is also limited in its range of observation in cases of stenosis or severe adhesions that do not permit passage of the scope, and difficulties in assessing lesions are frequently encountered, particularly in inflammatory disorders such as Crohn's disease. In such cases, many institutions introduce a water-soluble contrast agent (such as diatrizoate meglumine (Gastrografin®)) via the forceps port during BAE as a simple way of performing contrast. Good double-contrast images cannot be obtained, however, and investigation by this method frequently ends unsatisfactorily. The authors have devised a special probe for small intestinal radiography (made of polyvinyl chloride, which slides easily and is strong and flexible), and have reported the value of a new technique of retrograde ileography that improves on the conventional method [4]. This technique utilizes the overtube used in balloon endoscopy to enable safe, more selective contrast, and renders the guidewire unnecessary due to the improved probe, providing major improvements to the disadvantages of the conventional method (Fig. 2.11a–d). This approach can also be used following BAE via the peroral approach, and adapted for the jejunum or upper ileum. It may be necessary in future to develop investigative frameworks that utilize BAE and radiography in a complementary fashion, including this technique.

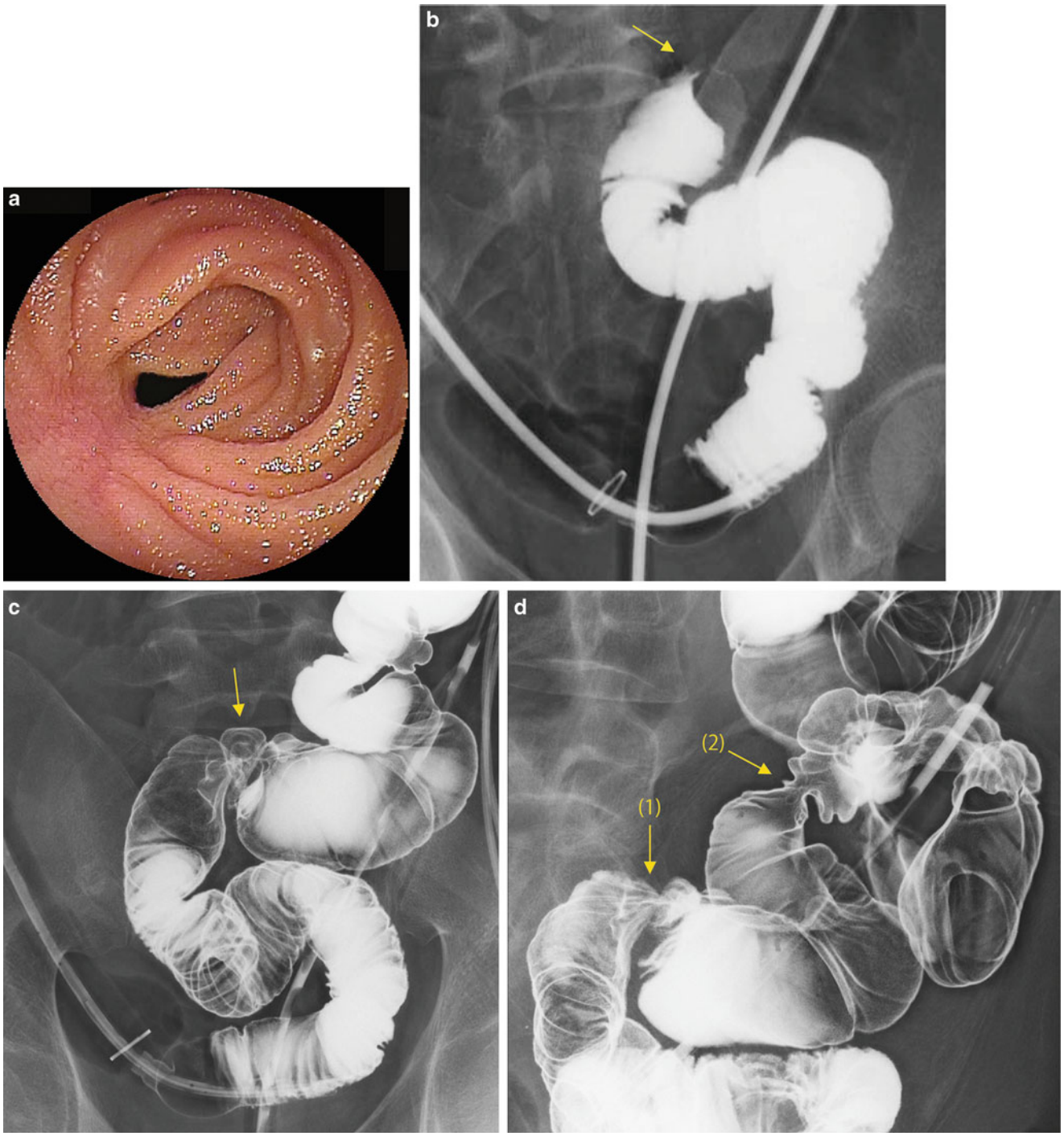

Fig. 2.11 Practice of retrograde ileography using double-balloon endoscopy. (**a**) Double-balloon endoscopy was performed via a per-anal approach in a patient with Crohn's disease, but stenosis prevented viewing any further toward the proximal end. (**b**) A contrast tube was placed on the tip of the over-tube, and 100 mL of barium introduced. The site of stenosis (*arrow*) observed endoscopically can be seen. (**c**) After the barium had been observed to flow in retrograde fashion through the site of stenosis (*arrow*), a total of 250 mL of air was slowly introduced. (**d**) Double-contrast observation of the proximal side of the site of stenosis (*1*) showed not only deformation of the intestinal tract, but also a second stenosis (*2*). Endoscopic balloon dilatation was performed the following day, enabling surgery to be avoided

2.3 CT and MRI Diagnostics

In recent years, the development of MDCT has led to dramatic improvements in spatial separability [5, 6]. It is now possible to visualize the gastrointestinal tract clearly by means of CT. Advances in the computers used for data-processing have also enabled detailed multiplanar reconstruction (MPR) based on the information acquired from CT. As CT is minimally invasive, this modality can be applied even when serious conditions such as intestinal obstruction or perforation are suspected (Fig. 2.12). In the field of small intestinal disease, CT is used for a wide range of indications, including obscure gastrointestinal bleeding (OGIB), suspected small intestinal tumor, and inflammatory bowel disease of unknown cause. In some institutions, CT enterography (Fig. 2.13a, b) is performed by filling the small intestinal lumen with a negative contrast agent such as air, water, or polyethylene glycol solution (PEG) or a positive contrast agent (including iodine and barium) to produce three-dimensional images [7–10]. Compared with small intestinal radiography, CT requires less expertise on the part of the practitioner. It can still be performed even if passage is obstructed, and has the advantage of providing information about the intestinal wall and areas outside the digestive tract. However, it is not possible to evaluate tiny bumps and depressions on the mucosal surface. CT also has the disadvantages that visualization of a target location may not be possible, depending on conditions, and that time is required for image production.

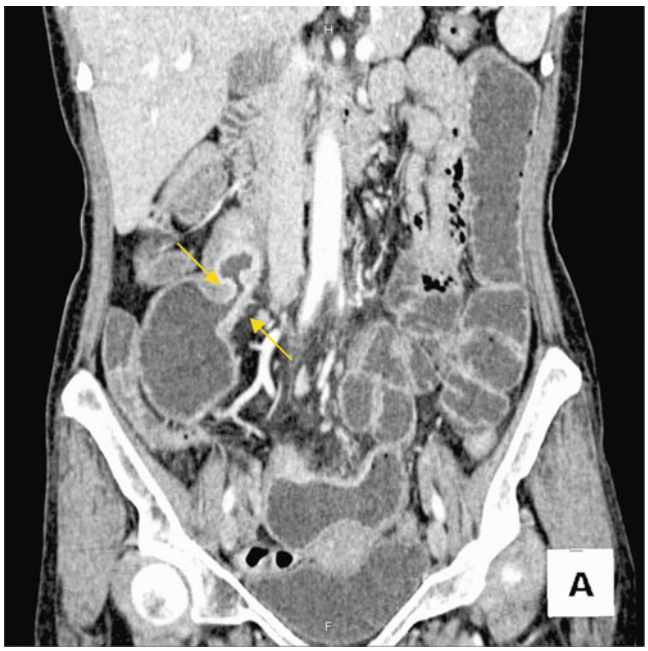

Fig. 2.12 Abdominal CT MPR image. MPR image of a patient with Crohn's disease and intestinal obstruction. The small intestine is visualized to a comparatively wide extent due to the backing up of intestinal fluid. Stenosis of the ileum is evident, with thickening of the intestinal wall, and the intestinal tract is dilated on the proximal side. This was regarded as the culprit lesion

Thanks to advances in MRI equipment that have reduced the time needed for imaging, this modality can now also be applied to small intestinal disease in the same way as CT. Although MRI has many similarities with CT in terms of imaging of the small intestine, its features include superior concentration resolution and the fact that no radiation exposure is involved. In Europe and the United States, there is a tendency to prefer MRI to CT or small intestinal radiography, both of which require radiation exposure, in chronic inflammatory conditions such as Crohn's disease that require repeated scanning. Studies comparing MRI with endoscopy have also been reported [7, 8] and MRI may be used with increasing frequency in future, particularly in Europe and the United States. MR enterography is also regarded as useful [9, 10] as, unlike CT enterography, it offers advantages such as dynamic evaluation, and there are hopes for its future development.

CT and MRI are expected to undergo further advances in engineering in future. At present, MPR imaging, which does not require the introduction of air or liquid, is the main form of imaging in all but a few institutions. There is no sign of the widespread adoption of CT enterography or MR enterography and the methods of dilatation of the small intestine also differ between institutions. Establishment of consistent methods to both enable clear visualization of the small intestine and offer superior simplicity and safety would thus be desirable.

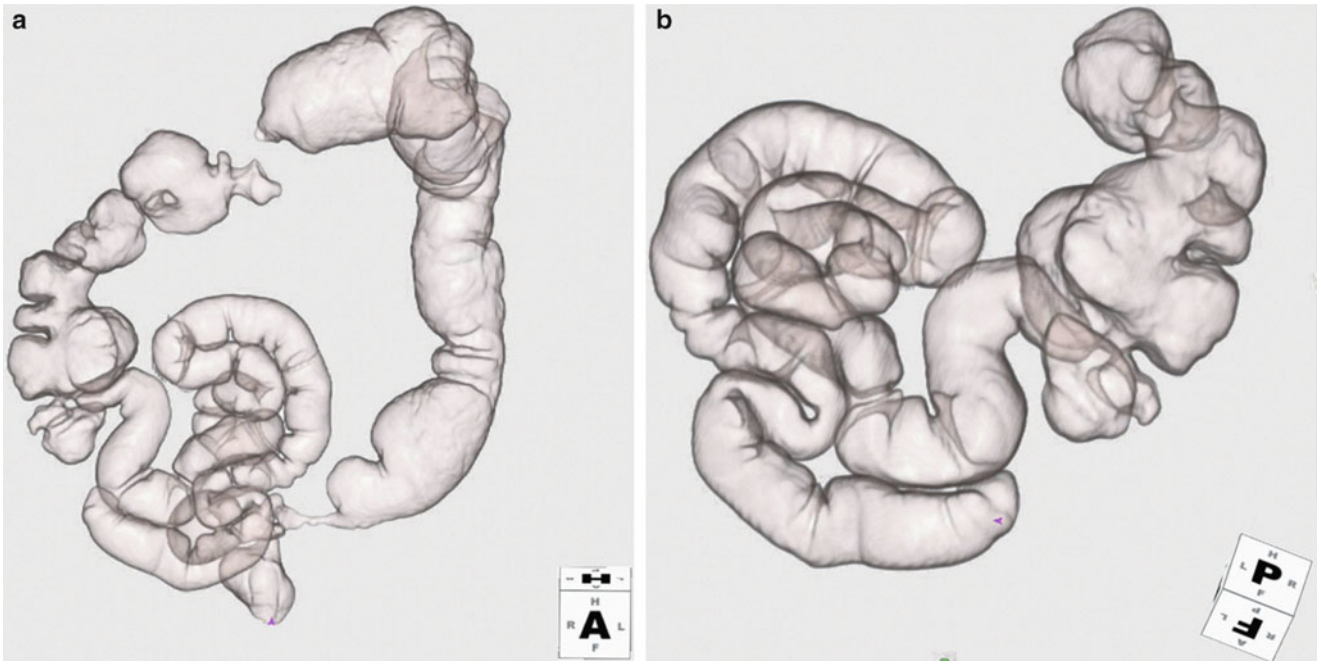

Fig. 2.13 Enterocolonography of large intestine stenosis. (**a**) Enterocolonography image of a patient with Crohn's disease with stenosis of the sigmoid and transverse colon. Air was introduced perianally, and the intestine was observed from the lower ileum to the colon. (**b**) There is clear visualization from the intrapelvic ileum to the terminal ileum, and this can be adjusted to any angle. Active lesions, fistulae, and the like can be ruled out, although it is not possible to evaluate small lesions such as aphthae

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