

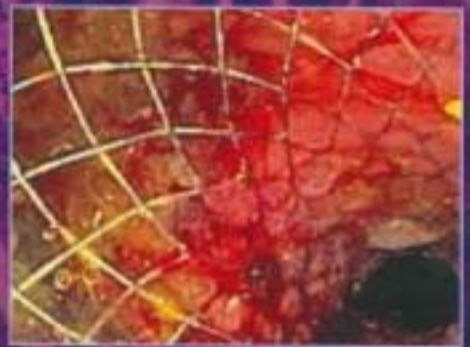
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Colonoscopy

Principles and Practice

EDITED BY
**Jerome D. Wayne, Douglas K. Rex &
Christopher B. Williams**



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Colonoscopy

Principles and Practice

Thanks to our wives—Meg Waye, Leslie Rex and Christina Williams—for their support in yet another time-consuming enterprise. Thanks also to those to whom we have taught colonoscopy and the many on whom we have performed colonoscopy. We have learned so much from you all, as we have from our friends the contributors to this book.

Colonoscopy

Principles and Practice

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Preface

Flexible endoscopy of the colon was introduced in 1963, six years after Basil Hirschowitz developed the fiberoptic gastroscope. Since the first attempts at intubating the entire colon, this procedure has now become a primary diagnostic and therapeutic tool for evaluation and treatment of colonic diseases. Using the ability to inspect, obtain tissue samples and remove colon polyps, colonoscopy has expanded our knowledge of the natural history of colonic neoplasia. Multiple large studies have shown that removal of benign adenomas will prevent colorectal cancer. Because of the increasing awareness of colorectal cancer being a common cause of death from cancer throughout the world, and the possibility to interrupt the adenoma to carcinoma sequence by polypectomy, the volume of colonoscopies around the world continues to be driven upward by widespread acknowledgement of the effectiveness of the procedure.

Colonoscopy is not merely a tool in the hands of a practitioner, but it is a discipline with an infrastructure built upon many areas of medicine, including internal medicine, the general practice of medicine, and gastroenterology in particular, as well as surgery, pathology, radiology, pediatrics, and molecular biology. The expanding horizon of colonoscopy was the stimulus for us to organize a new comprehensive textbook on this field. The chapters in this volume address every aspect of colonoscopy, and its interface with all of the other sections of medicine.

The editors of this book learned and indeed developed many techniques of colonoscopy when imaging was limited to the barium enema and there was no capability to visualize the intraluminal topography in the intact patient. This book represents the "state of the art" in colonoscopy. However, colonoscopy is a procedure in evolution and investigators around the world are

actively pursuing improvements. Colonoscopy is a relatively new discipline, and although tremendous strides have been made since its introduction, there are many unanswered questions such as how can we improve training in colonoscopy? Can bowel cleansing be made less toxic and less miserable? Can colonoscopy be made painless? Can we improve the detection of neoplasia? Can we make colonoscopy faster? Can we eliminate complications from both diagnostic and therapeutic procedures? The answers to these questions will determine the future of colonoscopy and its ultimate impact on colorectal disease. We look forward to the continuing pursuit of answers to all questions concerning colonoscopy, and urge future generations of colonoscopists to continue the quest for knowledge and add more information to each of the chapters in this book.

For many colonoscopists and certainly for ourselves, colonoscopy is not considered as part of a job, but rather as a passion. Every colonoscopy presents an opportunity to improve a patient outcome, to learn, often to reassure, to identify new questions and problems both clinical and scientific, and to enjoy the application of skills both manual and cognitive in nature. Thus, to edit a volume on colonoscopy has been for us a particular pleasure. We extend our most sincere thanks to the authors who contributed to this volume. The list of authors includes the world's most foremost practitioners from every aspect of medicine. Their expertise, diligence, and friendship are deeply appreciated. On behalf of all the authors, we thank the many, many thousands of patients who have trusted us and been our teachers.

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Chapter 1

History of Endoscopy in the Rectum and Colon

H. Niwa, Y. Sakai & C.B. Williams

Introduction—from rigid endoscopes to colonofiberscopes

Before endoscopes for colon examination achieved the remarkable technological progress that we see today, there was a long period when rigid proctosigmoidoscopes were used for examination of the distal half of the sigmoid colon and rectum.

Intracolonic photography of colonic mucosa, using a modification of the gastrocamera described as “sigmoidocamera” or “colonocamera,” was briefly used in Japan. Diagnosis was by examining pictures of the colonic mucosa obtained with the colonocamera.

Compared to today’s latest technically advanced colonofiberscopes and colonovideoscopes, the rigid hollow tube sigmoidoscopes were primitive and gave a limited view, but nonetheless had significant clinical value, as disease of the large bowel is most commonly found in the distal half of the sigmoid colon and rectum. Experimentation on these predecessors provided the foundations for endoscopic diagnosis made possible by use of current colonofiberscopes and videoscopes.

Any history of colonoscopy must take such devices into account, so this chapter therefore covers the topic of these early inventions.

Rigid endoscopes

Primitive specula

It was in the time of Hippocrates that people first attempted to observe inside the human body. An instrument called a speculum was used to examine the rectum and vagina, and with it cautery treatment of hemorrhoids was carried out. Primitive instruments that have similar structure and function to today’s anoscopes and coloscopes were discovered in the ruins of Pompeii, buried under volcanic ash after the eruption of a volcano in the 1st century AD (Fig. 1.1). Because the light source for a speculum was sunlight, observation was limited to areas at the openings of the body. After these primitive instruments, no significant progress was made until the 19th century.

Reverie of endoscopy

A Japanese writer predicted today’s endoscopes as early as 200 years ago, not inventing an actual endoscope, but imagining a kind of telescope closely resembling early rigid endoscopes. In the book called *Chikusai-Rou-Takara-no-Yamabukiuro*, published in 1794 in Japan by the author Zenkou Tsukiji, is a picture (Fig. 1.2) in which Dr Chikusai, the main character of this story, tries to look inside the human body through the navel with his special telescope. He examines the organs in the chest through the mouth, the organs in the epigastrium through the navel, and the organs in the hypogastrium through the anus, both to make a diagnosis and decide what treatment is appropriate. He enjoys a reputation as a discerning doctor and makes a lot of money.

Of course, this is not what really happened, but just an imaginary story. To mention the background which enabled the author to think of the story, mass importation of eyeglasses from Holland and China started in the mid 1600s; toward the end of 17th century production of eyeglasses started in Japan and in 1793, the year before publication of the book, a 3-m-long astronomical telescope had been produced in Japan.

Early endoscopes

Although the first telescopes were developed in Europe in the early 17th century, it was Philipp Bozzini who first actually tried to observe inside the human body, through a rigid tube without optics. He developed an apparatus called the light conductor (Lichtleiter) in 1805, which he used in his attempt to observe rectum, larynx, urethra, and upper esophagus [1]. Bozzini’s father was originally from Italy, but fled from his country after a duel. Bozzini was born in Mainz, Germany in 1773 and started to study medicine in this city, moving to Frankfurt in 1803. He was a man of a wide range of cultural accomplishments including medicine, mathematics, engineering, and the fine arts [1].

The main body of the light conductor was a rectangular box like a lantern (Fig. 1.3), used as the light source unit [1–3]. A replica of the light conductor is displayed in the Museum of Medical History in the Institute of



Fig. 1.1 (a) Roman speculum from the ruins of Pompeii in 79 AD and (b) anorectal dilator supplied with early Olympus colonoscopes in 1970 AD.



Fig. 1.2 Observing the inside of a patient's abdomen—a Japanese fantasy (1794 AD).

Medical History, the University of Vienna. It had round openings on the front and back walls of the light source box. The box was partitioned lengthwise into two areas, in one of which a candle was placed as the light source, with a concave mirror behind it. The position of the candle flame was kept unchanged with a spring. Observation through the unlit partition was from the back window of the light source unit, a speculum having been attached to the front opening. Several different specula were prepared for observation of different organs. For

inspection of larynx, pharynx, and esophagus, a special speculum was developed on the tip of which a concave mirror and a flat mirror were attached. The concave mirror was used for light transmission and the flat mirror for viewing the target area [4].

Using this device, Bozzini conducted experiments on corpses and patients. On December 9 in 1806, a public demonstration on corpses using his light conductor was held during a meeting of the Imperial Josephs Surgical Academy in Vienna. The details of this experiment are stored in archives in Vienna and later recorded in the paper by Lesky describing observation of the rectum, vagina, and uterine cervix of the corpse. In a second gathering of the Academy in 1807, using an improved version, observation was carried out of the rectum and the vagina, as well as an approach from a wound in the abdomen of the corpse. The first attempt to apply the device to a living patient was made in the same gathering.

The building of Josephs Surgical Academy, where the public experiments were held by Bozzini, is now the Institute of Medical History, the University of Vienna. The Museum of Medical History and the Museum of the Endoscope are in this building as well.

Based on the achievement of these experiments, Bozzini published a book on his light conductor in 1807. However, the Faculty of Medicine of the University of

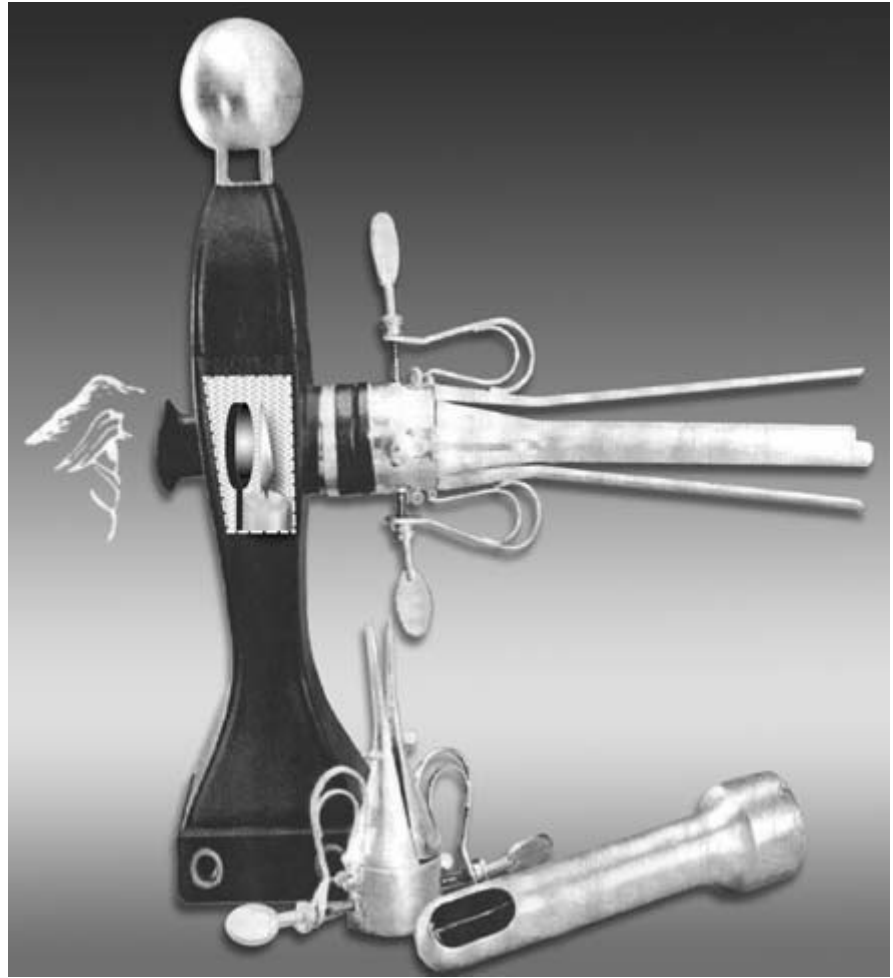


Fig. 1.3 Bozzini's "Lichtleiter" or light conductor (1706)—the dotted cutaway diagram shows the position inside it of the spring-mounted candle with a light shield behind it.

Vienna would not permit further study using the device. The authorities regarded it as nothing but a plaything, of no medical value but a "laterna magica in corpore humano." Use of the light conductor was forbidden, partly due to conflicts between the Surgical Academy and the University, but also due to the reluctance of the authorities to adopt anything new.

In 1826, Segales of France reported on a new method for examining inside the human bladder using a funnel-shaped metal tube, with a concave mirror and candle light as the light source. Fischer of America developed another cystoscope in 1827, while Avery of England developed an instrument designed for observation of urethra, bladder, vocal chords, and esophagus. Light for Avery's device was by reflecting candle light using a concave mirror. These achievements of our predecessors in development of cystoscopes and urethroscopes provided the foundation for development of gastrointestinal endoscopes, especially the open tube rigid proctosigmoidoscope.

In 1853, Désormeaux (1815–81) of France developed the first endoscope of practical value and called this

instrument an "endoscope" for the first time in history. Désormeaux utilized his instrument (Fig. 1.4) for diagnosis and treatment of urological diseases. The unit comprised a body tube and a light source unit. The light source was a gazogene lamp lit by firing a mixture of alcohol and turpentine. Inside the body tube, at its junction with the light source, was a mirror with a small hole in the center, which reflected the light provided by the source through the body tube and into the insertion part connected to end of the body tube. The diameter of the insertion part for urethra and bladder observation was about 6–8 mm. Observation was carried out from the small hole on the top end of the body tube. The body tube was freely rotatable around the axis of the connecting part, so that the light source unit would always stay vertical even though the main tube was moved. Désormeaux published a book in 1865 to summarize his achievements in observing urethra and bladder with the endoscope. In this book, he mentions that he succeeded in observing inside the rectum as well, although without details, and predicts that it should prove possible to observe inside the stomach.

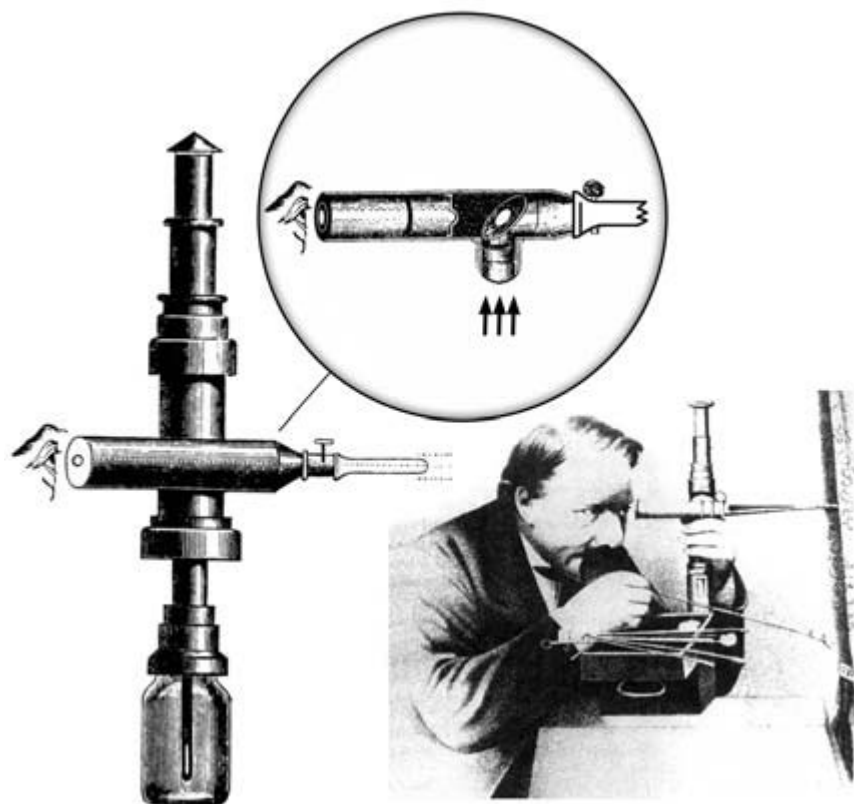


Fig. 1.4 Désormeaux's "endoscope" (1853)—with (inset) cross-section cutaway diagram showing the lensless view through a perforated mirror reflecting light from the source.

Désormeaux's endoscope was essentially a mere hollow rigid tube and did not have a lens in its optical system. It was Kussmaul who further developed Désormeaux's method and succeeded in making the first gastroscope in 1868. Kussmaul first tried observing the rectum and then the esophagus with Désormeaux's endoscope [5], succeeding in observing cancer of the upper esophagus. He then developed a new device with a longer insertion tube, as it was impossible to observe further than the upper esophagus with Désormeaux's endoscope.

It is said that Kussmaul got the idea of inserting a straight tube inside the stomach when he saw the performance of a sword-swallower. Happening to see the performer insert a straight rigid metal bar from his mouth into the esophagus, Kussmaul's assistant asked the performer to come to the university to carry out an experiment.

The gastroscope that Kussmaul made was a brass hollow tube of 47 cm in length and 1.3 cm in diameter, with two types of cross-sectional shapes, round and oval. No lens was used in the optical system. Although he succeeded in inserting the tube up to the stomach, the candle light source of Désormeaux's device was totally inadequate to supply enough light to illuminate all the way from mouth to stomach and this method had to be abandoned.

Leiter's rectoscope

Before the invention of the electric incandescent light bulb, it was known that bright light could be obtained by passing direct current electricity through a platinum wire, using a water-cooling system. This water-cooled electrical lighting system was applied to observation of the larynx in 1860s and subsequently to other endoscopes (Fig. 1.5). Nitze and Leiter made a cystoscope in 1879, and an esophagoscope and a gastroscope later on. Leiter, a Viennese optical instrument maker, developed a rectoscope with a similar light source, which appears in his catalogue, although it is not known whether it was actually used.

Modern proctosigmoidoscopes

With the introduction of Edison's electric incandescent bulb, the size of bulbs reduced. In 1886 Nitze and Leiter succeeded in developing a cystoscope with a miniature electric incandescent bulb at the tip, which became the basis for development of gastrointestinal endoscopes.

Nevertheless, this technology was not used for early proctosigmoidoscopes. In 1895 Kelly in the USA produced the first proctoscope of practical value [6]. It had a metal hollow tube, produced in various lengths, widening to the handle end except for one type which

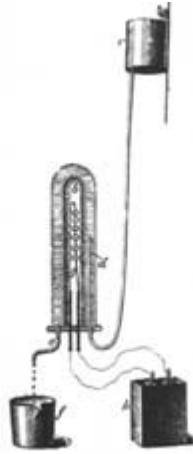


Fig. 1.5 "Stomatoscope" (1867, Breslau, Germany)—designed for oral illumination but also used up the rectum. Note the water-cooled electric lighting system.

had the same diameter through its length. There was an obturator for insertion and illumination was by a concave reflector, as used by otorhinolaryngologists. The rectum was well seen, but there was difficulty observing the proximal sigmoid colon with longer versions because of poor illumination.

In 1899, Pennington in the USA [7] sealed the eyepiece of the tube with a glass window and supplied air from a rubber ball to expand the sigmoid colon. He also inserted a small light bulb at the distal end for better illumination. In the same year, Laws used a thin metal rod with a miniature light bulb installed at the tip, inserted through the proctosigmoidoscope.

In 1903 Strauss in Germany followed the Laws' approach, developing a proctosigmoidoscope that distended the sigmoid colon with a rubber hand pump and safety bellows. This became the basis of commercially available Strauss-type proctosigmoidoscopes, which were very widely used until the arrival of fiber-sigmoidoscopes. Strauss proctosigmoidoscopes consisted of metal tubes 2 cm in diameter and of various lengths, inserted into the rectum or distal colon with an obturator in position. For observation the obturator was removed and a thin metal tube with a miniature light bulb inserted to the tip (Fig. 1.6). A magnifying apparatus was available that could provide six times magnified images, showing that there has been interest in magnification endoscopy for a long time. In 1910 Foges invented a proctoscope with a miniature light bulb installed at the eyepiece window. Another proctosigmoidoscope with a light source at the eyepiece end of the scope was developed by Yeomans in 1912 [8]. Illumination from an outside light source with a fiberoptic light guide is now widely used [9].

There are several lengths of rigid endoscopes for use in the rectum and sigmoid colon. Officially shorter

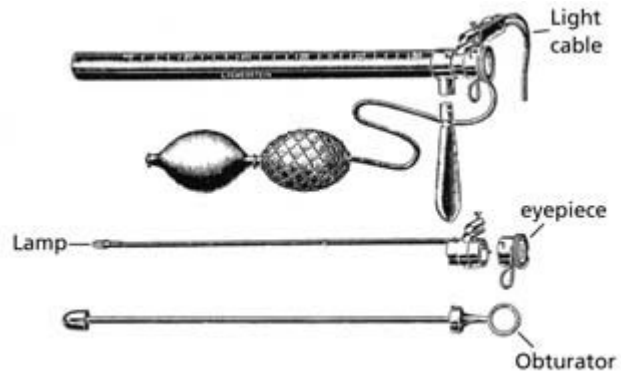


Fig. 1.6 Strauss type proctosigmoidoscope.

ones, for use in the rectum, are called rectoscopes or proctoscopes and longer ones, for use in the distal sigmoid colon, have been called sigmoidoscopes or proctosigmoidoscopes. However the terms rectoscope, proctoscope, sigmoidoscope, proctosigmoidoscope are effectively synonymous.

Sigmoidoscopy has been performed in various positions, in lithotomy, lateral decubitus or "chest-knee" position. It seems that Kelly was the first to carry out and emphasize the significance of chest-knee or "knee-elbow" position [6]. In this position air could flow into the sigmoid colon, with improved view.

Sigmoidoscope photography

Sigmoidoscopic photography was tried, for example using the Strauss sigmoidoscope with special apparatus for taking pictures. However it proved difficult to take good pictures through sigmoidoscopes until the early 1960s. Amongst other problems, the sensitivity of the reversal color film (Kodak) used for slides around 1960 was only ASA 10. Sufficient light was required, but this was difficult to achieve with the built-in sigmoidoscope bulbs available at this time. Therefore many solutions were tried, such as using multiple light bulbs or use of a high voltage light source. Picture-taking proctosigmoidoscopes were developed by Tohoku University in technical cooperation with a medical engineering company, Machida, and by Henning in Germany, using bulbs as the light source.

Apart from these types using light bulbs, Sakita, Niwa and their coworkers developed a different type of picture-taking sigmoidoscope in order to obtain better pictures in 1960. This used a Strauss type sigmoidoscope with tip light bulb for observation but a separate distal xenon lamp for photography. By integrating the xenon lamp and objective lens into the tip of this instrument, shutter speeds of 1/500–1/1000 were possible (Fig. 1.7). Figure 1.7(b) is a picture of a colonic polyp obtained with this instrument. Because the xenon lamp required high

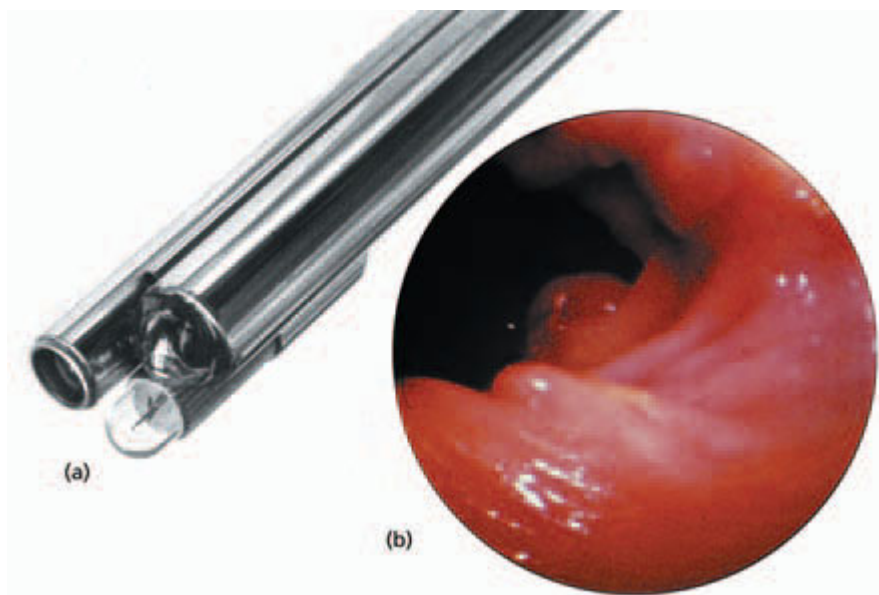


Fig. 1.7 (a) The tip of the optical tube for a picture-taking rigid sigmoidoscope, with (b) photograph of a colonic polyp.

voltage and other types of picture-taking sigmoidoscopes had poor illumination, these original picture-taking sigmoidoscopes gradually fell out of use. With the introduction of fiberoptic light guides sigmoidoscopic photography became more popular again, but colonofiberscopes and subsequently videoscopes have become the main means of taking pictures.

Special kinds of proctosigmoidoscope

Magnified three-dimensional proctosigmoidoscope

Special proctosigmoidoscopes allowing magnified three-dimensional observation of the rectal and colonic mucosa were used by Niwa in 1965 [10]. A special Kelly-type proctoscope (Fig. 1.8a) was coupled to a surgical stereomicroscope (Fig. 1.8b) on a stand (Fig. 1.8c). With this instrument, magnification of up to $\times 40$ was possible up to 15 cm from the anus, and up to $\times 64$ less than 10 cm from the anus. By this method, the surface of the normal rectal mucosa was observed to be transparent like gelatin, with thick blood vessels running horizontally underneath but also many thin vessels running vertically that could not be seen on conventional observation. With inflammation of the mucosa, the gelatinous transparency disappeared, with a red background and crypt openings showing up white. If toluidine blue was sprayed onto the surface of the mucosa, the pits became more obvious (Fig. 1.8c), which helped clarify the changes in the appearance of pit pattern in polyps or the mucosa of ulcerative colitis.

The method of dye spray in diagnosis has been used since the early days of otorhinolaryngology and gynecology. Besides Niwa's work using stereomicroscopy in gastroenterology, pontamine sky blue and toluidine

blue were used in 1961 for intraluminal microscopic observation of rectal mucosa by Yamagata and Miura [11], although the first referenced report of dye methodology in the field of gastroscopy was by Tsuda *et al.* in 1966 [12].

Intraluminal microscopy of rectal mucosa

Yamagata and Miura invented an intraluminal microscope for *in vivo* rectal mucosa. Observation using this apparatus was performed by first using a conventional sigmoidoscope, then inserting the intraluminal microscope through the sigmoidoscope in order to observe the pit openings of the rectal glands close up, the microscope tip being positioned immediately onto the target area. This device could provide between $\times 5$ and $\times 130$ magnified images of rectal mucosa surface by switching modes.

Development of intraluminal microscopy of the rectal mucosa (by Yamagata and Miura) or magnified three-dimensional observation of the rectal mucosa using stereomicroscopy (by Niwa) was in the days that the Japanese medical world was still under the influence of German medicine. German medical opinion was that inflammation of the colonic mucosa was accompanied by an intense inflammatory cell infiltration, which should not be described as ulcerative colitis but as "chronic idiopathic proctocolitis"; microscopy was expected to help diagnose and discriminate between the types of inflammation.

"High colonic" endoscopy

Another example of a special kind of sigmoidoscope, was one made by Regenbogen in Germany and pre-

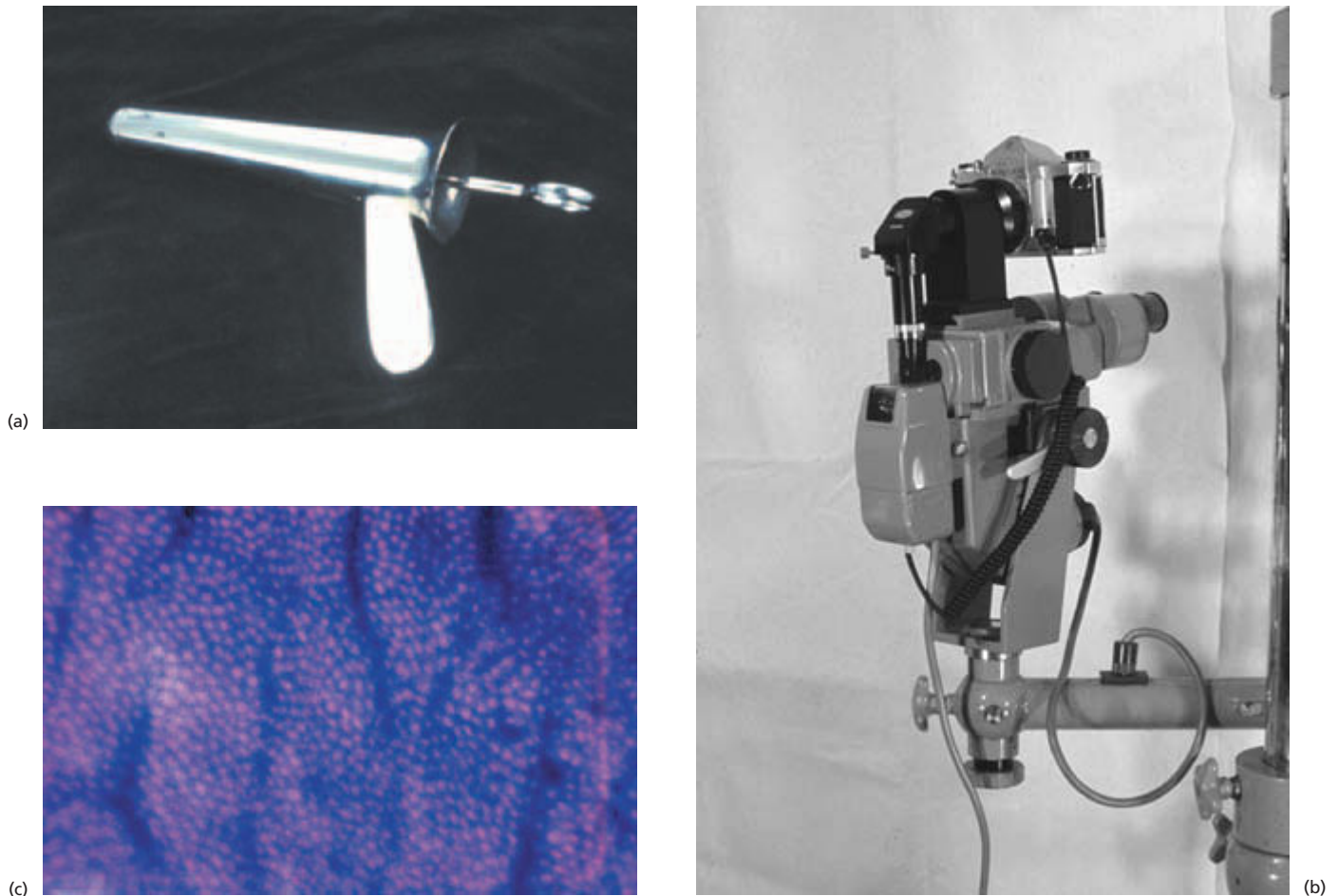


Fig. 1.8 Magnifying three-dimensional proctosigmoidoscope. (a) Scope body. (b) Surgical stereomicroscope. (c) Crypt openings of rectal mucosa with dye method.

sented at the First Congress of the International Society of Endoscopy in Tokyo in 1966. Using Regenbogen's sigmoidoscope it was possible to observe more proximal segments of the sigmoid colon (high colonic endoscopy) [13]. For this purpose, his sigmoidoscope had a rounded tip to help insertion round the sigmoid colon when there was acute bending or contraction. In order to assure insertion and observation of the proximal sigmoid further improvements were made (Fig. 1.9). Two slits in the body of the sigmoidoscope and a rubber covering allowed the atraumatic arms of an "extender" to open out of the slits. With the extender arms open at the tip end of the slit, the bowel fixed by the arms could be pulled back over the sigmoidoscope, rather as a glove is pulled over the fingers. The area observed depended on the anatomy of the bowel and the experience of the operator, but Regenbogen reported that he could observe at least 15 cm deeper than with an ordinary sigmoidoscope.

Some laughed at Regenbogen's report, questioning its benefits. However, since current colonoscopes are advanced into the proximal colon by straightening the bowel as much as possible, looking back at Regenbogen's report we can say that it actually anticipated some of the basis of current technique.

Sigmoidocamera and colonocamera

In 1929, Porges and Heilpern reported the "Gastrophotor" (Fig. 1.10), a pin-hole stereoscopic camera for use in the stomach and rectum. At the tip of Gastrophotor was an eight-pin-hole stereoscopic camera, allowing taking of pictures of a wide area of stomach or rectum. The Gastrophotor set, as supplied commercially, contained two instruments: one for the stomach (black shaft) and one for the rectum (red shaft). Using this apparatus, trials were made of taking pictures of the rectal mucosa, but there are no reports in the literature of its clinical use in the rectum.

The sigmoidocamera was first developed by Matsunaga and Tsushima in 1958, modifying the type II gastrocamera [14]. A conventional sigmoidoscope was first inserted into the sigmoid colon and the sigmoidocamera

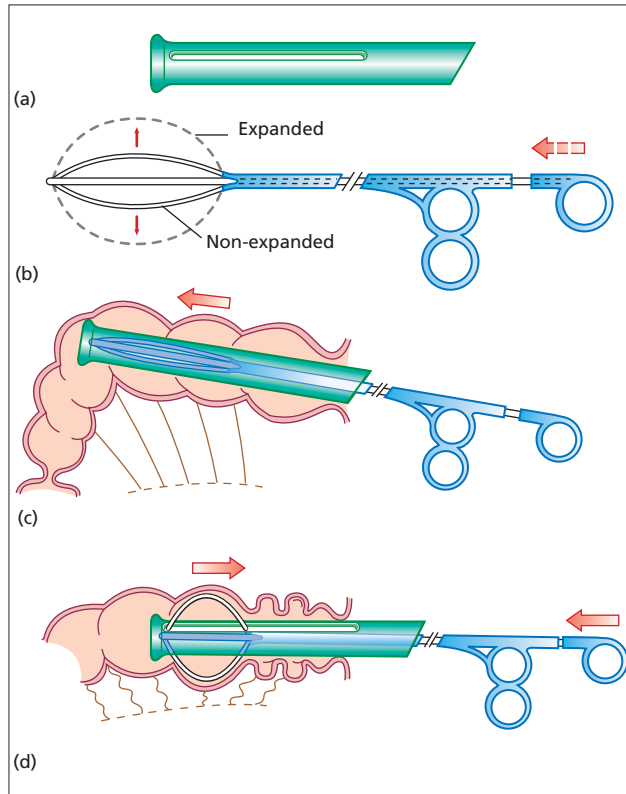


Fig. 1.9 Regenbogen's sigmoidoscope. (a) Slotted end of tube. (b) Wire 'extender' mechanism, closed and open. (c) Sigmoidoscope insertion stretches and angulates sigmoid colon. (d) Expanded 'extender' grips and straightens colon on withdrawal.



Fig. 1.10 Gastrophotor.

then inserted through the hollow body of the sigmoidoscope to take pictures. In other words, this instrument was developed as a way of photographing endoscopic findings of areas visible on sigmoidoscopy, which was otherwise impossible at that time.

In 1960, Niwa developed the prototype of a new colonocamera (Fig. 1.11) [15], a modification of the mass survey gastrocamera (later called the type V Gastrocamera) but with a much longer shaft. The visual angle of the lens was 80° and the film used was 5 mm in width. With this prototype, photography up to the left (splenic) flexure was successful, indicating for the first time that observation of the proximal colon was possible.

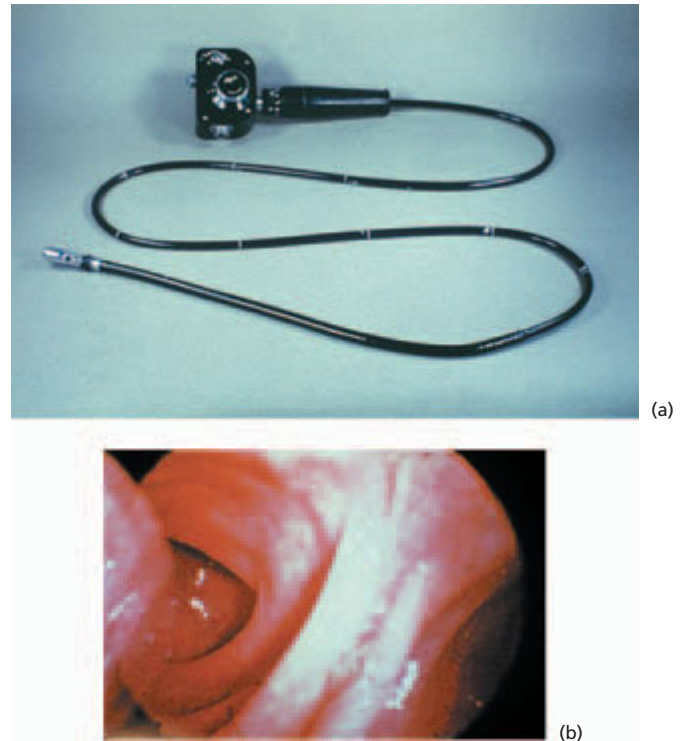


Fig. 1.11 (a) Colonocamera (Niwa, 1960) and (b) image of sigmoid colon.

Figure 1.11(b) shows an example of the pictures taken by this instrument.

Further improvements were made to this prototype colonocamera and its length extended (Colonocamera type III). The instrument was inserted into the proximal colon under fluoroscopic guidance. The mechanism of picture-taking was the same as with the gastrocamera; however, the colonocamera was not always able to take good pictures due to the narrow colonic lumen, its lateral-viewing optical system and the limited number of pictures it could take.

American fiberscope development

Whilst gastrocamera and colcamera development proceeded in Japan, Hopkins and Kapany in the UK in 1954 had demonstrated image transmission down a short fiberoptic bundle and speculated on its potential use for gastroscopy [16]. Hirschowitz and Curtiss at the University of Michigan developed a fiberoptic viewing bundle by 1957, used it to perform the first flexible gastroduodenoscopy [17], and then worked with American Cystoscope Makers Inc. (ACMI) to produce prototype endoscopes. By 1961 the ACMI "Hirschowitz fibergastroscope" was commercially available, creating excitement in Japan and around the world.

In 1961 Overholt, also at the University of Michigan, obtained US government funding to develop fiberscopes



Fig. 1.12 Prototype fiberoptic sigmoidoscope: Illinois Institute of Research (Overholt, 1963).



Fig. 1.13 The first fiberoptic sigmoidoscope—four-way angling: Eder Instrument Co. (Overholt, 1963).

for colonic use. By 1963 three different US manufacturers had prototype short colonoscopes and Overholt was able to perform the first flexible sigmoidoscopy with a crude four-way angling instrument (Figs 1.12 & 1.13). ACMI, a relatively small company, had been pre-occupied with gastroscope development and unwilling to accept governmental conditions for colonoscope



Fig. 1.15 Commercialized Hirschowitz fiberoptic gastroscope (American Cystoscope Makers Inc., ACMI, 1964), as also used in colon. Side-viewing, no angulation controls (focussing lever only), with transformer for distal tip light bulb.

development. ACMI did however supply both passive viewing bundles and prototype side-viewing fiberoptic gastroscopes which were used in 1966–8 by pioneer colon enthusiasts in the USA [18], the UK [19], and Italy. By 1967 Overholt could report 40 successful flexible sigmoidoscopies [20]. A fourth company, American Optical, was able to produce fiberoptic bundles [21] and sold some to Japan for use in prototype development.

ACMI, partly because of the small and very flexible fibers produced by their development of the Hirschowitz and Curtiss two-glass drawn-fiber method of production (Fig. 1.14), were able by 1971 onwards to produce highly robust colonoscopes (Fig. 1.15). These were capable of acute tip angulation without damage to the fibers, and had an innovative “flag-handle” method of controlling four-way angulation (Fig. 1.16), although

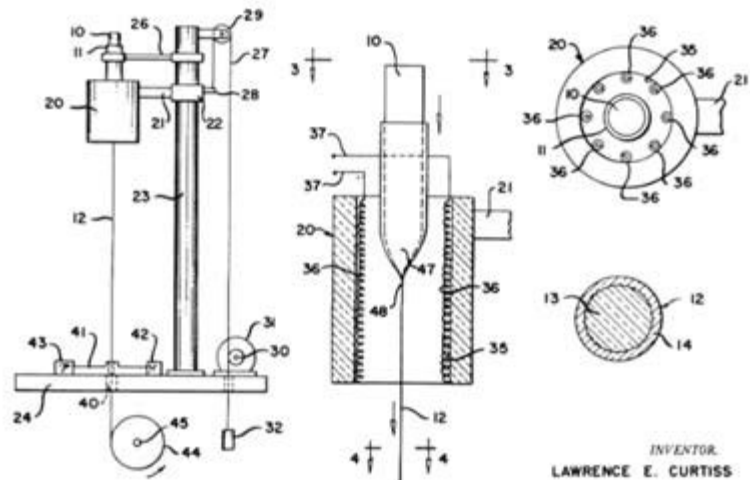


Fig. 1.14 The original patent diagram (Curtiss and Hirschowitz, filed 1957; registered 1971). This shows the technique for drawing a “two-glass” fiber through an electric furnace.



Fig. 1.16 ACMI F9A “flag-handle coloscope” (1974) with single-lever giving four-way angulation control.

with mechanical construction and torque-stability characteristics somewhat inferior to Japanese instruments of the same period.

The US endoscope companies were too small to sustain the costs of quality improvement in the long term and larger American corporations proved uninterested in the medical market, so by the late 1980s colonoscope production ceased. ACMI at least had the satisfaction, on behalf of Hirschowitz and Curtiss, of winning the battle to establish their patent rights on the critical underlying principles for fiberoptic manufacture.

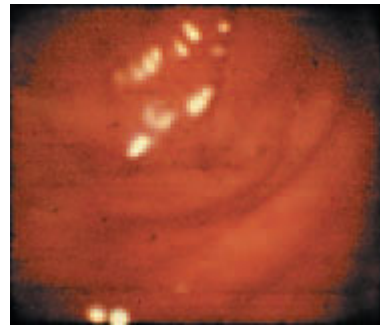
Japanese colonofiberscope development

With the spread of “gastrocamera with fiberscope” (GTF, an instrument combining gastrocamera and fiberscope produced in 1964), attempts were made to utilize it for colonic examination. However, insertion into the proximal half of the sigmoid colon proved extremely difficult because of the shaft characteristics of the scope and the field of view, which was very limited due to the side-viewing optical system. To adapt to the narrow and tortuous lumen of the colon, modifications were necessary to make the shaft of the colonofiberscope more flexible and to alter the direction of optical view.

A prototype forward-viewing colonofiberscope was first made for Niwa in 1965 [10] by Olympus (Fig. 1.17). The visual angle of the lens was 35° , there was no angulation mechanism, it used a fiberoptic light guide for illumination, and the shaft was 2 m in length. Partly because the shaft was too stiff, insertion into the descending colon was still very difficult. When inserting into the proximal sigmoid colon, the tip pressed into the colonic wall, so losing the view. Observation during withdrawal was also difficult because of poor illumination at a distance. This passive prototype instrument



(a)



(b)

Fig. 1.17 (a) Prototype forward-viewing colonofiberscope (Niwa, 1965). (b) Example through the forward-viewing colonofiberscope.

therefore proved impractical, although Niwa tried, without much success, to avoid impaction by attaching a centering balloon at the tip end.

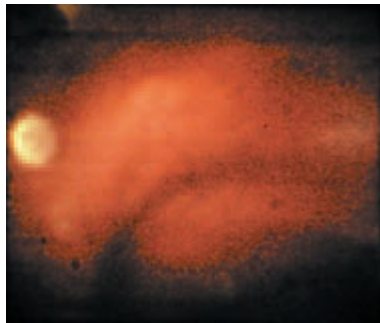
The next prototype was the forward-/side-viewing colonofiberscope shown in Figure 1.18, which could be used as either a forward- or side-viewing scope by changing the lens at the tip [22]. However the image was not good, either in forward view because of poor illumination, or side viewing, due to an inner reflection at the cover glass of the lens.

A “rotating prism” colonofiberscope was developed next [22,23] (Fig. 1.19). The prism could be rotated in either direction from the control body. The visual angle was 40° , it had four-way angulation of the bending section, and the shaft was 120 cm in length. Insertion into the descending colon remained very difficult with this model too, because of shaft stiffness and the long rigid metal tip. The image was also poor because of internal reflections from the illuminating light caused by rotation of the prism.

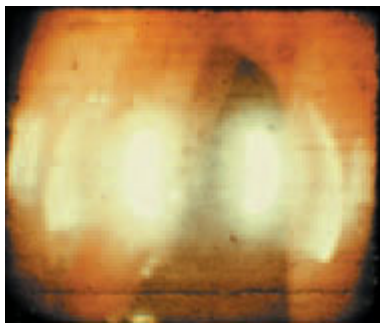
From the experiments carried out on these various prototypes, the conclusions were that the colonofiberscope should have a more flexible shaft and needed a forward-oblique-viewing lens. Oblique viewing was adopted to compensate for the narrow visual angle of the forward-viewing model, resulting from the limited



(a)



(b)



(c)

Fig. 1.18 (a) The prototype forward- plus side-viewing colonofiberscope (Niwa *et al.*, 1966) (detachable side-viewing lens is on right). (b) Image through forward-viewing lens. (c) Image obtained with side-viewing attachment, showing limited view and unacceptable reflections.

resolution of the fiber bundle at the time. As the result, a prototype short colonofiberscope was produced with only up/down angulation (Fig. 1.20) [24,25]. The same handle mechanism was used as in the esophagoscope,

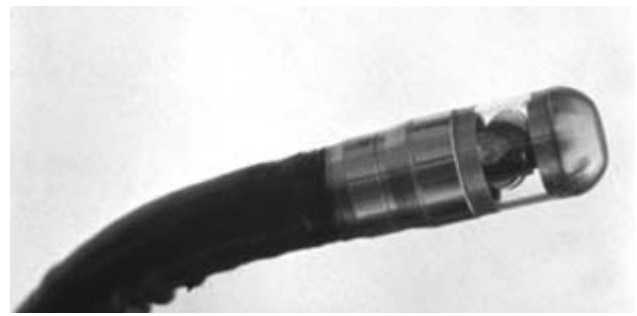


Fig. 1.19 "Rotating prism" colonofiberscope—side-viewing with 30° view (Niwa *et al.*, 1966).

already commercialized at the time. This colonofiberscope was deliberately made shorter than the earlier prototypes which had proved difficult to use in the sigmoid colon. The author realized that, rather than aiming at the proximal colon from the beginning, it was preferable to simplify design in order to observe the sigmoid colon effectively, the site of most disease. Examinations were much easier with this prototype and images were good, as shown in Figure 1.20(b).

The first practical colonofiberscope had been invented at this point. Later the length of the shaft was extended by 25 cm and the forward-oblique viewing was changed from downward to upward, to coincide with the direction of bending of the sigmoid colon. This colonofiberscope became the basis of the SB type short colonofiberscope manufactured by Olympus, shown in Figure 1.21.

In contrast to the small fibers produced by the two-glass method used by the American manufacturers the Japanese fiber bundle manufacture was, from an early stage, by the three-glass method [26]. This entailed orderly rows of coated glass rods being drawn out in a matrix of acid-leachable glass, which was finally dissolved away leaving the characteristic orderly rows of glass fibers at each end. Olympus bundles were therefore better looking than the ACMI bundles, but had thicker fibers which limited resolution and angle of view, and were more easily damaged (Fig. 1.20b), so angulation of early Olympus colonoscopes was limited to only around 90°.

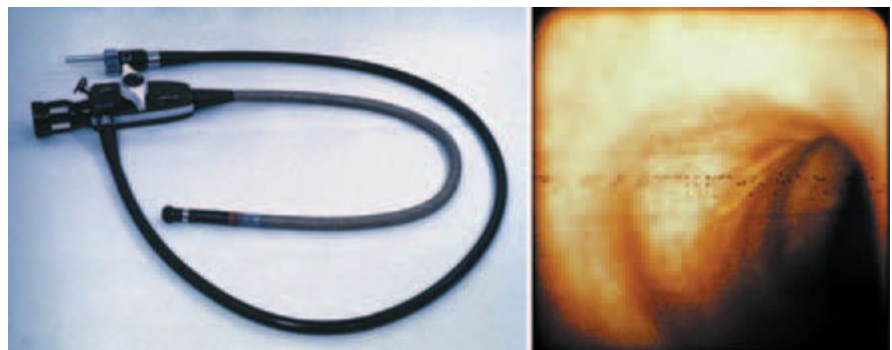


Fig. 1.20 (a) Prototype short colonofiberscope (Niwa, 1968). (b) Image through prototype short colonofiberscope—note typical broken glass fibers.



Fig. 1.21 Olympus colonofiberscopes (1970–1).

In contrast to Niwa, Matsunaga's group had aimed at reaching the right side of the colon from the beginning, using a prototype fiberscope in 1968 which had a 120-cm long shaft and four-way angulation [27]. They extended its shaft length to 2 m in 1969, the basis of the Olympus LB type long colonofiberscope (Fig. 1.21). However insertion into the proximal colon was extremely difficult and their success rate for insertion into the ascending colon was reported to be 8% in 1970.

Yamagata and his coworkers developed yet another type of colonofiberscope in cooperation with Machida Seisakusho (medical & optical equipment manufacturer). At first they used a scope designed for duodenoscopy in the colon, but insertion proved difficult. They later developed a scope with an olive-shaped tip (Type IV) in 1966, other prototypes in 1968 and 1969, and finally achieved a practical colonofiberscope with the development of Type VII in 1970. The shaft of this prototype was 190 cm long with four-way angulation. It was the basis for the excellent fibercolonoscope later manufactured by Machida (Fig. 1.22).

However, problems still remained after commercialization, including difficulty of insertion into the proximal colon and blind areas to observation. Therefore research into optics, flexibility and stiffness of the shaft and structure were carried out [18,28–30]. For example, Niwa *et al.* made a prototype 30° forward-oblique-viewing colonofiberscope in 1974, which had greater flexibility of the first 20 cm of the shaft compared to the stiffer shaft overall [28]. With such developments, colonofiberscopes became much easier to use.

Further improvements continued subsequently, especially in fiber bundle technology, so current Olympus



Fig. 1.22 Machida fibercolonoscope control body (1970)—note right- and left-hand controls, giving four-way tip angulation.

colonofiberscopes have 140° angle of view, up/down distal angulation of 180°, and left/right angulation of 160°. The outer diameter of the standard distal end is 13.8 mm. There are three different body lengths available with the same optical specification. There are also two channel types for therapy and thinner diameter models. Other manufacturers (Fujinon, Pentax) have similar products in their endoscope range.

Other attempts at insertion to the proximal colon

During the course of colonoscope development various attempts were made to facilitate insertion into the

proximal colon. In the early days Kanazawa inserted a polyethylene tube under fluoroscopic control from the sigmoid colon to descending colon beforehand. Through this tube, a colonocamera or gastrofiberscope could be inserted to the descending colon with improved success. Fox, in the UK, devised a similar method for suction biopsy through a flexible polyvinyl tube inserted under fluoroscopy, and then utilized this method to insert a passive bundle (ACMI) or fibergastroscope into the proximal colon [31].

There were many other attempts to facilitate insertion. These included supplementary instruments such as a guiding split-sigmoidoscope, which was withdrawn and dismantled after inserting the fiberoscope through it [32], a stiffening wire method [33], intestinal string pull-up methods [34–36], intestinal string guidance method [37], and a sliding tube method [38].

The stiffening wire method was a way of maintaining the straightened shape of the sigmoid colon, initially by inserting a steel wire through the biopsy channel to enhance the stiffness of the body [33] (see later). For the intestinal pull-up methods (end-to-end method), an intestinal tube was swallowed by the patient the day before examination. In the “pulley” approach a loop was then made in the tube when it emerged from the anus, threaded through with another string connected to the tip of the colonofiberscope. The looped tube was pulled back from the mouth into the proximal colon and used as a pulley through which the anal pull-string could be used to tug the endoscope into the proximal colon [36]. In the “string guidance” method, the tube coming out from the anus was inserted through the biopsy channel as a guide to help insertion proximally.

The “splinting tube” or “sliding tube” method (see later) was used to maintain straightening of the colonoscope [38]. It was necessary to apply the sliding tube over the colonofiberscope before the procedure and use of fluoroscopy was desirable for safety. Improvements were made on sliding tubes (demountable assembly or split-type) so that they could be put together when necessary [39].

Early researchers went through considerable difficulties, since colonoscopy requires much greater skill compared to that of upper digestive endoscopy. Even if a colonofiberscope was successfully inserted, it took great effort to make full use of it and achieve good routine results.

Other countries involvement in fibercolonoscopy

Only limited manufacture of short colonoscopes occurred in other countries, and used Japanese fiber bundles. In Germany the Storz and Wolff endoscope companies achieved small-scale production, whilst in Russia and China larger-scale manufacture was licensed.

Researchers around the rest of the world, however, did pioneer in developing and establishing many aspects of the technique of colonoscopy. In the USA, Waye [40] and Shinya [41] played the leading role. Deyhle in Germany [33], Rossini in Italy, and Williams in England [42] all made great contributions. Colonoscopic snare polypectomy was pioneered by Deyhle and Shinya. Recently Williams participated in the development of the position-detecting device (Scope Guide/UPD, Olympus), which makes it possible to know the shape and position of an endoscope during the procedure without using fluoroscopy. Magnetic position-indicators installed inside the endoscope communicate to the main device which detects the magnetic fields and displays the configured images on the TV monitor [43].

The transition to electronic endoscopes

Fiberoptic endoscopes enabled examination of body cavities, but by only one person—the operator. “Lecture scopes” (teaching attachments) were developed to overcome this problem. A prism was attached to the scope eyepiece with a fiber bundle to send the same visual information to another eyepiece, allowing two people to observe the same image. However, the attachment resulted in insufficient brightness for the operator, caused difficulty in operating the hand-held control unit, and increased the risk of scope dislodgement during complex maneuvers. The second observer received an image transmitted via glass fiber over a distance of about 1 m, so lacked clarity and definition. The lecture scope thus permitted multiple observers to view the same endoscopic image, but was far from ideal.

To improve image quality, endoscopists began direct connection of video cameras to the scope eyepiece lens. Initially a three-tube camera was suspended from the ceiling and attached to an endoscope (Ikegami, Tokyo), but proved cumbersome and the scope was often dislodged on rotation. Nonetheless the images obtained were displayed on a large television monitor and easily recorded on videotape, adding to the interest of the procedure not only for the operator but also for the many observers. A commercially available TV camera was subsequently used (Keymed, London), connection between eyepiece and camera being by 30-cm straight tubes and prismatic joints. Maneuverability was improved, but the scope had to be disconnected for derotation and the TV trolley was too large and heavy to move around conveniently.

A single-tube camera was eventually developed (OTV-E, Olympus) that could be directly attached to the eyepiece, similarly to a lecture scope. It was rectangular (length 14 cm, weight 290 g plus cable) but caused strain on the examiner’s left hand, because of its attachment to the end of the control body and eyepiece. Compared

with the larger cameras, brightness was poorer but nonetheless it proved popular with endoscopists. Units continued to become smaller with the introduction of charge-coupled device (CCD) technology, decreasing to 7.5 cm in length and 150 g in weight (OTV-F3, Olympus). However the poor quality of the enlarged fiberoptic images displayed on the TV monitor encouraged development of electronic endoscopes.

Early electronic endoscopes

Progress in electronics led to the American development in 1969 of silicon CCDs containing picture elements (pixels) able to generate electric signals in response to light. Even though Japanese glass fibers were reduced down to 7 μm diameter, with reduced “packing fraction” between fibers and superior resolution, CCD images were able to be made several-fold higher in quality. Early CCDs were too large for small-diameter gastroscopes, so the first “videoendoscope” was a colonoscope produced in the USA by Welch-Allyn Company in 1983 [44]. Placement of the CCD directly behind the objective lens made the instrument tip more bulky and stiff. The bending section was less agile than that of a fiberoptic colonoscope, so more difficult to retrovert and sometimes restricting angulation and view. Videoendoscopes were initially received with surprise and skepticism by Japanese manufacturers, but market forces soon led to their adoption—videocolonoscopy sales rapidly overtaking those of fiberoptic instruments.

Because CCDs could transmit monochrome brightness of their individual elements but not color (the glass fiber was only for illumination), two methods were devised to display images in color, the “sequential system” and the “white light” or simultaneous system (see Chapter 22). With the sequential system, light emitted from the light source was converted into strobed colored light by means of rotating red (R), green (G), and blue (B) filters. The light-based information was recorded in separate R, G, and B image memory-stores in the processor, before being combined into a color screen image. The sequential method permitted use of a smaller CCD, i.e. a small number of image elements, but color blurring or break-up often occurred. By contrast, the simultaneous system used R, G and B filters superimposed in a mosaic pattern over the CCD pixels. Each pixel thus received color information, simultaneously sent to the processor and displayed on the monitor. Although this system had no color blurring, a larger CCD was necessary, and the greater ratio of G relative to R and B in the filter mosaic altered the color tone on the monitor, creating an unusual hue for endoscopists used to fiberoptic endoscopes. Gradually, with miniaturization, CCDs became smaller and the number of pixels increased, resulting in high-quality images.



Fig. 1.23 “Standard” and “slim” fibercolonoscope tip/bending sections.

Further developments in colonoscopy

Ultra-thin endoscopes

The need for ultra-thin endoscopes is less in the colon than in the upper gastrointestinal tract. However, whilst an external diameter of 10–13 mm permits good maneuverability, the instrumentation channel should have an internal diameter of at least 2.8 mm (larger if possible) to facilitate the passage of accessories. The diameter of the upper gastrointestinal tract is 10 mm or less in some patients. Ultra-thin fiberscopes were technically easy to manufacture and were commercially available from the earliest days of endoscopy—ACMI in the USA had a 2.5-mm passive “ureteroscopy” in 1967 (R Wappler, personal communication). However, since a thin diameter led to a scope that was too flexible, efforts were made to increase rigidity, even in thin scopes for adults. These stiffer scopes could not be used in children or in some adults with colonic strictures, pronounced tortuosity, or severe adhesions. Very flexible ultrathin scopes were therefore also developed and manufactured at the same time (CF-SV, Olympus, Fig. 1.23). To produce ultra-thin scopes, the length of the tip had to be shortened and the radius of curvature during maximal bending reduced. The technology involved was used to improve the performance of standard adult endoscopes, permitting acute angulation but also allowing accessories to pass.

Stiffening methodology

When shaft characteristics are too soft, looping of the scope occurs when there is resistance produced by the tip passing through acute flexures. Such bending most frequently occurs in the sigmoid colon and pressure was

applied to the abdominal wall to oppose it and/or stiffening devices used from the early days of the fiberoptic endoscope. From the spring steel stiffening wires used by some colonoscopists in the early 1970s there developed a stiffening wire and stiffening tube. The ACMI internal stiffening wire of 1974 consisted of a core tensioning wire surrounded by a 3.5-mm-diameter coil. Tensioning the core wire, the outer coil contracted and stiffened. The large diameter required to achieve effective stiffening restricted use to large-channel “therapeutic colonoscopes,” such as the ACMI F9A. Thinner wires for standard colonoscopes did not produce the desired stiffness.

Stiffening, “splinting” or “overtubes” were, for the same reasons, also in use from the start of colonoscopy. The commercialized, rather rigid, Olympus stiffening tube had to be put in place over the scope before insertion, and its length reduced the effective working length of scope. Prototype Gortex “split-overtubes” overcame this problem and were floppy enough to be inserted without using fluoroscopy. However with the development of “one-man” colonoscopy handling technique and better understanding of loop control, less flexible scopes became more popular and stiffening overtubes are currently rarely used.

Looping can sometimes not be avoided, even if a very stiff scope is used—and formation of a loop in a stiff scope generally causes the patient considerable discomfort. Scopes using the same principle as a stiffening wire were therefore developed, based on a 1975 prototype

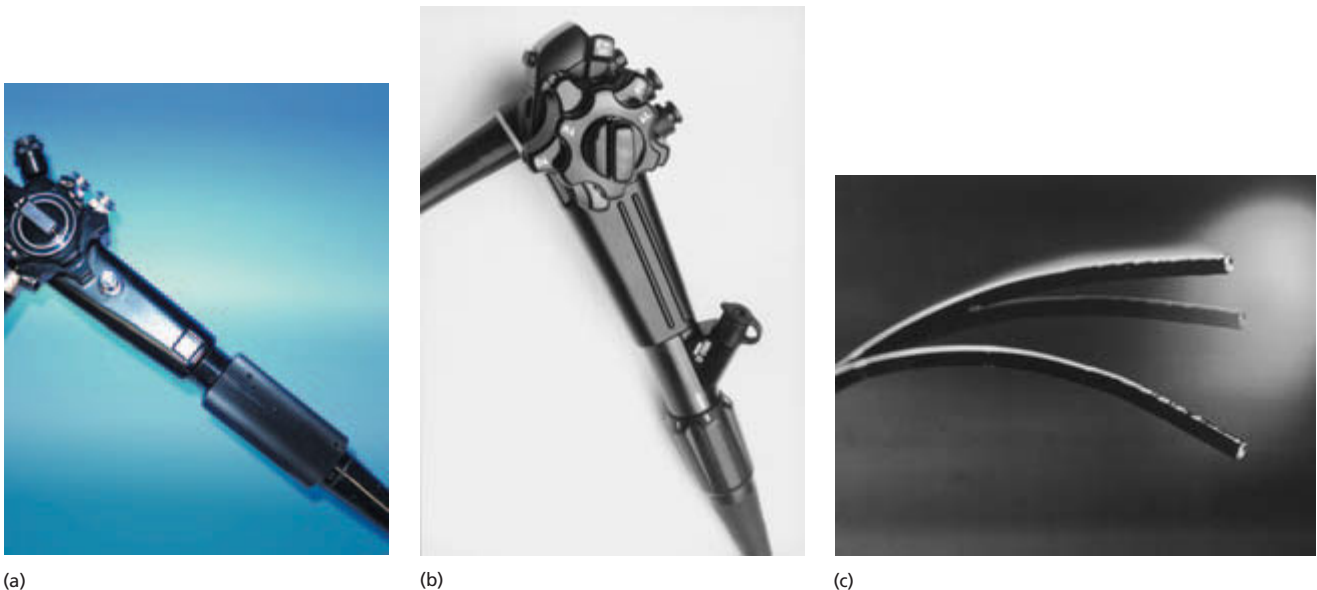
made for UK use (Fig. 1.24a) commercialized in 2000 (Olympus CF240AI/L, Fig. 1.24b). Stiffness is applied by twisting the tensioning-ring installed between the control body and shaft. The shaft characteristics are designed to be only slightly stiffer than a pediatric scope when set to “floppy,” but similar to a hard scope when set to “stiff” (Fig. 1.24c). An ultra-thin colonoscope incorporating the same mechanism was also produced. More improvements are needed because shaft looping remains a problem in colonoscopy.

Imaging endoscope configuration

It is important to know the configuration of the scope during colonoscopy without the use of fluoroscopy, particularly when difficulty and persistent or atypical looping occurs during the procedure, when the patient suddenly complains of pain, or to allow the endoscopist to confirm the site of lesions. To overcome such uncertainties two different UK groups produced prototype “3-D magnetic imaging” systems in 1993–4 (Williams 1993 [43], Bladen 1994 [45]), finally commercialized as the Olympus “Scope Guide” or “UPD” 3D imager in 2002. Small electromagnet coils are installed inside the scope at about 5-cm intervals from the tip (Fig. 1.25) and each coil is activated at a different frequency. A sensor dish detects the magnetic fields produced by each coil, and position-sensing information for all the coils is processed by a computer and displayed as a three-dimensional real-time screen image of endoscope shape. The strength of the magnetic fields is minimal by international specifications, so that the system is safe for continuous use.

Images showing the shape of the scope can be displayed from the direction desired by the operator,

Fig. 1.24 Shaft-mounted stiffening control of Olympus Innoflex “variable” colonoscopes: (a) 1975 prototype; (b) 2000 commercialized version; (c) effect on shaft stiffness demonstrated.



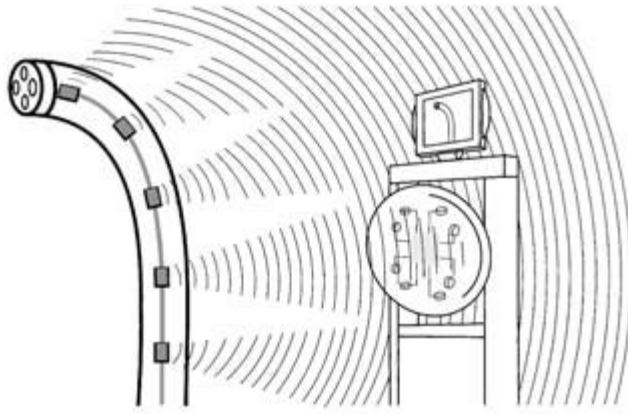


Fig. 1.25 Diagrammatic representation of three-dimensional imaging system (Scope Guide/UPD, Olympus), showing field(s) from within-scope electromagnets computed to produce an image of shaft configuration.



Fig. 1.26 Lateral view of alpha loop shown by “3D imager” (Scope Guide, Olympus).

independent of the patient’s body position. In addition, both frontal (AP) and lateral views can be displayed simultaneously split-screen. To facilitate 3-D image presentation, gray-scale shading is used, close-up regions of the scope being displayed bright and distant regions dark (Fig. 1.26).

In addition to the commercialized coil-fitted “imager colonoscopes” (CF240AI, Olympus), 2-mm-diameter “imager probes” containing the coils can be inserted into the biopsy channel of conventional scopes (Fig. 1.27), which interferes with suction. A hand-coil can be used during abdominal manipulation to ensure that the assistant’s hand pressure is correctly located over a loop.

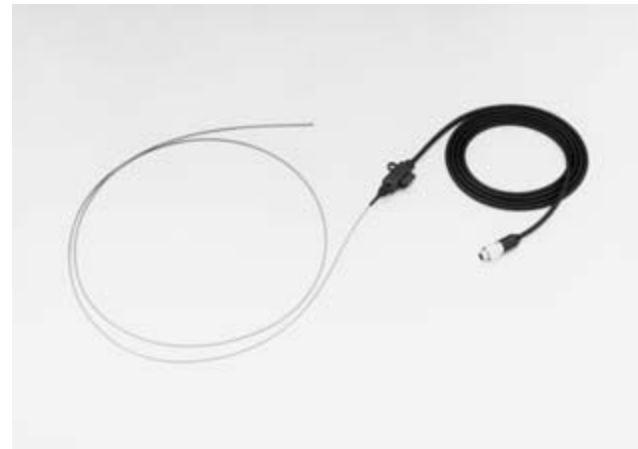


Fig. 1.27 “3D Imager” probe for insertion down instrumentation channel of any endoscope.

Magnification and dyeing

Prototype magnifying fiberoptic colonoscopes were developed which could magnify objects up to 170 times, resolving even the nuclei of superficial epithelial cells. At that time there was no clinical need for such a degree of magnification, since commercially available magnifying scopes were able to magnify objects up to 35 times (CF-HM Olympus), physically moving some of the objective lenses at the tip of the scope, giving a depth of focus of up to 2–3 mm. These principles were also applied to electronic scopes, using a piezoelectric method to zoom the objective lenses move smoothly and simply (Fig. 1.28). As CCDs became even smaller and resolution increased, minute changes visible only on magnification could be displayed in full detail on a high-resolution television monitor. Compared with the upper gastrointestinal tract, the colon is less susceptible to pulsation,

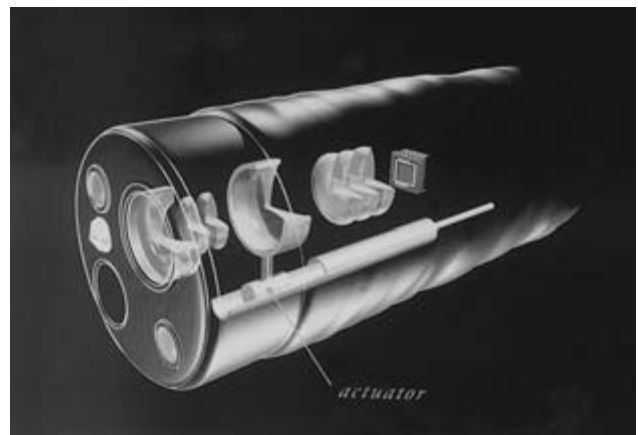


Fig. 1.28 Zoom lens mechanism of magnifying scopes—piezoelectric actuator adjusts position of the moveable lens.

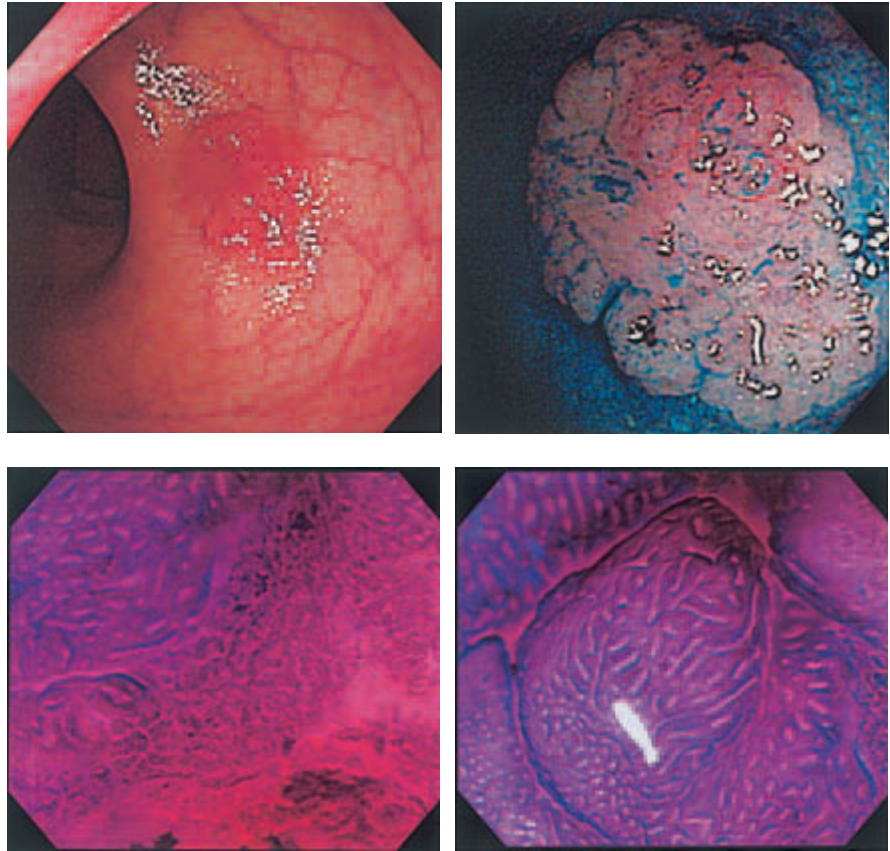


Fig. 1.29 Dye-spray, staining, and magnification of a 9-mm malignant polyp. (a) Initial view of lesion (b) Close-up after indigo carmine spray. (c) Magnified view after cresyl violet staining—deformed crypts in depressed area suggest malignancy. (d) Adjacent elevated area—appearances typical of benign adenoma.

has minimal peristalsis and less adherent mucus, all of which characteristics facilitate magnifying endoscopy.

Magnifying endoscopy may provide a good view, but the images are flat and monotonous if not processed correctly, making it difficult to identify surface irregularity. The use of dye can make pathologic changes stand out either by contrast or staining (see Chapter 43). With the contrast method, dye solution (0.1–0.2% aqueous solution of indigo carmine food dye) accumulates in depressed areas and grooves and highlights the margin even of very slight protrusions, allowing lesions to be more easily identified, compensating for the disadvantage of magnifying endoscopy. Vital staining is usually by methylene blue (0.05–0.1%) or crystal violet (0.05%), and these dyes are absorbed by the surface epithelium, particularly the cells surrounding crypts.

In the colon, the shape of the crypts not only reflects the histologic characteristics of lesions but can also suggest the depth of invasion of carcinomas, helping to determine whether a lesion is suitable for endoscopic resection. Classification of types of colonic polyps by surface appearance started in 1975 with description of four types on examination with a dissecting microscope. Tada in 1978 reclassified these into three types on the basis of magnifying endoscopy [46], later adding a fourth type when the crypts are absent in advanced

carcinomas. These findings were forgotten and not applied to magnifying endoscopic examination for many years. Interest in Tada's classification was revived with increasing interest in superficial type cancer, especially by Kudo *et al.* (1992) [47] who used the previous classification of types I–V. There are some exceptions to the classification system, i.e. the fine surface architecture of the colon does not always correspond to deeper histologic changes, so magnification serves only as a partial aid to diagnosis (Fig. 1.29).

Enhancement

Endoscopic images comprise an extremely large amount of potential imaging information. With electronic scopes, imaging information consists of different electronic components. Manipulation of electronic information such as color, clarity, and color intensity may improve diagnostic capability (see Chapter 22). At first, enhancement was used for overall modification and for processing of gentle curves. Because light/dark enhancement effectively highlighted the outline of lesions, it was used for the diagnosis of superficial type lesions and the identification of minute structural changes on magnifying endoscopy (Fig. 1.30). It also became possible to enhance specific frequency bands, i.e. specific colors such as hemoglobin.

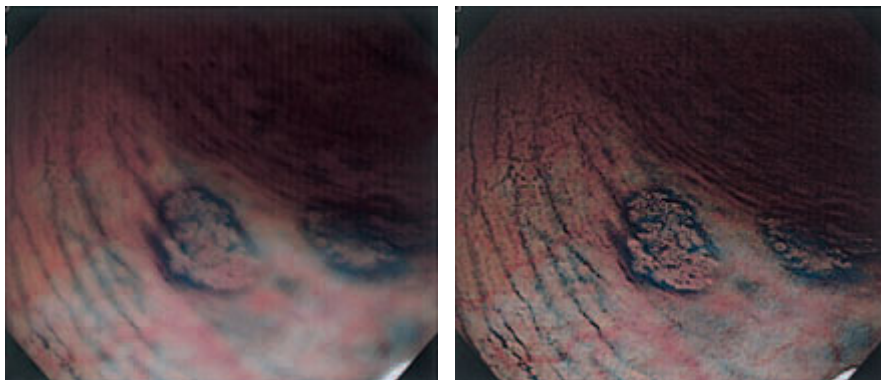


Fig. 1.30 (a) Hyperplastic polyp without image edge enhancement. (b) Same polyp as in (a) after image edge enhancement.

Moreover, the color of a lesion could be enhanced without modifying the color tone of the surrounding mucosa, so making lesions more easily identified.

Autofluorescence and infrared light

The use of light outside of the visible spectrum was attempted during the days of fiberoptic endoscopy, but was found to be impractical. Electronic scopes have been revived for research purposes, and the ease of processing electronic information may lead to the future development of electronic scopes.

Autofluorescence (see Chapter 44) is a technique that uses minute quantities of fluorescence inherent in tissue. This technique has received considerable attention because it does not require the use of fluorescein or other dyes. The observed findings are displayed with the use of an absorption filter. Minute quantities of fluorescence in the range of 500–600 nm can thereby be visualized. This technique is useful for the detection of tumors with high autofluorescence.

Infrared light has a wavelength of about 1000 nm and can be detected by the endoscope CCD. In particular, blood vessels can be clearly observed by the intravenous injection of indocyanine green (ICG) and the use of an appropriate filter, compatible with the degree of infrared light absorption. Even deep blood vessels that cannot be observed on conventional examination can be visualized. This feature is useful for determination of the presence and distribution of nutrient vessels before tumor resection.

Endoscopic ultrasonography

Attempts to use ultrasonography for diagnosis during endoscopy date back to the days of the fiberoptic endoscope. An ultrasound transducer (radial or linear) is incorporated into the tip of the scope (see Chapter 45). Ultrasonic waves are delivered perpendicularly to the scope axis. For radial scanning the transducer must be rotated mechanically, whereas for linear scanning, ultra-

sonic waves are delivered in a single direction from the side of the scope. To attach a transducer to the scope the length of the rigid part of the tip of the scope has to be longer, especially so for linear scanning, making the passage of the scope through curved sections of the intestine more difficult. Radial scanning of the colon was therefore introduced initially.

Until the development of specialized instruments for colonic endoscopic ultrasonography (EUS), side-viewing scopes designed for EUS of the stomach were used in the colon. Placement was through an overtube put in position over a conventional colonoscope, which was then withdrawn after the EUS gastroscope was inserted, and scanning performed during withdrawal under degassed water. Forward-viewing EUS colonoscopes were then developed (CF-UM3, Olympus, Fig. 1.31). The presence of the fiberoptic bundles and instrumentation channel limited radial imaging to 300°. The scope had a control panel located between the control body and the eyepiece, containing the transducer rotation motor and EUS switches. At first there were two kinds of transducers: a 7.5-MHz one and a 12-MHz one, but later it became possible to switch frequencies. EUS video



Fig. 1.31 Tip of EUS radial colonoscope (Olympus CF-UM3)—can be used with or without water balloon in place.



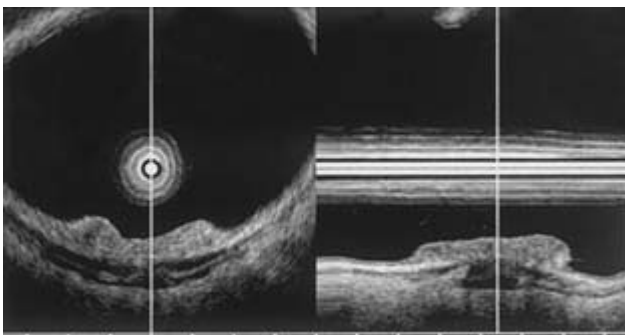
Fig. 1.32 EUS colonoscope (Olympus CF-UMQ 230).

colonoscopes were similar, but smaller and somewhat lighter (Fig. 1.32).

EUS probes had to pass through the biopsy channel of the scope, so their diameter was limited to 3.2 mm or less. This made it technically impossible to develop a 7.5-MHz probe, although 12- and 20-MHz probes were possible. Recently, 30-MHz probes have become commercially available (Fig. 1.33). Scanning is by mechanical radial rotation, obtaining transverse images of the intestine. Even small lesions can be targeted and diagnosis of the depth of invasion of superficial type lesions is facilitated by the use of a 20- or 30-MHz transducer. EUS is not suited for the evaluation of abnormalities outside the colon wall because of attenuation of the ultrasound beam at a distance.

Helical scanning can be achieved by moving the transducer of the ultrasonic probe at a constant rate to allow tomography or three-dimensional reconstruction. Up to 160 tomographic images covering a region of 4 cm can be saved in a computer and dual plane reconstruction then results in findings quite similar to those obtained

Fig. 1.34 (a) Helical EUS radial and longitudinal scan views of depressed polyp. (b) Three-dimensional reconstruction of helical EUS scan. (c) Endoscopic view.



(a)

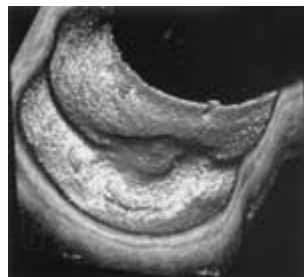


Fig. 1.33 EUS probe with motor-driven rotating transducer inside.

by linear scanning. Transverse and longitudinal images of a lesion can be displayed instantaneously (Fig. 1.34) or incorporated into a graphic display, displaying both types of images simultaneously. Dramatic images, including three-dimensional scans, can now be produced (Fig. 1.34b).

Summary

The long history of rigid endoscopy was essentially limited to the rectosigmoid area, but later transformed by the introduction of the electric light bulb. Gastrocamera technology had limited impact on colonic diagnosis, but gave Japanese manufacturers the mechanical expertise to produce torque-stable shafts and superior angulation and control mechanisms. Introduction of fiberoptics from the USA in 1957 and a sustained period of prototype development during the 1960s and 1970s resulted in the highly sophisticated fiberoptic colonoscopes available at the end of the millennium. The invention of the CCD brought application of digital electronics to videocolonoscopy, through CCD and a further new dimension. Other supportive innovations and parallel methodologies continue to be developed, but still more are needed to guarantee the future of colonoscopy.



(b)



(c)

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Chapter 2

The Colonoscopy Suite

Martin E. Rich

The introduction and general acceptance of the video endoscope in the early 1980s initiated a transformation in the design and planning of spaces for endoscopic procedures. The 1990s saw the expansion of this technological transformation worldwide as well as the onset of shrinking insurance reimbursement, particularly in the USA. Consequently, in the first decade of the 21st century, planning for endoscopy confronts three established conditions:

1 *Technology based on digital video imaging and its supporting systems.* Gastrointestinal endoscopy is now routinely performed with video devices. This technology fundamentally affects the endoscopist's relationship to the physical space in which he/she works. It influences how equipment is handled, how images are viewed, and how information is processed. It places important requirements on the infrastructure that makes it all possible.

2 *The use of computers and computer connectivity to manipulate, process, store, and transmit images.* The dependence on the computer in every facet of medicine has been keenly felt in the endoscopy setting. The natural extension of the video endoscopic procedure is the ease with which digital images and information are utilized. As bandwidth has increased and becomes readily accessible, the sharing and moving of information to remote locations has become routine. The endoscopy practice of the future may be a collection of sites linked by the internet to central locations for information, with the opportunity for physicians at many locations to participate in procedures, research, or administrative activities.

3 *Economic constraints that are influenced by managed care and government reimbursement policies.* These necessitate careful use of available resources and funds in order to provide safe and efficient settings. The benefits of screening colonoscopy and the approval in the USA of Medicare coverage for this procedure in average risk individuals creates additional economic pressure. The challenge of creating a viable facility in light of ever narrower operating margins mandates the need for economically and efficiently designed facilities.

The need to acknowledge these factors has changed the way we think about and design endoscopy facilities. These issues are in addition to the normal problems associated with construction projects.

The purpose of this chapter is to offer basic concepts and layout principles that can be generally applied, as well as guidelines and detail requirements that will help address current and future needs. While the primary experience of the author is with issues particular to units in the USA, most principles are universal and will apply in many other countries.

Whether the project is large or small, office, ambulatory center or hospital, new construction or renovated space, effective planning is critical. The commitment to create, expand or redevelop an endoscopy center must include provision of appropriate lead time for planning and construction, and for operational activities to be put in place. Lead time for a small to medium size project can require 12–24 months of effort (Fig. 2.1).

The impulse to repeat past experience should be resisted, and planning should focus on understanding underlying principles and preparing a sound analysis of current and future needs. Establishing the requirements for a proposed facility can occupy half of the overall project schedule, depending on the complexity of the facility. It is important to document this decision-making process so that goals, findings and priorities are kept in focus, particularly where the personnel involved with the process may not see it through from beginning to end.

There are four principal phases of implementing any project:

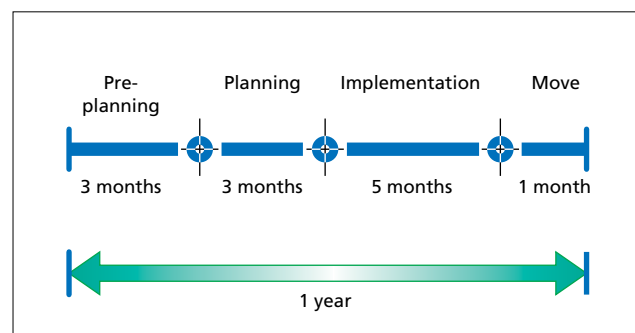


Fig. 2.1 Project schedule.

Phase 1: defining needs, collecting and assessing data

- (a) Location and type; existing or new; office, ambulatory center, or hospital.
- (b) Case load, facility size, and overall objectives.
- (c) Licensure and accreditation requirements; certification and agency approvals.
- (d) An outline of requirements to satisfy present and future needs.

Phase 2: design and layout

- (a) Arrangement of components and flow patterns.
- (b) Block layout and preliminary design.
- (c) Design development and detailed layout:
 - equipment type, size, and installation;
 - electrical wiring and video networking;
 - environmental considerations—heating, air-conditioning, and ventilation;
 - procedure room design;
 - operational consideration—quality control;
 - certification requirements;
 - interior design.

Phase 3: documentation and enumeration

- (a) Construction documents.
- (b) Engineering specifications.
- (c) Equipment integration.
- (d) Voice and data networks.
- (e) Agency approvals, licensing certification.
- (f) Estimation of cost and schedule.
- (g) Furniture and equipment specifications.

Phase 4: implementation and operation

- (a) Construction and finish work.
- (b) Equipment and furniture installation.
- (c) Inspection and approvals.
- (d) Moving logistics.
- (e) Organization and operation.

Step one/start planning

Before physical planning begins, basic decisions must be made about the character of the project. Generally, an office facility will be small, with few practitioners involved and a relatively simple decision-making process. An ambulatory facility will be more complex, and planning will involve more people to work through the basic issues as well as the necessities of licensing, code compliance, and certification. An endoscopy unit in a hospital must satisfy the requirements of many diverse groups and planning is needed for manifold and sophisticated procedures.

Getting appropriate help is essential since the planning and construction process is a team endeavor. It requires the vision of the physicians and medical staff, and the participation of architects and engineers, medical equipment and technology specialists, computer and communications consultants, and legal, business and licensing advisors. There is no substitute for an experienced planning professional who can facilitate the process and help integrate the varied requirements into a unified whole. The effort to develop a creative approach to communication among the various planning participants will be rewarded with less chance of costly errors later on.

Spaces designed for colonoscopy are equally suited for esophagogastroduodenoscopy (EGD) examinations and rooms for these procedures will be designed in all types of gastrointestinal units, including hospitals, medical offices, and ambulatory centers. Hospitals have unique and complicated requirements apart from office and ambulatory locations. However, there are significant (and legal, in the USA) differences between office units and ambulatory centers that require some clarification.

Offices

The gastrointestinal office is usually a place where general practice is combined with procedure work. In a start-up practice procedures might be performed in any available area that is large enough for both patient and physician. Many of these spaces are inadequate and do not fully bring patient comfort or safety into account. As a practice becomes more established, dedicated areas for performing procedures are usually developed to provide more efficient facilities for the increased caseload. The office endoscopy environment is not generally subject to specific minimum standards other than local building codes and inspections. Currently, there are pressures to regulate the construction of offices to accommodate gastrointestinal procedures. The American Gastroenterological Association has published a list of recommended standards for office-based gastrointestinal endoscopy services in an attempt to establish a minimum level of compliance. These standards could have significant impact upon the size, layout, and design of offices and may become part of the equation in the not too distant future.

Ambulatory facilities

In the USA an ASC (ambulatory surgical center) or AEC (ambulatory endoscopy center) is a dedicated and certified facility entitled to receive specific facility fee reimbursement from Medicare and third party insurers. This certification is granted to facilities that comply with

state licensing regulations (where applicable) and receive certification from CMS or another accrediting agency. Some state laws do not differentiate between ASCs and AECs in so far as where endoscopy must be performed, while states that do differentiate may have less restrictive requirements for AECs. As a rule, in the USA, requirements in the licensing codes incorporate recommendations from the *Guidelines for Design and Construction of Hospital and Health Care Facilities*. This is a set of national standards published by the American Institute of Architects and the Facilities Guidelines Institute with assistance from the US Department of Health and Human Services. These standards include specific room sizes, minimum corridor widths, plumbing provisions, air-conditioning standards, and requirements for emergency power, among others. The recommendations insure a level of safety and quality equivalent to those found in hospital facilities but are at a considerably higher cost than a typical office installation. The many requirements dictated by codes and regulations in the USA for Ambulatory Surgical Centers are summarized on pp. 42–43. Similar codes regulate minimum standards, particularly in the case of hospital ambulatory units, in most industrialized countries (p. 43).

In all endoscopic facilities, the design objective, whether or not decreed by law, concerns balancing requirements of patients and staff with technological and equipment needs to enable the realization of high-quality endoscopy in a safe, efficient and reassuring setting. If planning is successful, a specific volume of endoscopic procedures can be handled smoothly, and a corresponding management of costs is achieved. In addition, the basis for design should provide a comfortable and convenient work environment for both physicians and staff. These underlying considerations are appropriate whether the volume of the particular practice is large or small, and whether the space is a hospital endoscopy unit, an AEC, or a single office room used for an occasional procedure.

Assessment and programming

With a general vision of the objectives, physicians and staff can articulate needs with the help of a critique of existing arrangements and examples of successful operations. These general issues must be translated into specific requirements such as range of services, caseload projections, and concepts of how the practice will be managed. Ultimately, this is expressed in a written synopsis or program brief. Architectural services generally include a programming phase, resulting in an organized list of the type, size, quantity, and quality of the rooms, spaces and supporting services required in the design.

The functional space program is the basis for physician and designer to reach a common understanding of

the composition of the facility. Program preparation involves collecting, organizing, and evaluating criteria. The information may be assembled through individual interviews with staff or through a designated person who has been assigned the task of coordinating the collective staff effort to articulate the requirements of the new facility.

It is important that planning activities are formalized and separated from the regular events of the workday in order to establish a framework in which the physician and architect or planner can interact without distraction. During the planning phase, 2–3 hours per week should be set aside for review meetings.

The program is a summary of the quantity and area (feet squared (ft²) or meters squared (m²)) requirements of all spaces. Before it can be prepared the following basic decisions must be made:

- the number and size of procedure rooms to be provided;
- the amount of recovery area;
- scope cleaning and storage requirements;
- the size and seating requirements of the waiting area;
- the size of the administrative operation and number of stations needed;
- the amount of space needed for computers and related equipment;
- the number of physicians' offices.

Number of procedure rooms

The benchmark for an endoscopy facility is the number of procedures that are performed in a given time-frame. There is a direct relationship between the number of rooms and the volume of cases that can be performed. In hospitals, additional factors such as teaching requirements, the use of anesthesiologists and fluoroscopy, and the performance of complex procedures have a notable impact on the number of rooms required to accommodate a given caseload and the range of endoscopy services offered.

An endoscopist can generally establish data on how many colonoscopies and EGD procedures were performed in the past year, and the amount of time required for the completion of the examination. It is helpful to formalize the process of data collection.

From this information it is possible to project the number of procedure rooms required, as well as the amount of space that will be needed for recovery and other functions. For planning precision it is useful to determine the total number of colonoscopies and EGD endoscopies that will be performed per year and then calculate an *average daily caseload*. This is done by dividing the yearly case total by the number of working days, generally in the neighborhood of 250 days per year (DPY). A growth rate should be estimated from historical data, and with

this it is possible to project a potential volume of cases to be performed 5 or 10 years in the future. Planning should always be done for a future volume, not from present numbers. While planning for the future it is also important to anticipate whether physicians will be added to current staff, as this will affect how efficiently the rooms will be used in light of scheduling complexities. In addition, some attempt should be made to assess the potential impact on growth rate caused by new technologies such as virtual colonoscopy and the Given Imaging Capsule for wireless endoscopy.

A raw count of cases is not an absolute measure of volume since a colonoscopy will occupy an endoscopy room for considerably longer than EGD procedures. Hospital units must add complex procedures to the overall number of cases, as they may take more time than standard endoscopies. These procedures include endoscopic ultrasound and ERCP. If these procedures are not currently performed, but are possible in the near future, space and time must be factored into the plans. Some assumption must be made as to the balance of colonoscopy to upper endoscopy (and other complex examinations) in a typical day's procedure work and the average duration times of these procedures. An individual assessment of each group's characteristics (some may have a greater demand for fluoroscopy) must also be made to determine whether scheduling issues or other factors might affect the amount of work that may be performed. By assessing the individual characteristics, the speeds of the physicians, and the efficiency of the staff, *the average procedure time*, including room preparation, needs to be estimated. It should be noted that these data gathered at one facility are not usually transferable to any other facility.

Dividing the working hours in a typical day by *the average procedure time*, including room preparation, results in an approximate daily capacity of procedures per room (PPR). Dividing the projected number of cases per day by the capacity per room will provide the number of rooms required ER. The accompanying formulae express the relation between time, room output, and the resulting number of procedure rooms required:

$$\text{Daily projected volume (PPD)} = \frac{\text{Annual projected volume}}{\text{Working days per year}}$$

$$\text{PPR} = \frac{\text{Number of working hours}}{\text{Av. procedure time} + \text{Turnaround time}}$$

$$\text{ER} = \frac{\text{Daily projected volume}}{\text{Capacity per room (PPR)} \times 0.8 \text{ (efficiency factor)}}$$

A range of six to eight procedures per day should be expected from this analysis, assuming average conditions and an operational efficiency of about 70–80%. This is based on an assumption of equal proportions of upper

and lower cases, a 45-minute average turnaround time, and sufficient recovery space to keep the procedure room reserved for the performance of gastrointestinal procedures. As time and efficiency factors change, so will resulting room capacity.

Maintaining a high operational efficiency is dependent on skilled teamwork by staff and good scheduling of procedures, which must take into account the varying times required for completion of specific procedures and the equipment required by different endoscopists.

Units that schedule more than six procedures per day will generally require more than one dedicated room, with procedures being performed simultaneously by multiple endoscopists. For example, if eight cases per day could theoretically be performed, a single room could accommodate up to 2000 procedures per year (PPY). However, it is prudent to factor in a loss (20–30%) for inefficiencies caused by cancellations, equipment breakdown, and staff absences. Taking operational inefficiency into account, the same room with supporting recovery, handling an average of six cases per 7-hour day and assuming 250 working days per year, will have a volume of about 1500 procedures performed. This 1500 PPY is generally a realistic number to use for planning purposes and allows some flexibility in scheduling. Increasing the length of the working day above 7 hours will increase the numbers. However, in the long run overscheduling will lead to inability to maintain a steady pace, with loss of flexibility and a resultant lowering of staff morale and patient comfort.

The accompanying formulaic table shows a typical relationship between caseload and the number of required procedure rooms based on the variable input to the computer. Altering any of the parameters (such as hours of operation, number of working days, or the percentage of colonoscopies) will affect the required number of rooms (Fig. 2.2).

Maintaining room productivity at current levels will be challenged in the future as the number of more therapeutic, and therefore lengthier, procedures increases. Productivity numbers may also be affected by more stringent infection controls, which will require longer room preparation times.

Recovery space

Units that perform more than four procedures per day will require a dedicated procedure room with separate recovery space and skilled staff to operate both these areas. The capacity of the endoscopy rooms will be limited by the ability of the recovery space to handle the flow. The recovery area should be close to procedure rooms and ample in size to handle the volume of cases. This aspect becomes more important as the complexity of both procedures and endoscopy equipment increases.

Projected Volume:

Procedures per Year:	Working Days per Year:	Daily Volume
4500	250	18.00

Procedure Profiles:

Percentage:	Avg Time	Total Time	Avg Procedure Time
Gastro/GI 1350ppy 30%	30 min	40500 min	53 min
Colon/GI 2700ppy 60%	60 min	162000 min	
ERCP 450ppy 10%	75 min	33750 min	

Working time per Day:	Avg Procedure Time	Capacity per Room	Procedure Rooms
hours minutes		w/o Loss 70% Eff procedures procedures	
5.0 hours 300 min	53 min	5.71 4.00	4.50 Required
6.0 hours 360 min	53 min	6.86 4.80	3.75 Required
6.5 hours 390 min	53 min	7.43 5.20	3.46 Required
7.0 hours 420 min	53 min	8.00 5.60	3.21 Required
7.5 hours 450 min	53 min	8.57 6.00	3.00 Required
8.0 hours 480 min	53 min	9.14 6.40	2.81 Required

Fig. 2.2 Endoscopy room projections.

The high cost of equipment and infrastructure in the endoscopy room can only be fully amortized by a continuous and efficient usage of these specialized procedure spaces. It is impractical to have a patient recovering in the procedure room, preventing another procedure from commencing. Through exact scheduling of procedures with varying recovery times, one can create a smooth flow with no fewer than 1.5 recovery spaces per procedure room. However, this assumes optimal conditions without inefficiency and it may well lead to scheduling backlogs if, for example, patients are slower than predicted in coming out of sedation. A more practical ratio is two recovery spaces for each planned procedure room. When the recovery space is used for changing of clothing and preparation before procedures, additional capacity should be considered. In this case a safer ratio would be two and a half to three recovery spaces per procedure room.

A recovery space should be secure, comfortable and appropriate to an ambulatory setting, to some degree separated from inpatient holding areas in hospital units if possible. During the recovery phase, ambulatory cases will usually have accompanying persons who need some access to the patient. This suggests an extra space

requirement in the recovery area for these visitors and some element of privacy. Individual combination dressing and recovery rooms may be used in private offices. This type of space provides the privacy and sound isolation that results in a more comfortable experience, but does require more monitoring effort. A minimum size for this type of recovery room is 5 ft wide by 9 ft long (1.5 m by 2.7 m). Group recovery spaces are common in hospitals and ambulatory centers where direct monitoring is required by regulation. Generally designed with curtained cubicles, these need to be a minimum of 6 ft by 8 ft in size (1.8 m by 2.4 m). However, they lack the private quality of fully enclosed, separate recovery spaces. Providing solid side walls and curtained fronts provides better psychological separation while allowing for adequate observation. New patient privacy regulations in the USA (HIPAA) may require side-wall partitions as a requisite for physician-patient conversations in any recovery room situation. Another compromise is a group-type area used in conjunction with a more commodious separate step-down or second stage room. A step-down room is a space in which the ambiance is more relaxed and where families can join the patient after the medication has worn off. The step-down room can be a lounge or similar space with reclining chairs, music, television, etc.

Private changing areas are desirable in almost any type of unit, especially in larger ones with combined preparation and recovery areas. The use of individual lockers for storage of clothing and valuables is a good idea and avoids the problem of damage or loss of personal possessions. Recovery areas should have daylighting if possible, pleasant décor, and appropriate artificial lighting. Storage should be provided either within or near the recovery space for blankets, bedpans, etc. There need to be provisions for oxygen and patient monitoring, as well as emergency provisions. Ample patient toilets should be located within preparation and recovery areas as well, particularly in the colonoscopy suite where patients have been prepared with enemas or cathartics. A good ratio is an average of one patient toilet for every two procedure rooms. These toilet spaces should be designed for disabled access and equipped with grab bars and high toilet level, which are also appropriate accommodations for patients who may still be under the influence of medication after procedure. An emergency nurse call system is also advisable.

Scope cleaning and storage

Prevention of infection transmission is an important factor in the colonoscopy suite, and following any examination the scopes must be cleaned and fully disinfected. With the increasing problems of HIV, hepatitis B, tuberculosis, and other communicable infections, the risk of contamination must be monitored and eliminated from the gastrointestinal setting. This involves prevention of cross-contamination between clean and soiled scopes. A scope washing room separate and apart from the procedure room is essential. Proper cleaning is the goal and cleaning rooms should be planned with adequate space and ample plumbing and power provisions for automatic high-level disinfecting or sterilization equipment. Adequate counter areas for manual scope cleaning are essential, as well as space for accessory cleaning equipment and tubs for soaking scopes if the automatic washing machines are disabled. A rule of thumb is 3 ft to 6 ft (1 m to 2 m) of counter space free of sinks per procedure room. Several oversized, deep sinks are required whether scopes are washed by hand or automatic equipment is used. The room should be large enough and planned to separate clean instruments from the soiled scopes waiting to be processed. An array of small hooks at the sink area facilitates the handling of the small accessory articles that must also be cleaned each day.

Safe and secure storage for the full inventory of clean scopes and accessories should be provided at convenient locations adjacent to, and in, the endoscopy room. Cabinets for storing of endoscopes must have ventilation provisions to insure that any moisture, which may be

trapped in the instrument after drying, does not promote the growth of microorganisms. Ventilation holes or fan-assisted storage units can be planned.

Room size standards and the written program

A first measure of the success of a facility is whether enough space has been provided for all the planned needs. Once the number of procedure rooms is decided, the amount of recovery space factored in and a list of other spaces assembled, information on room sizes must be determined to complete the program. Standards for general spaces can be found in a variety of source books and published recommendations. However, these are open to review and ongoing evaluation since size requirements will vary somewhat with the particular needs and circumstances under which the spaces function. Reference points and experience are useful in evaluating room sizes; physical measurements of similar spaces are important for comparison purposes. Endoscopy units that perform well should be visited and compared (the program examples below show typical listings of room and room size requirements).

The impact of electronics has been dramatic, and a survey of anticipated and evolving equipment is critical in determining space requirements. This may include space for a fluoroscope, magnetic endoscope imaging, argon plasma coagulator, and so on. Comprehensive data, including electrical power specifications for equipment, ventilation needs, and subjective issues such as sound privacy and lighting quality, are also needed. Building codes, licensing guidelines, and certification standards contain minimum requirements for room and corridor sizes, mechanical services and construction classification information.

Storage requirements must be calculated for both supplies and records and a list of storage needs incorporated in the program. Corridors, storage, and utility rooms will represent up to 30% of the net space in a facility, and this should be included in the total. Certification guidelines have specific requirements for medical records. While record keeping may eventually become electronic, presently it relies on paper in ever growing quantities. Storage and filing for paper needs must be estimated, as well as space for the storage of medical supplies. Most storage should be lockable for both security and privacy reasons. Another measure of the success of the final plan will be the capability of the facility to expand if needed and to be versatile and efficient over its years of service. Therefore, it is advisable to factor in some expansion allowance of additional area (minimally 10–20% beyond projected needs) to accommodate growth and change.

Lastly, projections for staff needs should be factored into the program to insure that enough space has been allotted to provide comfortable and efficient support areas for both physicians and assistants.

Examples of two typical programs are shown, one for an ambulatory center (Fig. 2.3a) and another for a medium-sized office unit (Fig. 2.3b). The program for the ambulatory center, for example, has a total net useable requirement of approximately 8700 ft² (808 m²) for four procedure rooms with a separate general exam zone. The total also reflects requirements most often included in licensed units in the USA. The office endoscopy program describes a total need of 3250 ft² (301 m²) with two dedicated procedure rooms and other needs required for the gastrointestinal practice.

A final program may be represented in different formats. However, the result needs to be a complete enumeration of the particulars including a list of space requirements complete with dimensions and net areas. Numbers for corridor circulation, utility spaces, miscellaneous functions, and a contingency allowance for growth and unforeseen changes must be factored in for a calculated total gross area need. The completed program is a useful guide in evaluating available locations for a new facility. The total area requirement as estimated from the list of particulars may be the first indication that desires are not compatible with the business plan or budget or with available properties, and that compromises must be made. The program can be continually refined and adjusted to reality as well as a more precise awareness of needs. It is a statement of goals and useful as a checklist throughout the project to determine whether all the requirements are included in the final drawings and will be included in the finished facility. If thoroughly executed much time will be saved in later design stages and costly mistakes will be avoided in construction.

Tip—information to collect

A loose-leaf notebook can be helpful for collecting the following information that is developed in the program process. Descriptive notes should be recorded whenever they are thought about, and checked against the plans on a regular basis (Table 2.1):

- caseload and utilization projections;
- space sizes and total areas desired;
- equipment list;
- electrical power demands for equipment;
- areas requiring ventilation for hospital suites where colonoscopy is to be performed;
- provisions for negative pressure where airborne contagious disease may be prevalent;
- areas requiring sound privacy;
- lighting needs;
- interior design goals.

Arrangement

A successful design for an endoscopy project provides for effective movement patterns of patients and staff and can be critical in controlling operational costs. These flow patterns are dependent largely upon decisions about the arrangement and placement of procedure areas, recovery spaces, and other key elements that are decided on when planning the unit. When a layout is inefficient, causing staff to cover large distances to get supplies, clean scopes and monitor recovery, or when bottlenecks occur in the patient flow, the potential of the unit is limited, additional staff will be needed, and operating expenses will be higher.

A dedicated endoscopy facility is composed of two core elements, the procedure zone and the administration operations area.

Table 2.1 Descriptive notes.

1	Remote monitors on procedure imaging network
2	Walls which surround the procedure rooms, as well as doors to these rooms, should have acoustical ratings to contain procedure sounds
3	The procedure rooms should be designed with two modes of lighting
4	A double monitor system should be planned for the procedure rooms. In a two-monitor system, both physician and assistant can have a comfortable view of the procedure image
5	Procedure spaces should be equipped with a means of exhaust and ventilation to remove odors. Provide 15 air changes per hour with direct exhaust of used air to outside
6	In cleaning rooms exhaust grills should be located near the floor and at counter height
7	Scope washing rooms should be located with pairs of procedure rooms
8	Oxygen, suction, and medical air should be located in procedure rooms, recovery areas, etc.
9	Emergency call button system
10	Exam table, writing area, cabinets, X-ray viewer
11	Locked cabinets for drugs
12	Emergency communication system
13	Emergency (crash) cart

Room Name	Room Size		Area		Qty	Descriptive Notes	Total Area	
	feet	metric	feet	metric			feet	metric
Administration Areas								
Waiting Room	20' x 30'	6.1m x 9.1m	600 sf	56m	1	individual seating for 30 persons	600 sf	56sm
toilet	6' x 8'	1.8m x 2.4m	48 sf	4m	1	disabled accessible(9)	48 sf	4sm
patient education area	7' x 9'	2.1m x 2.7m	63 sf	6m	1		63 sf	6sm
Reception station	8' x 12'	2.4m x 3.7m	96 sf	9m	1	scheduling and appointments	96 sf	9sm
computer station	6' x 8'	1.8m x 2.4m	48 sf	4m	2	billing area	96 sf	9sm
files and records	12' x 20'	3.7m x 6.1m	240 sf	22m	1	high density filing	240 sf	22sm
copier/fax	6' x 8'	1.8m x 2.4m	48 sf	4m	1		48 sf	4sm
Offices, physicians	12' x 15'	3.7m x 4.6m	180 sf	17m	3	monitors,(1)	540 sf	50sm
nurse's office	8' x 10'	2.4m x 3.0m	80 sf	7m	1		80 sf	7sm
computer-server	12' x 18'	3.7m x 5.5m	216 sf	20m	1	computer-(1)	216 sf	20sm
conference room	13' x 16'	4.0m x 4.9m	208 sf	19m	1	videomonitor	208 sf	19sm
exam rooms	8' x 10'	2.4m x 3.0m	80 sf	7m	3	discussion,exam,desk,sink	240 sf	22sm
patient toilets	6' x 6'	1.8m x 1.8m	36 sf	3m	2		72 sf	7sm

Procedure areas

Dressing areas/prep-M/F	6' x 8'	1.8m x 2.4m	48 sf	4m	4	male,female	192 sf	18sm
locker area	6' x 12'	1.8m x 3.7m	72 sf	7m	2	male,female	144 sf	13sm
patient toilets	6' x 6'	1.8m x 1.8m	36 sf	3m	4		144 sf	13sm
waiting	10' x 14'	3.0m x 4.3m	140 sf	13m	1		140 sf	13sm
nurses desk	6' x 10'	1.8m x 3.0m	60 sf	6m	1		60 sf	6sm
Endoscopy (general)	15' x 18'	4.6m x 5.5m	270 sf	25m	4	Colonoscopy(2,3,4,5,8,11,12,13)	1080 sf	100sm
nurse's station	8' x 8'	2.4m x 2.4m	64 sf	6m	1	handwashing sink	64 sf	6sm
utility/storage	12' x 17'	3.7m x 5.2m	204 sf	19m	1		204 sf	19sm
dictation area	7' x 12'	2.1m x 3.7m	84 sf	8m	1		84 sf	8sm
Scope washing	8' x 15'	2.4m x 4.6m	120 sf	11m	2	scope washer-(5,6,7,8,11)	240 sf	22sm
scope storage	5' x 12'	1.5m x 3.7m	60 sf	6m	1		60 sf	6sm
Recovery	6' x 12'	1.8m x 3.7m	72 sf	7m	9	curtain cubicles (8,9)	648 sf	60sm
toilet	5' x 6'	1.5m x 1.8m	30 sf	3m	1		30 sf	3sm
nurse's station	8' x 12'	2.4m x 3.7m	96 sf	9m	1	central, good view -(14)	96 sf	9sm

Support Services

Staff Room-M/F	12' x 14'	3.7m x 4.3m	168 sf	16m	1	refrigerator, microwave etc	168 sf	16sm
staff toilet	6' x 6'	1.8m x 1.8m	36 sf	3m	1	shower stall	36 sf	3sm
staff lockers	10' x 12'	3.0m x 3.7m	120 sf	11m	2		240 sf	22sm
Storage supplies	8' x 12'	2.4m x 3.7m	96 sf	9m	1	bulk style carts	96 sf	9sm
clean area	6' x 10'	1.8m x 3.0m	60 sf	6m	1		60 sf	6sm
soiled area	8' x 10'	2.4m x 3.0m	80 sf	7m	1		80 sf	7sm
janitors cl	4' x 4'	1.2m x 1.2m	16 sf	1m	1		16 sf	1sm

Space Total

SubTotal Area

6429 sf 597sm

Circulation factor 35% (corridors, shafts, columns etc.)

2250 sf 209sm

TOTAL NET AREA

8679 sf 806sm

(a) Measurement excludes space occupied by stairs, elevators electrical closets and mechanical spaces

Room Name	Room Size		Area		Qty	Descriptive Notes	Total Area	
	feet	metric	feet	metric			feet	metric
Administration Areas								
Waiting Room	13' x 15'	4.0m x 4.6m	195 sf	18m	1	individual seating for 14 persons	195 sf	18m
toilet	6' x 7'	1.8m x 2.1m	42 sf	4m	1	disabled accessible (9)	42 sf	4m
Reception station	6' x 10'	1.8m x 3.0m	60 sf	6m	1	scheduling and appointments	60 sf	6m
computer station	6' x 8'	1.8m x 2.4m	48 sf	4m	3	billing area	144 sf	13m
files and records	12' x 15'	3.7m x 4.6m	180 sf	17m	1	high density filing	180 sf	17m
copier/fax	6' x 6'	1.8m x 1.8m	36 sf	3m	1		36 sf	3m
Physician's Consult	12' x 12'	3.7m x 3.7m	144 sf	13m	2	monitors,(1)	288 sf	27m
patient education	7' x 10'	2.1m x 3.0m	70 sf	7m	1		70 sf	7m
nurse manager	10' x 12'	3.0m x 3.7m	120 sf	11m	1		120 sf	11m
toilet	6' x 6'	1.8m x 1.8m	36 sf	3m	1		36 sf	3m

Procedure areas

Prep-Recovery/Dressing	6' x 10'	1.8m x 3.0m	60 sf	6m	4	male,female	240 sf	22m
patient toilet	6' x 6'	1.8m x 1.8m	36 sf	3m	1		36 sf	3m
exam rooms	8' x 10'	2.4m x 3.0m	80 sf	7m	3	discussion,exam,desk,sink	240 sf	22m
Endoscopy (general)	12' x 15'	3.7m x 4.6m	180 sf	17m	2	Colonoscopy- (2,3,4,5,8,11,12,13)	360 sf	33m
nurse's station	3' x 10'	0.9m x 3.0m	30 sf	3m	1	handwashing sink	30 sf	3m
storage	10' x 10'	3.0m x 3.0m	100 sf	9m	1		100 sf	9m
Scope washing	8' x 12'	2.4m x 3.7m	96 sf	9m	1	scope washer-(5,6,7,8,11)	96 sf	9m
scope storage	5' x 2'	1.5m x 0.6m	10 sf	1m	1		10 sf	1m

Support Services

Staff lounge	8' x 12'	2.4m x 3.7m	96 sf	9m	1		96 sf	9m
Storage supplies	6' x 10'	1.8m x 3.0m	60 sf	6m	1		60 sf	6m
clean area	6' x 8'	1.8m x 2.4m	48 sf	4m	1		48 sf	4m
janitors cl	3' x 4'	0.9m x 1.2m	12 sf	1m	1		12 sf	1m

Space Total

31 SubTotal Area

2499 sf 232m

Circulation factor 30% (corridors, shafts, columns etc.)

750 sf 70m

TOTAL NET AREA

3249 sf 302m

(b) Measurement excludes space occupied by stairs, elevators electrical closets and mechanical spaces

Fig. 2.3 Endoscopy unit profile: (a) ambulatory center; (b) private office. See also Table 2.1 for the numbering of descriptive notes.

Procedure rooms, changing and prep areas, recovery, and scope cleaning form the heart of the procedure zone, while business office, waiting room and consultation offices are part of the administration area. The two components function interdependently; however, each is a self-contained work center with different types of staff. Their functions should not be mixed. For example, medical business records should not be stored in the procedure zone and medical supplies should not be kept in the administration area. Patients should be able to move from one zone to the other without traveling excessive distances through complicated corridor pathways requiring additional staff to monitor traffic. On the other hand, waiting areas should be located remotely from the endoscopy zone for purposes of sound isolation, patient and visitor control, and for esthetic reasons as well. Whether the planning is being done for a large multi-room facility or for the reworking of an existing office for occasional endoscopy, there are fundamental patient handling and movement principles that should be addressed in planning the space.

As facilities become more complex, additional elements surround and interrelate with this core. Hospitals will often have teaching areas, and ambulatory units may have clinical examination areas that operate in close cooperation with the endoscopy activities. In certified ambulatory centers in the USA there are very strict rules about the separation of endoscopy areas from all other activities, medical or otherwise.

In any project, flow diagramming can be a powerful tool for understanding and evaluating arrangement options prior to preparing preliminary plans. In a simple flow diagram, rooms are represented as oval shapes or bubbles. Arrows indicate relationship between activities and are an expression of adjacencies and resulting movement patterns (Fig. 2.4).

The following sequence of steps routinely occurs for every patient undergoing an endoscopic procedure. This workflow can be translated into a simple, one-directional movement pattern in the final layout.

- 1 The patient arrives at registration and completes necessary paperwork and administrative information.
- 2 The patient waits.
- 3 The patient is brought from waiting to preparation area where clothing is stored and exchanged for a gown.
- 4 The patient is transported from the preparation area to the procedure room.
- 5 The patient is sedated and a procedure is performed.
- 6 The patient is transported from the procedure area to a recovery room.
- 7 The patient meets with the physician.
- 8 The patient leaves the procedure zone and completes any unfinished administrative business related matters.
- 9 The patient exits the unit.

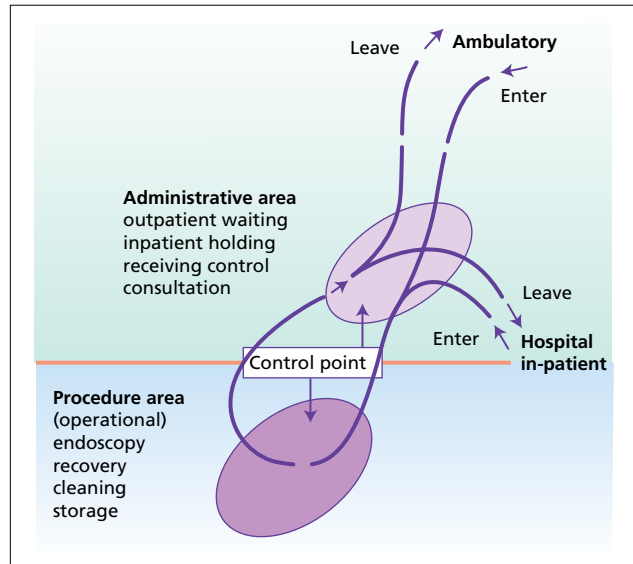


Fig. 2.4 Patient movement patterns.

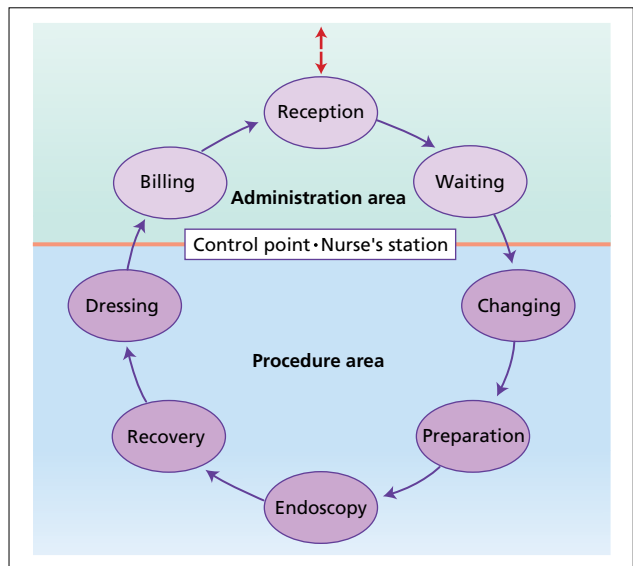


Fig. 2.5 Patient flow sequence.

This sequence of stages can be diagrammed as a circle. Patients travel a sequential path from reception through preparation, procedure and recovery, finally returning to administration for processing and departure (Fig. 2.5).

The most efficient layout for a project is achieved by grouping interdependent elements with minimum distances between one another. Waiting should be reasonably close to preparation/recovery, which should be adjacent to the procedure areas. Preparation/recovery is a transitional area due to its central role in the patient sequence. Its placement with respect to the other

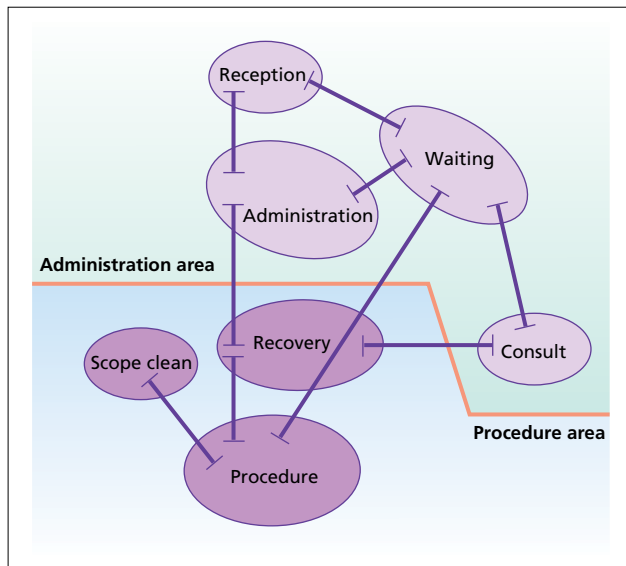


Fig. 2.6 Endoscopy suite—critical relationships.

components in most cases is the key to satisfactory design and efficient movement pattern (Fig. 2.6).

The same principles of proximity apply to staff movement patterns. If close together, recovery, procedure, and scope cleaning areas facilitate the many tasks that must be performed by staff. It is desirable to group endoscopy procedure rooms with scope washing and other support functions. The result is a localized travel pattern for staff activities pre and post procedure. Clustering procedure rooms around scope washing areas with direct access between the rooms is an ideal arrangement for achieving this kind of efficiency. If it is not possible to achieve direct access, the scope washing room or rooms should be positioned close to the group of procedure rooms. This ideal relationship is expressed in a flow diagram with arrows indicating important functional proximity and patterns of movement (Fig. 2.7).

Tip—questions to ask

- How many of the staff are typically assisting in procedures?
- Who is responsible for preparation of the procedure area?
- How do assistants monitor the recovering patients?
- How are scopes and other equipment cleaned?
- Who will be responsible for the organizing of supplies and cleaned equipment?

When patient and staff movements are superimposed, maintaining the separation of each activity circulation pattern is optimal. In the hypothetical endoscopy unit diagram (Fig. 2.8), patient movement is expressed as

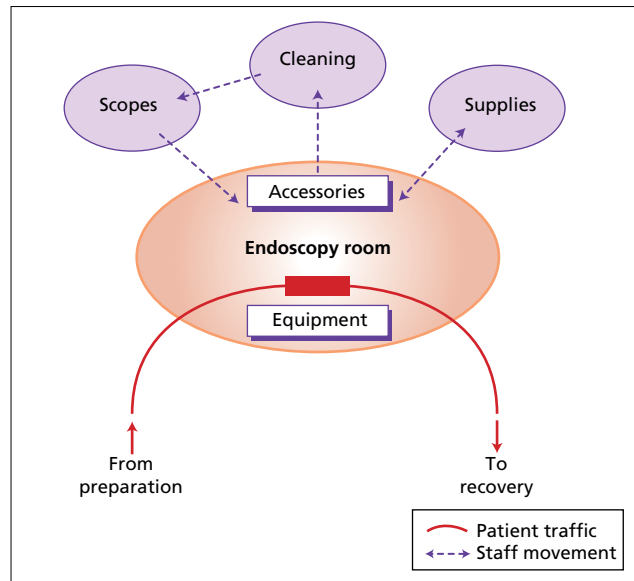


Fig. 2.7 Flow pattern in the procedure room.

a sequential flow extending from the waiting room to preparation and changing, then to procedure and recovery spaces. The patient exits from the recovery room past the administration area and through the waiting room with minimal retracing of steps. The ideal patient path does not overlap or result in conflicts with the movement pattern of the staff. In the hospital, stretcher traffic and movement patterns of patients on foot should be kept separate.

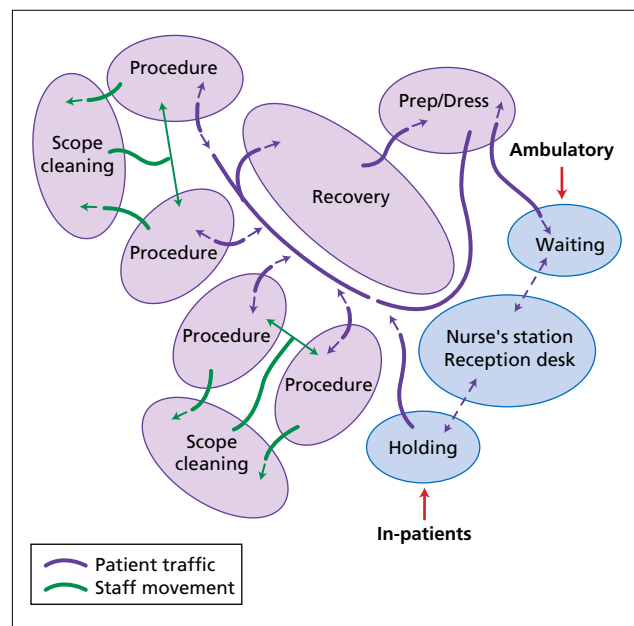


Fig. 2.8 Patient and staff movement pattern.

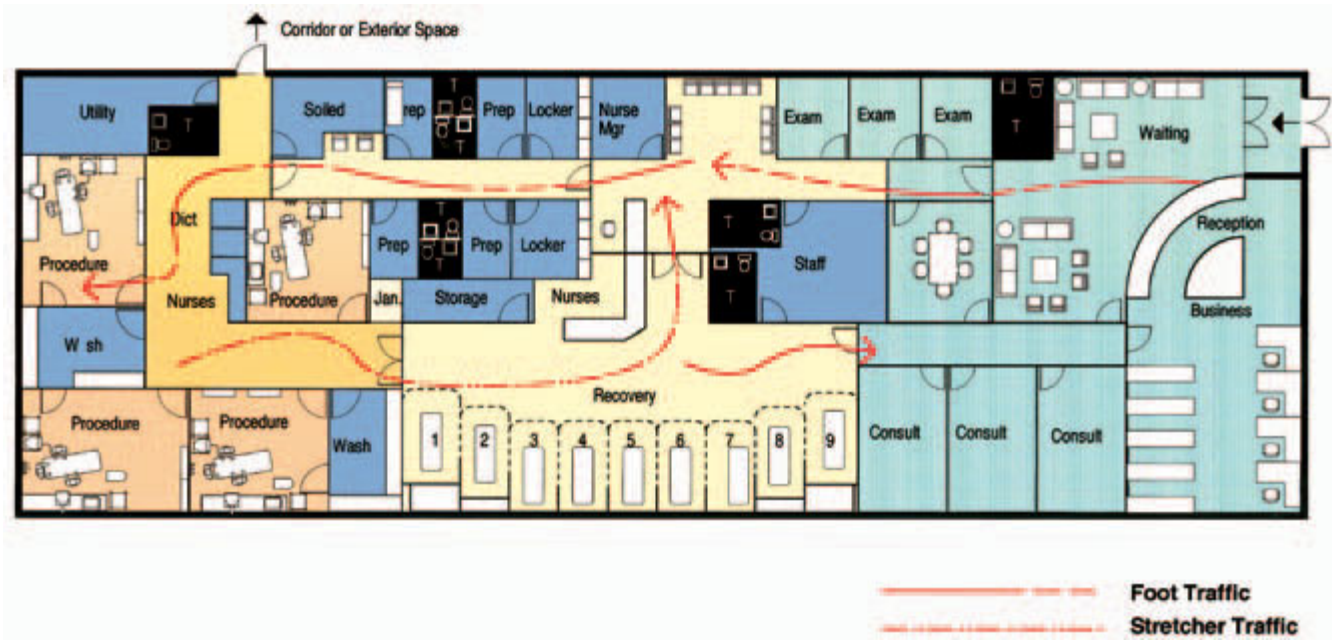


Fig. 2.9 Ambulatory endoscopy suite.

With ideal movement patterns clarified, a schematic block diagram can be prepared to approximate specific space configuration. Block diagrams vary widely but generally are a more realistic flow study, can be true to scale, and may factor in existing elements such as elevators, stairs, and other conditions. These studies are easy for physicians to understand and are a useful tool for evaluating alternative solutions and confirming flow patterns without expending large amounts of time and money. The block diagram example (Fig. 2.9) here represents a mid-sized ambulatory endoscopy unit with four dedicated procedure rooms and recovery space for 9. The diagram has been drawn with superimposed arrows indicating the patient flow pattern.

Preliminary planning solutions

The purpose of a preliminary plan is to represent a realistic overall layout of the unit or suite, taking into account room size, actual areas, and site conditions. At this stage a floor plan is prepared, room arrangements are finalized, and length and width dimensions are verified. It is important that preliminary drawings be precise and show the general locations of equipment with enough detail to make certain that everything will fit. Details such as door placement and size, pathways between areas, and the particular movement of medicated patients on stretchers from procedure rooms to recovery should be obvious and clearly stated. As the design develops toward a workable stage, aspects of the

plan should be periodically reviewed for adherence to the original movement and flow objectives.

This example (Fig. 2.10) of a preliminary plan shows the ambulatory center design in a more developed state. The patient movement pattern and arrangement is consistent with the block diagram and general goals. The procedure zone of this ambulatory unit is arranged with four dedicated endoscopy rooms flanking a core of preparation, washing and laboratory support functions.

Design development

Procedure room design

Design development furnishes a full elaboration of the specific layout coordinated with other requirements. The drawings and other supporting material such as outline specifications, cost estimates, etc. form a final planning tool that describes the total scope of work. In this phase the location of equipment is finalized and requirements are established for physical supports as well as power and communications connections. Particular emphasis at this stage is on the complete development of procedure room layouts.

There is ongoing discussion, sometimes verging on controversy, about appropriate procedure room size. Recommendations ranging from 190 to 300 ft² (17.5–28 m²) have been proposed by experts in the field. These differing points of view have validity in specific situations. Judgements about which room size configuration works in a given situation can be facilitated by analyzing the workflow of the endoscopist and assistant as well



Fig. 2.10 Preliminary plan of ambulatory centre.

as the constraints dictated by scope umbilical lengths, viewing distances and clearances required.

Licensing laws in the USA generally require that rooms have a net or clear floor area of 200 ft² (18.6 m²). The clear area requirement excludes fixed elements such as built-in counters and nonmovable storage cabinets. Carts on casters and other easily movable components are generally permitted to be included within the clear area of the room.

The well-planned endoscopy room breaks down into several primary components. First is the endoscopist's work zone, which generally requires a relatively small clear space of 28 in. (0.7 m) to 32 in. (0.81 m) between stretcher and equipment, which allows room for the physician to maneuver and is within the limits of the length of the umbilical. The assistant needs 36 in. (0.91 m) to 40 in. (1.0 m) of space, the ability to move easily around, and adjacent counter space or an accessory cart so that supplies and implements are readily accessible. Lastly, a minimum clear floor area of 7 ft 6 in. (2.3 m) between fixed elements is required for positioning and rotation of the typical stretcher measuring 31 in. by 83 in. (0.79 m by 2.1 m). These elements are common building blocks in all procedure rooms (Fig. 2.11).

There are two categories of procedure room organization that directly apply these concepts. Classified here as parallel layout and corner layout configurations, they

tend to be appropriate to smaller and larger rooms, respectively. In concept, both these configurations closely surround the patient, doctor, and assistant with primary equipment, supplies, and controls. Each arrangement enables monitor locations to be within acceptable distances with clear comfortable viewing sight-lines and makes possible concealment or elimination of cables from the floor area.

In a parallel room plan, equipment areas 24 in. (61 cm) deep are arranged on the two opposing long walls establishing work zones and clearances on either side of the stretcher. A 12 ft (3.7 m) dimension is optimal for the width of a parallel configured room and places the endoscopist at a comfortable viewing distance of 6–7 ft (2 m) from a monitor wall-mounted across the space. Since all equipment is on one wall or the other, the 12-ft (3.7 m) width also facilitates the concealed interconnecting of cables through walls and ceiling areas (Fig. 2.12(a) and (b)).

The corner layout approach solves problems inherent in the use of large rooms. Larger sized (square shaped) rooms are routinely planned to meet a specialized need; for example, the minimum 200 ft² (18.6 m²) in ambulatory centers, hospital rooms, and those used for teaching purposes. Additionally, there is a school of thought that somewhat convincingly suggests that larger rooms in hospitals allow greater flexibility and accommodate the greater variety of complex procedures encountered there. If rooms are large but not planned well, open floor space becomes excessive, resulting in wasted space and inefficient and tiring movement patterns for those who

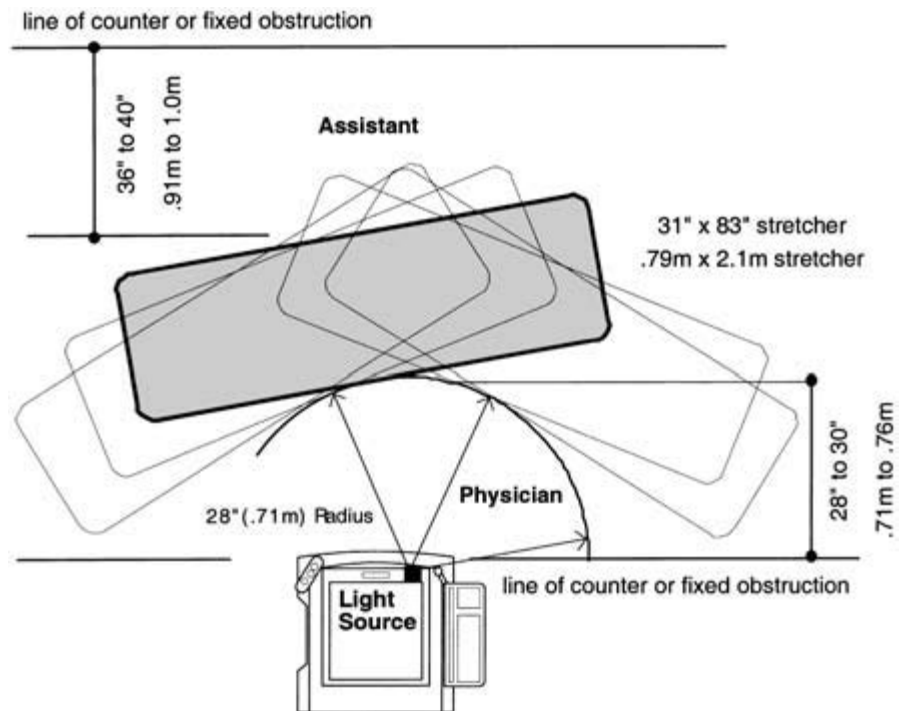


Fig. 2.11 Basic clearances.

work there. In these cases cables can often be found lying across floor areas creating a tripping hazard. Corner layouts work well by clustering the key building blocks of the work zones in a smaller part of the room, incorporating the same space principles outlined above for the parallel approach. In the corner alternative the light source and processor are located to the right of the physician. The monitor is located on the perpendicular wall and is to the front of the physician at a distance of approximately 6–7 ft (2.0 m).

Figure 2.12(c) and (d) show examples for both parallel and corner designed rooms. Each set shows variations on specific needs and indicates where specialized or ancillary equipment can be placed.

A 12 ft by 19 ft (3.7 m by 5.7 m) general purpose colonoscopy room is an example of a parallel configuration that works well and demonstrates the underlying principals. This room size (228 ft² or 21 m²) provides ample space for equipment and storage, comfortable work zones, clear floor space for stretcher movement, flexibility for future growth, and the ability to easily conceal most cabling. It also represents room dimensions that satisfy the minimum area of 200 ft² (18.6 m²) clear of the built-in cabinetry that meets most US license requirements for room size. Where minimum area requirements do not govern, in private offices for example, the room may be shortened to 15 or 16 ft (4.6–4.9 m) in length without compromising the essential qualities. The resulting total area is 190 ft² (17.5 m²) including cabinets and fixed elements. This use of this particular

room size is advantageous in light of construction cost savings and reduced real estate expenses (Fig. 2.13).

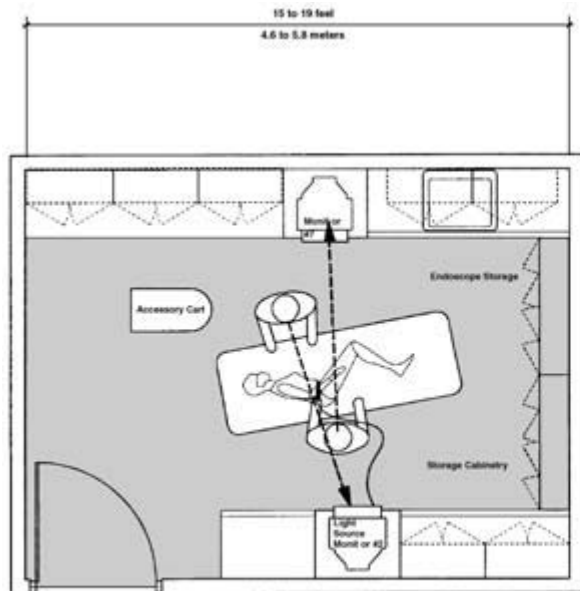
Tip—key recommendations

- Connection points on the walls and concealed cabling pathways in the wall and over the ceiling.
- Optimal viewing distances—7 ft (2.0 m) maximum.
- Clear areas in center for work zones and stretcher.

Equipment arrangement options

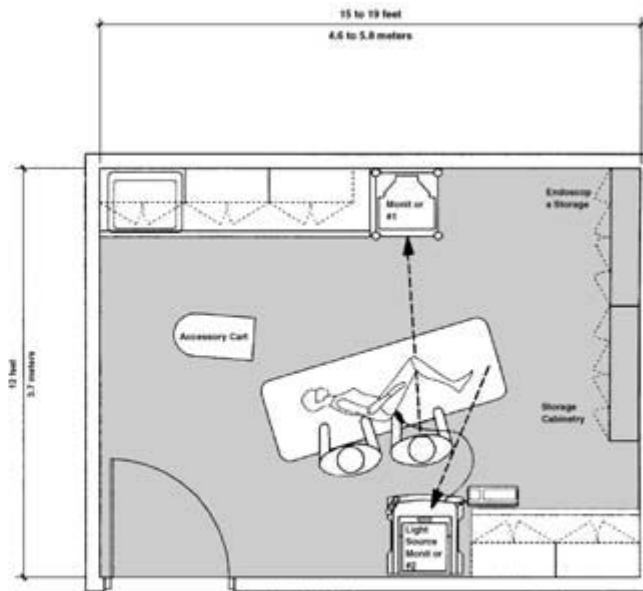
Considering the large amount of equipment now routinely found in the procedure room, some form of vertical arrangement or stacking of devices is logical. This economizes floor space and helps to concentrate and define the work zone areas. There are three basic approaches to implementing this concept. Equipment can be organized in custom-designed cabinetry towers, placed on a combination of tall manufactured equipment carts and wall mounts, or placed on structurally supported articulating arms that float from the ceiling plane. Each system is capable of holding three or more devices on shelves or mounts, one above the other with cables and power connections along the back.

Because in most cases procedure rooms divide naturally into two work zones (the endoscopist and the assistant), separate and interconnected equipment stacks should be planned opposite each other in the space. The first stack behind (or to the side) of the physician will



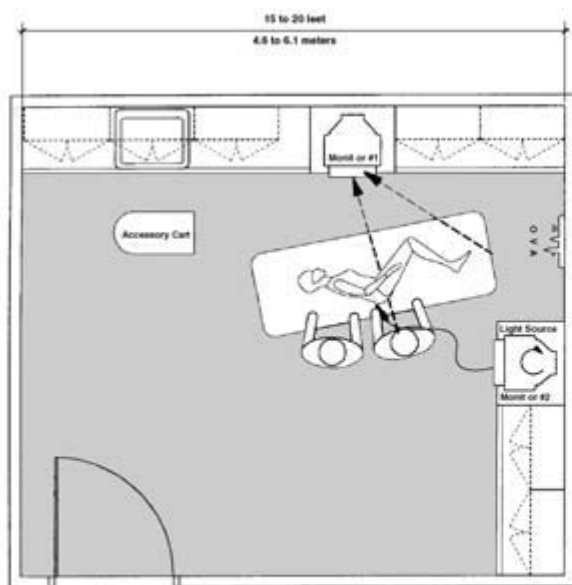
Parallel Room with Equipment Cabinets

(a)



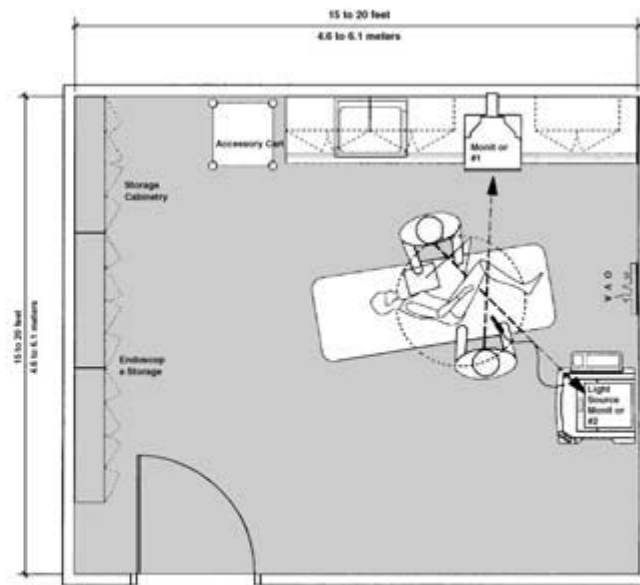
Parallel Room with Equipment Carts

(b)



Corner Room with Equipment Cabinets

(c)



Corner Room with Equipment Carts

(d)

Fig. 2.12 Procedure room comparison.

hold a light source and video processor, secondary monitor, and other peripherals. The second stack on the gastrointestinal assistant (GIA) side will hold recording equipment, image printer, electrocautery devices, and principal viewing monitor, with room for more. In a parallel room design the two stacks will be on the long walls opposite each other. In the corner layout they are at right angles to each other defining the work zones.

Comparative room diagrams and photographs show these three alternative arrangement methods.

Option one (Fig. 2.14a) has two tall cabinetry units in which the equipment items (light sources, suction devices, controllers, and monitors) are arranged vertically. Each cabinet has adjustable shelving and an adjacent vertical compartment that holds a power strip and the necessary cables and wires.

Option two (Fig. 2.14b) shows a manufactured cart placed below a wall-mounted monitor on a bracket support. This creates a vertical assemblage of devices

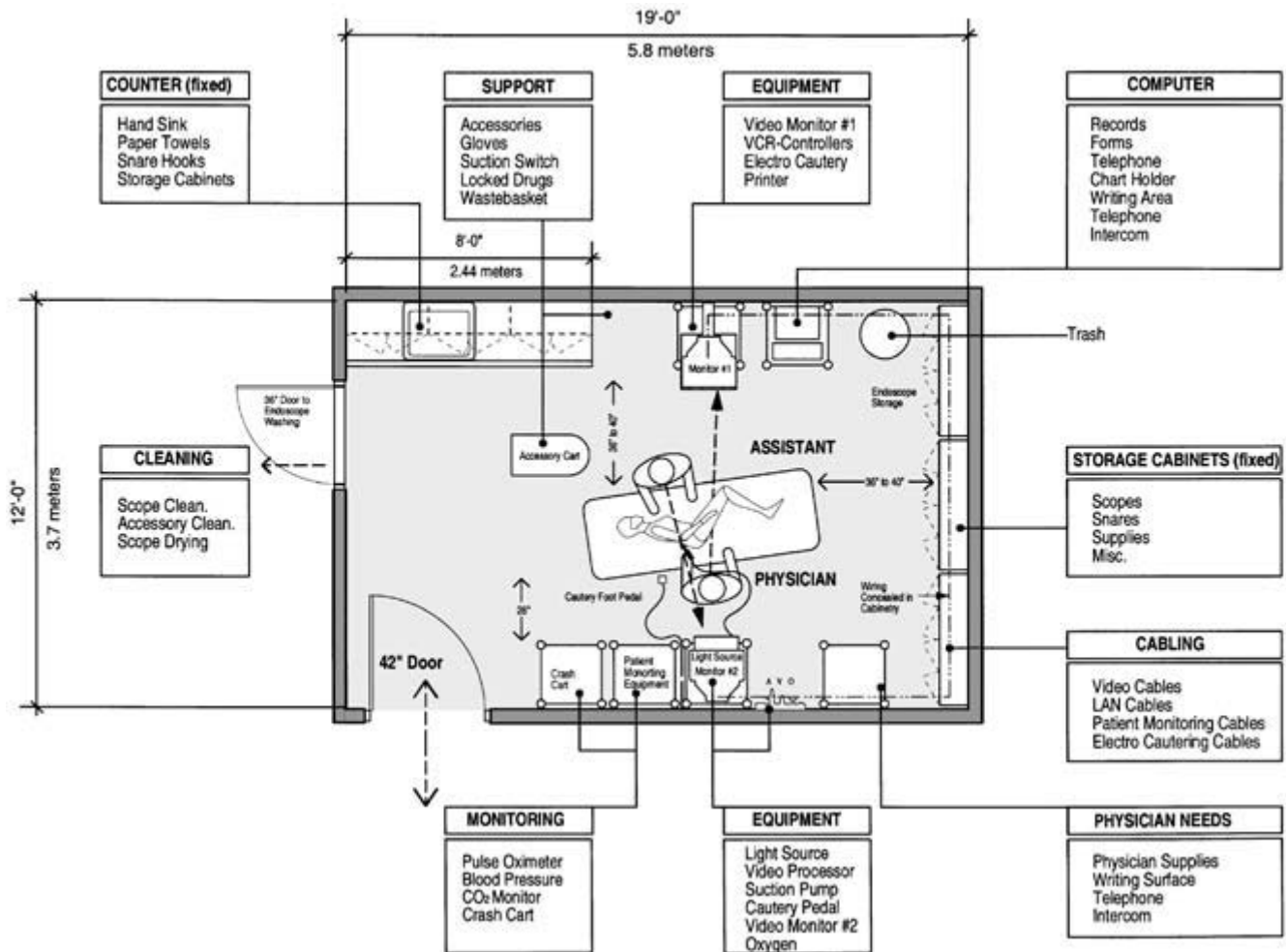


Fig. 2.13 Typical procedure room arrangement (parallel configuration) 200 ft² (18.6 m²).

interconnected through wall channels or within the cart.

The third option (Fig. 2.14c) is the floating ceiling mounted arm. These are available in many configurations and in varying load capacities. They provide adjustability and can be easily repositioned to suit different individual needs. Cables are fed through the arm from the ceiling and therefore kept off the floor. However, these arms are expensive, require costly structural provisions to install, and may be realistic in only select circumstances.

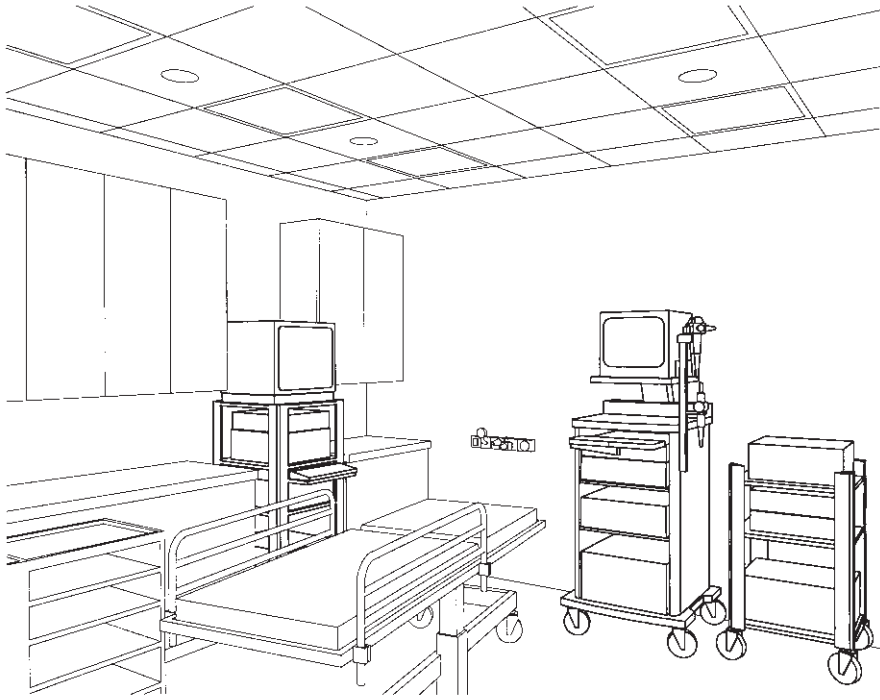
In all of these options, decisions on where TV monitors are located should be resolved with "sightline" studies. As mentioned previously monitors need to be within a distance of 6–7 ft from the endoscopist for clear viewing of a 20 inch (51 cm) CRT or flat screen device. Some physicians prefer a closer image. In addition, monitor height is extremely important. If placed too low the image can be obstructed from view by other people mov-

ing in the room, while monitors placed too high on a ceiling bracket can cause unnecessary neck strain and discomfort for the physician. A suggested height is 6 ft (2 m) to the center of the monitor. It is also important for the assistant to be able to view the endoscopic image along with the endoscopist. If the assistant stands opposite the physician, as is common in most instances, this will necessitate a second monitor located on the physician side of the room. If the assistant stands next to the physician they can both observe the same monitor. An additional set of devices for patient monitoring can be incorporated in one of these stacks or placed on a third independent cart or ceiling arm.

In order to keep floor areas clear of wiring, pathways provided in cabinetry, in raceways, or in accessible ceiling areas should be incorporated into procedure room design for all cabling. This includes provisions for coaxial cables to video monitors, power wiring for all equipment, telephone cords, computer network cables, and connections to patient-monitoring devices. The interconnection of equipment with cables and power cords is basic to the planning and should not be an afterthought.



(a)



(b)

EQUIPMENT IN CARTS

Fig. 2.14 (a) Two tall cabinetry units. (Photograph courtesy of Kenneth Perry, Kingsport, TN.) (b) Equipment in carts.



Fig. 2.14 (cont'd) (c) Floating ceiling mounted arm. (Photograph by Bernstein Associates, Mt Vernon, NY. Courtesy of Dr B. Kummer.)

The primary planning requirement is that power receptacles and video and data connection plates need to be located in close proximity to the devices they serve (Fig. 2.15).

Endoscopy carts should be selected with an eye towards wire and cable management. These include provisions for cable conduits at the rear of the cart and multiple plug strips directly on the cart to power all the devices. The cart itself is then plugged into a nearby receptacle.

When designing cabinetry used to house equipment, empty spaces can be incorporated where cables can run freely behind or to the side of the various devices that need to be interconnected. These compartments are best accessed by doors or removable panels. Cabinets may also have internal power distribution through continuous plugmold strips installed within the accessible cabling space.

Walls should be constructed with empty piping or metal conduits 1 in. (2.54 cm) in diameter leading to every point of connection for the required cabling. These empty channels usually terminate above the ceiling and provide clear pathways from one point in the room to all other locations where devices need to be connected. This plan assumes that the ceiling is an empty void that will allow cabling to be extended to the opposite side of the room. Therefore, the ceiling should be constructed with a lay-in accessible tile suspension system or with access doors installed in the Gypsum board plane. Conduit pathways in ceiling areas provide additional protection against damage and shield cables from magnetic field

interference caused by fluorescent light ballasts and fans or other motors.

Additional considerations

Doors into procedure rooms should be at least 36 in. (0.92 m) wide to allow stretchers to pass freely between rooms. It is good policy to have locking devices on the inside of the doors to prevent wandering patients from entering unannounced.

A charting surface should be planned for each procedure room. This may be combined with a computer area but should be close to the head of the patient to be within easy reach of the physician and assistant.

Suction where provided through central systems should be provided at multiple locations, including one in proximity to the patient and one directly behind or adjacent to the light source cart or cabinet.

Locked drug cabinets are required in or near procedure rooms, and scope storage cabinets can be located in the procedure room or centrally. Ample space should be provided for garbage cans and receptacles for special disposal needs such as sharps, etc.

Continuous plug-in strips of electrical outlets may be installed along the entire length of equipment counters to cover contingencies and add flexibility.

Soundproofing and privacy

Walls that surround procedure rooms should be acoustically insulated to prevent procedure noises and staff

(c)

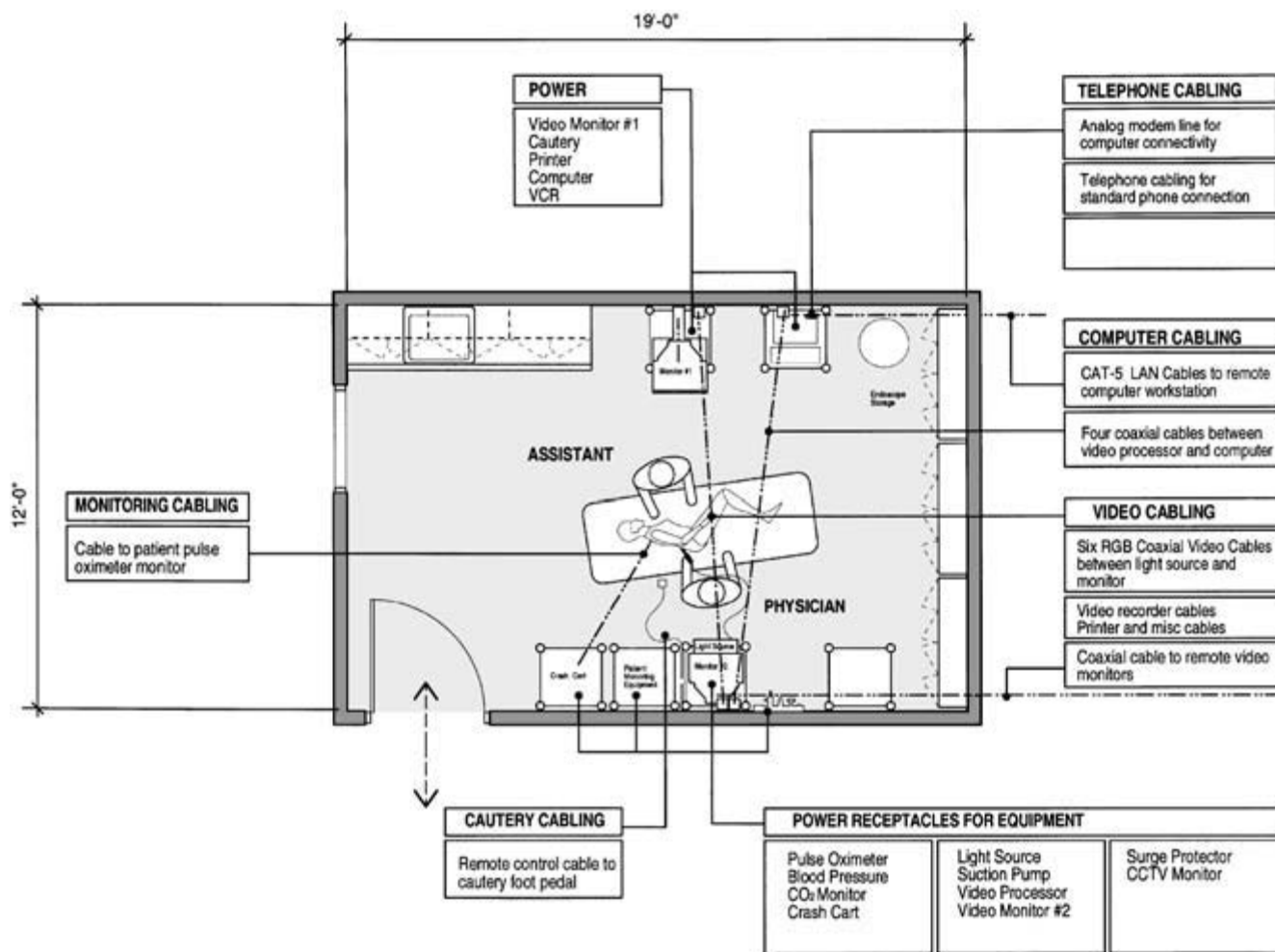


Fig. 2.15 Typical cabling and power requirements.

discussions from being overheard by patients in recovery areas or adjacent rooms and corridors. Doors in these walls should be sound rated and provided with bottom seals and sound gasketing. There are various standard details for constructing sound partitions but generally these partitions must fully extend to the structural slab above the ceiling. Manufacturer's installation recommendations must be followed carefully to achieve the full intended sound value. Wall systems are judged acoustically by their STC (sound transmission) ratings. A rating of STC 49 or higher should be used around procedure rooms. Door ratings can be slightly less but are always the weakest point in a sound isolation system. They must be installed perfectly with all gaps closed or sound will pass through and around the perimeter. Acoustic tile ceilings are recommended to further absorb sound and reduce transmission.

Materials

Wall materials can be light colored and washable to present a clean and bright environment. Coated paper, vinyl fabric, or spray-on composite paint application will allow easy cleaning of the surfaces. Flooring should be made of resilient material for comfort, and should be fully washable with no gaps, spaces or seams to collect dirt. Sheet vinyl with chemical or heat-welded seams and an integral coved base is the best choice. Counters and cabinetry surfaces should be covered in high-pressure laminate materials, stainless steel, or metal with baked on enamel coatings. Counter areas should have full backsplash areas with completely sealed seams at counter joints. All these materials will take wear and are easily cleaned.

Emergency facilities

Every endoscopy unit should be equipped to deal with emergency situations. In the office or ambulatory setting

this means that a patient may have to be transferred quickly to a hospital for care. For this purpose, it is wise to have an exit area that will be discreet, with easy access to an ambulance driveway or street. This exit should be remote from the main entry to avoid transporting a sick and sedated patient in discomfort through a crowded waiting room. The endoscopy unit should also have an area set aside for storage of emergency equipment that can be moved rapidly to wherever it is needed, usually a crash cart with oxygen, an EKG machine, and a defibrillator.

Heating, ventilating, and air conditioning

Air conditioning and heating systems should be designed to provide a degree of control appropriate to the different functions within the unit. Endoscopy rooms should be separately zoned and easily adjusted for the range of temperatures required for patients who can be sensitive to cooler settings and for staff who are active and desire air conditioning. These spaces should also be equipped with a means of supplemental exhaust capable of extracting odors and refreshing the air providing 10–15 air changes per hour. The endoscope cleaning area must be well ventilated against the build up of irritating fumes from disinfection agents, which are unpleasant and potentially harmful to staff. Fume extraction grills in cleaning spaces should be located at counter level and low in the room to deal with vapors that are heavier than air.

New buildings generally provide central air conditioning systems; however, the degree of heating/cooling and ventilation control may be inappropriate for colonoscopy procedures and existing systems can be difficult or costly to modify. Early evaluation of the capability of existing systems will pinpoint potential problems that may be encountered and help to avoid complications later on. If the air conditioning systems are self-contained and dedicated to the facility or the procedure zone rooms, adequate space and power must be provided for the central equipment and its servicing requirements. To accommodate dedicated air conditioning equipment a separate room with some access to the exterior may need to be planned. Requirements for negative pressure in specialized circumstances should be considered.

Plumbing

Multiple plumbing connections are required in any endoscopy center. In multistorey buildings the planning of sinks, toilets, and other plumbing items can be complicated by the need to run drainage lines in the ceiling of the floor below. It is important to determine that plumbing lines can be run easily to the many locations required

at procedure, scope cleaning and toilet spaces. If the location for the new unit is on grade, special care must be taken to plan all plumbing connections before the concrete floor slab is poured in place. Local regulations about disposal of chemicals used in the process of disinfecting and washing of endoscopes must also be taken into consideration. Backflow prevention systems, while now routinely incorporated in automatic scope cleaning units, may be additionally required by codes as part of the plumbing roughing to prevent contamination of the domestic water supply.

Lighting

Lighting requirements will vary throughout the office. In endoscopy rooms, good general lighting of approximately 100 foot-candles is required for preparation and cleaning, but excess light must be eliminated during procedures for optimal viewing of video monitors. A dual system that can provide both low-level dimmed light and brighter light is desirable. The dim light will not interfere with the endoscopist's view of the monitors, while the brighter light will provide enough illumination for staff to work at other points in the procedure. This is easily achieved with two modes of lighting. In a two-mode system, fluorescent fixtures provide the required level of work light (100 foot-candles), while adjustable low-voltage or mini spotlights are positioned to provide low levels of light during procedures, to be directed on specific areas where needed. Fluorescent fixtures can be operated with special dimming systems; however, a few separate directed fixtures will add illumination to specific work areas. If windows are present, elimination of light with blackout shades or other daylight control devices will be required. Recovery rooms should be planned with soft, pleasant adjustable lighting. Particular attention should be paid to prevention of light sources shining directly into the eyes of a supine patient. This can be accomplished by using indirect or upright fixtures also on dimmers. In the administration areas, a good level of general and task lighting (50–75 foot-candles) is adequate for performing clerical activities. The light should be glare free, and attention should be directed to the placement of light sources because of the increased use of computer monitors.

Communications systems

It is no longer possible to operate any medical organization without depending heavily on electronic communication systems. The degree to which voice and data communications systems have changed in just one decade hints at the rapid pace with which these systems will continue to change. The endoscopy facility will benefit from the range of options available.

The telephone service network is the communications backbone common to every facility, and has been traditionally depended upon for contact with the public as well as with other professionals. It has evolved into a multifaceted system that provides access to wireless networks, pagers, email, fax connections, high-speed internet access, and potentially internet voice communications. Competitive internal voice systems with a vast array of features allow great choice. Features such as voicemail, automated answering, call forwarding, and conferencing are normally available even in the economy systems. The basic requirement is a multiline system with enough expansion capabilities to handle the projected volume of calls. A speakerphone feature in the telephone system is desirable for hands-off use in procedure rooms and can substitute for a separate intercom system. Modern phone systems with microprocessors have very compact central switching units. These require relatively small dedicated and accessible areas with separate power provisions for the processing units. A basic telephone closet for a small system will require a width of 4 ft (1.2 m) of clear wall space for equipment mounting and cable connections.

Wireless systems are a recent addition to the communications arsenal. Beepers and cellular phones, essential tools for medical providers over the last several years, are being supplemented or replaced by wireless network services which allows small groups to communicate with each other instantly. Wireless charting, email, and personal digital assistant (PDA) devices capable of receiving messages are the beginning of the next step in communications. As medical infomatics become more sophisticated with central databanks of patient information, wireless and broadband connections to these will become commonplace. All portable devices will require charging stations and multiple power receptacles must be provided for this purpose.

A good intercom system is still essential for smoothing the internal operation, particularly as the endoscopy unit gets larger with multiple procedure rooms. An intercom should have hands-off operation with selective station calling. Telephone systems with built in intercom capability can eliminate duplication. The telephone system can also provide link-up to the entry intercom and activate door-release devices where desirable.

Connectivity

Cabling pathways for the telephone network must be planned. As mentioned previously, procedure rooms equipped for video endoscopy will have multiple video cabling requirements. For best results, direct connections between video processor and (analog) monitors are typically made with multiple individual RGB broadcast video coaxial cables grouped together. (This provides

for the most accurate depiction of the image recorded by the endoscope). This cable bundle is bulky and requires a minimum of a 1 in. (2.54 cm) diameter clear conduit between video processor and remotely located video monitors. Recording of procedures on tape and documentation with digital capture photography and computer interfacing require cabling networks and multiple connection points. A computer interface requires installation of both video coaxial cabling and high-quality (twisted pair) category 5e (or better) cables. Such a network allows viewing of data and captured endoscopy images at multiple locations where a computer is connected to the network server. Software is available to facilitate and speed record entry to a central server of specific case information as well as images taken during a procedure. This information can be retrieved for reporting, research and distribution purposes. In addition to the connectivity within the room, it might be desirable to have analog video images transmitted to other locations in the facility for teaching purposes or for viewing convenience by other physicians. This can be accomplished by use of broadcast video coaxial cable networks using NTSC (the US standard) or similar signal transmission. If this type of option is needed or planned for future implementation, precabing or empty and accessible conduit should be planned and provided (Fig. 2.15).

Patient monitoring at recovery can be supported through the use of an open circuit intercom, and/or by closed circuit television cameras linked to one or more observation points. With CCTV assistants can accomplish other tasks while maintaining visual contact with recovering patients. Video cabling from camera locations to monitoring points must be planned.

Most facilities will consider the installation of a LAN (local area network) with a central server for the business office and for record storage, as well as a network for archiving and retrieval of data and digital images recorded during procedures. Connections using high-speed ethernet cable are required, as well as operating hubs for an ethernet or similar network. LAN connections may also be provided at copiers to take advantage of new multitasking equipment.

Broadband internet connections allow the transmission of reports and images to remote sites for distribution, archiving, or other purposes. Services such as DSL and cable are experiencing rapid growth throughout the USA and are increasingly reliable and affordable. DSL is now becoming readily available in many areas through phone service or internet service providers, enabling information to be transmitted at high speed. Its use is expected to grow significantly as local telephone service providers upgrade their cabling and equipment. Many digital cable vendors also offer cable modem broadband service, which has some advantages over DSL. While at

present it is aimed primarily at the residential consumer market, it could be an option for smaller offices or ambulatory units. For larger and/or less budget-conscious practices, T1 and T3 lines provide superior speed and reliability. This type of connection may also be available through a hospital infrastructure to a unit connected to that hospital. Any of the above options would, of course, have to be considered in planning for connectivity, which will require a high-quality category 5e or better data cable.

Wiring plans need to incorporate a host of other connections for various electronic systems. Panic or emergency call buttons at each recovery place and in the patient's toilet area are important for overall safe operation. Low-voltage wiring needs to be run to a central monitoring annunciator panel with both audible and visual alarm indicators. Emergency lights above the doors to the respective rooms indicate where a call originated.

Music systems, CCTV and commercial cable television service require additional cabling and wiring where desired. A built-in sound system should be considered for waiting areas and at recovery spaces. This has the added benefit of providing sound masking to reduce background noises. Speaker cables to these locations will be required. Commercial cable television might also be considered for recovery areas or waiting rooms to occupy patients' and/or visitors' attention.

Security systems are common wherever expensive equipment, drugs, etc. are present. A secure access and door-release system with intercom should be enhanced with video entry cameras and monitors at strategic locations. Miniaturized video surveillance systems allow units to be mounted discretely and can be built directly into the entry door area. Electronic security systems should be considered, with central station monitoring covering entry doors and windows, alarms, and a zone-type coverage providing a second level of protection. Space must be provided for security control panels with dedicated telephone connectivity and power for the processing devices.

The administration area

The same detailed planning should be directed at the layout of the administration area as to the medical spaces. The complexity of clerical operations in medicine, coupled with the impact of the use of computers to organize and process information, have placed constraints on design of this area. Space must be provided for computer equipment at every workstation, for the many additional devices required, and for the personnel needed to operate them comfortably. Each person working with a computer needs from 5 to 7 linear feet (1.5–2.1 m) of desk space from 26 in. to 30 in. (0.66 m

to 0.76 m) deep (depending on equipment) for both machines and paperwork. Computer workstations, desks, or large expanses of built-in counter space can all satisfy the need if ergonomically designed. Keyboard drawers or articulating keyboard arms should be installed to prevent repetitive motion disorders. Additional and ample counter space should be set aside for the various laser printers, color ink jet printers, dot matrix form printers, label printers, etc. that may be needed. Space must be provided for copiers, mail-processing equipment, fax machines, surge protectors, UPS (uninterrupted power supply) units, wireless chargers, PDA cradles, and other devices. As with any machine, particular attention should be given to noise factors, heat output, and adequate electrical provisions. All this equipment requires paper, toner cartridges, ink and other supplies, and space in supply closets or cabinets must be planned. The administration area and consult rooms should have extra power receptacles available for charging stations for wireless and portable devices.

The business office should be zoned for several defined functions. Space and staff areas should be allocated to these four specific task functions:

- 1 reception;
- 2 appointments and scheduling;
- 3 general correspondence, filing, and record keeping;
- 4 billing and insurance affairs.

Other than the reception area, the remainder of the business office works best if it is separated visually and acoustically from the waiting room. A small area should be set aside for discussing bills or insurance matters with patients on their way out of the office.

Still a pressing subject in administrative areas and business offices is the solution to the filing problem. The amount of filing space required for records that need to be accessed continues to place demand on available space. Records normally increase at a fixed rate per year and at an accelerated rate as a practice grows, and long-term expansion space must be programmed. It is common in poorly planned facilities for medical records to be stored in coat closets, toilets, and procedure rooms. A more useful approach is to provide as much file space as possible directly in the business office and provide a separate inactive file storage room or combination supply and file room with space for 100% expansion. Consider some of the more sophisticated paper filing systems with cabinets that slide or rotate, resulting in more efficient usage of available floor space.

In addition, look ahead to what computer storage and record systems will do in the next 5–10 years to reduce this pressure. Whether the increased power and mass storage capabilities of computers will ultimately solve this problem is still a question. Scanning of documents and electronic data record operations may allow more of the paper to be eliminated or moved to remote locations

while keeping the information accessible. Software with an easy and usable interface is currently available to bring scanned paper records and information to any computer on the network.

In the USA be aware of recent legislation (HIPAA) concerning the privacy of patient matters. Files must be kept locked and all material dealing with a patient must be treated in a sensitive and secure manner. This could include files that might be carelessly left out, computer screens that are easily read, and telephone conversations that can be easily overheard by patients in the waiting area.

Waiting room

The size of the waiting room depends on the type and volume of the practice. A minimum of 8–10 seats is advisable in an office setting, while ambulatory centers will require larger rooms commensurate with the size of the facility. Since each procedure room will have three patients in various stages of treatment (one in the room, one in the postprocedure recovery room, and one waiting to go into the room), and each will have at least one person accompanying, it is recommended that for each procedure room six waiting spaces be planned. *Therefore, for two procedure rooms a minimum of 12 seats should be planned.*

Space can be used efficiently by selecting small comfortable chairs rather than large deep sofas. Banquette seating offers an alternative and can be more flexible than individual chairs. Variety is important as the number of seats grow in order to avoid the look of an airline terminal waiting room. The waiting room must have provisions for visitors' coats, a toilet, possibly a telephone, and amenities such as magazine racks, umbrella stands, pleasant artwork, etc.

Environmental factors

A vision for the physical surroundings should be established with the architect or with an interior designer early in the process. A pleasant and comfortable setting can help to both alleviate patient anxiety and increase staff motivation and productivity. This involves a conscious effort and a sufficient budget to achieve a high level of quality with good materials, varied lighting, and color schemes that contribute to the overall impact of a comforting environment. A professionally executed plan will be complete with furniture selections, artwork and door signs for room identification coordinated with surface materials. Choosing materials solely on the basis of their ability to withstand the wear of a busy office often results in an institutional setting. On the other hand, a successful interior, if maintained regularly, can age well, and consideration must be given to how

surfaces will hold up over the years. Medical spaces take a great deal of wear and tear and a maintenance program to keep the space in its best possible condition should be established.

Summary

This chapter has attempted to provide a synopsis of some of the many issues that must be faced when planning for the endoscopy units. The purpose here is to give physician and staff an appreciation of the scope and complexity of the planning process and to help them formulate objectives that must be articulated to the design professionals. In summation, there are 10 points worth repeating that will be useful in getting started and completing a successful planning process:

- 1 Allow adequate time for planning.
- 2 Choose experienced design professionals with whom you can work and communicate comfortably.
- 3 Set aside a regular block of time for discussion, review, and program development.
- 4 Get staff involved in writing down their needs and wishes.
- 5 Write a statement of your vision and goals, from which a detailed program can be prepared.
- 6 Make an inventory of equipment that will be used, including information on potential future acquisitions.
- 7 Visit examples of facilities whose ideas are worth incorporating.
- 8 Use flow studies to evaluate where functional elements are to be placed.
- 9 Use block diagrams to study options.
- 10 Review preliminary drawings and construction documents carefully against the program.

Summary of regulatory requirements for licensing ambulatory centers in the USA

1 Certification steps

- (a) Application for *Certificate of Need*—some states require this to apply for license.
- (b) Application for *State License*—some states exempt certain facilities; some states have no license.
- (c) Application for *Accreditation*—accepted in lieu of licensing in some instances.
- (d) *Application to CMS for Medicare number.*

2 Certification (CMS requirements)

- *Governing body*—full legal responsibility.
- *Written transfer agreement*—with nearby hospital.
- *Ongoing self-assessment of quality.*
- *Complete medical records.*

- *Specific standards for staffing, drugs, emergency procedure, etc.*
- *Separate staff and separate records.*
- *Exclusive use of surgical spaces*—other parts of the ASC may be used for other purposes when no surgery is being conducted.
- *Physical separation from office*—permanent walls with 1-hour fire rating.
- *Comply with state license requirements.*
- *Safe and sanitary environment*—architectural and code implications.

3 Physical requirements

A Guidelines for Design and Construction of Hospital and Health Care Facilities, version 2001–2003

- 1 (9.9A1)—200 ft² room size (clear of fixed cabinet).
- 2 (9.9A1)—Monolithic floor covering (seamless).
- 3 (9.9A2)—Hand-washing fixture in suite.
- 4 (9.9A3)—Oxygen and vacuum in procedure, recovery and cleaning.
- 5 (9.9A5)—Emergency communication system.
- 6 (9.9B2)—Negative pressure in procedure room and scope cleaning room.
- 7 (9.9B2)—Dedicated cleaning room.
- 8 (9.9B2)—Hand-washing fixture in cleaning room.
- 9 (9.9B3)—Changing and storage of clothing.
- 10 (9.9B3)—Toilet facility.
- 11 (9.9B3)—Clean utility room.
- 12 (9.9B3)—Dedicated recovery area.
- 13 (9.9B3)—Janitor's closet.
- 14 (9.2.H1)—Minimum corridor width 60 inches—outpatient areas.

B Life Safety Code NFPA (National Fire Protection Association #101)

- 1 (12.6.2.4.2)—Two means of egress if facility is 1000 ft² or more.
- 2 (12.2.3.3)—Corridor width 44 ft² minimum in ambulatory centers.
- 3 (12.2.3.3)—Corridor width 96 ft² minimum in hospitals.
- 3 (12.1.2.2)—2-hour separation if adjacent to another healthcare use.
- 4 (12.6.3.7.1)—1-hour separation in mixed occupancies uses.
- 5 (12.6.2.9.2)—Emergency power where general anesthesia is used.

- 6 (12.6.3.7.2)—1-hour smoke separation in units over 2000 ft².

C Accessibility ADA (Americans with Disabilities Act)

- 1 (4.1.11)—Toilets (public), all must be accessible.
- 2 (4.1.11)—Toilets (private), must be adaptable.
- 3 (4.1)—General accessibility for path of access to all spaces.

D JCAHO (Joint Commission on Accreditation of Healthcare Organizations)

- 1 (PL.4.2)—Emergency power source.
- 2 (SH.1.13.6)—Recovery area equipped and monitored.
- 3 (SH 1.21.1.14)—Cardiac life support services.

Further reading

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Chapter 3

The Colonoscopy Assistant

Louise E. Taylor and James A. DiSario

Introduction

A trained gastrointestinal assistant is a necessary and important part of the endoscopy team. During the procedure, the assistant works closely with the endoscopist, often preparing the necessary equipment in advance of the physician's request, and anticipates the next set of actions. However, the intraprocedure part of the assistant's task is only one part of the overall responsibility. Other duties of the gastrointestinal assistant include: preparation of the room, ordering supplies, speaking with the patient and allaying apprehensions, cleaning and maintaining the equipment, coordinating outgoing specimens and incoming reports with the pathology laboratory, keeping track of narcotics and their proper requisition. Many of the remarks in this chapter are written from the information and requirements of the assistant in the USA, and can be adapted to conditions throughout the world. Safety is a universal obligation for endoscopy units everywhere, and the task of the assistant is generally the same in any setting. Because of the complex nature of the colonoscopic examination and the multiple elements that must be learned, proficiency of the assistant and efficiency of the endoscopy unit mandates that proper training is required in order to be a gastrointestinal assistant.

The role and responsibility of the assistant during colonoscopy varies according to level of licensure. The nurse and associate must function within these prescribed guidelines and hospital or facility policy.

There are two categories for the assistant in the gastrointestinal endoscopy setting, the first category is the nurse, which includes the registered nurse (RN), licensed practical nurse (LPN), and licensed vocational nurse (LVN). The second category is the unlicensed assistive personnel which includes the medical assistant, gastrointestinal assistant, and gastrointestinal or other medical technician. Staff in the latter category have direct patient-care responsibilities and are under direct supervision of a registered nurse [1].

The Society of Gastroenterology Nurses and Associates has published a position statement on minimal registered nurse staffing in the endoscopy center [1,2]. This standard of care applies to the USA but similar

guidelines are necessary regardless of the setting which includes hospital and out of hospital endoscopy centers. One registered nurse should be in the preprocedure area to perform and document the patient assessment. One registered nurse should be in the postprocedure area to perform patient assessment during recovery from intravenous sedation and analgesia. One registered nurse should be in the procedure room to assess and monitor the patient during sedation and analgesia.

When a patient is scheduled for the procedure, instructions for colon preparation are supplied. The patient's medical history is important in the decision of which method is used for cleansing the colon. It is at this time that the teaching process is begun. Brochures are often helpful for this initial contact, as it gives the patient a statement to take home and read in a less stressful surrounding. The American Society for Gastrointestinal Endoscopy (ASGE), the American Gastroenterological Association (AGA), and the Society for Gastroenterology Nurses and Associates (SGNA) are some of the sources to obtain preprinted brochures. Each organization has a website available to use as a resource (ASGE: www.asge.org; AGA: www.gastro.org; SGNA: www.sgna.org), as well as a source to obtain printed information.

The patient's visit generates a medical record. This should encompass the entire encounter from the preprocedure phase, through the procedure, recovery, and discharge [3]. Depending on institutional policy, a postprocedure or follow-up call may be required and should be documented. Each endoscopy unit is responsible for establishing their own documentation procedure and forms. In addition to printed forms, a number of computer programs are available. These can often be individualized for the needs of the unit and state requirements. Some programs interface with programs used by the physician to document the procedure.

After arrival at the endoscopy center for the procedure, the patient is escorted and instructed to change into a procedure gown. The SGNA has stated that the preprocedure assessment should be performed and documented by the registered nurse. It is critical to obtain a basic medical history, including allergies, current medications, and a record of past surgical procedures.

Physical limitations and psychological issues should be included and addressed. Of special note are any medical conditions that put the patient at increased risk of developing a complication related to sedation. These include severe cardiac, pulmonary, renal or central nervous system disorders, and obesity, sleep apnea, pregnancy, and drug or alcohol abuse.

The medication list should include all drugs that the patient is taking on a routine or PRN basis. This includes prescription drugs, over-the-counter medications, vitamins, and herbs. The endoscopist should be notified if the patient is taking medications that affect coagulation including warfarin, aspirin, nonsteroidal antiinflammatory drugs, and ginko. The assistant should be aware of possible adverse medication interaction with agents used for sedation, analgesia. Examples include benzodiazepines, opioids, psychoactive drugs, and monoamine oxidase inhibitors. Meperidine should not be given to a patient who has taken a monoamine oxidase inhibitor within 2–3 weeks as coma, severe hypertension, hypotension, respiratory depression, convulsions, malignant hyperpyrexia, and death may occur. There can also be a potentiating effect with the administration of any narcotic agent.

The effectiveness of the colon preparation should be established during the interview. The nurse should ask the patient what preparation he/she took and for a description of the last results. If there is a questionable or poor result, the endoscopist should be notified for a decision to perform the procedure, give an enema, or reschedule after re-prepping the patient.

Informed consent is obtained according to hospital or individual center policy (see Chapter 4). A guideline provided by the ASGE states that the endoscopist is best advised to personally obtain the informed consent. This duty is not generally one that can be delegated, although individual state and hospital policies may vary. Depending on facility policy, the assistant may serve as a witness.

Setting up the room

The equipment should be turned on and all operating systems initiated. Water bottles should be sterilized or high-level disinfected daily. If high-level disinfectant is used, a thorough rinse with sterile water should be performed to remove chemical residue. Water bottles should then be filled with sterile water to the level indicated, and the top secured and positioned according to manufacturer's instructions.

The assistant should check the procedure room for the availability of supplies (medication, accessories, biopsy forceps, specimen containers, etc.) and test all equipment for functionality. The colonoscope should be tested to assure that air and water channels are working.

Lubricant should be ready for the endoscopist to use for rectal examination and lubrication of the instrument prior to insertion.

Monitoring and sedation

There is a critical nature to the assignment of monitoring the patient who is receiving sedation and analgesia. For very ill patients and/or the complex procedures, a second nurse or associate is required to assist the physician while a registered nurse concentrates on monitoring the patient [4].

Basic life support is a standard requirement for all healthcare workers. In some centers, advanced cardiac life support is required for licensed personnel. Emergency equipment should be available and staff should be familiar with this equipment and its location. Several sizes of oral airways, and mask and bag equipment for respiratory support should be readily available. There should be immediate access to an emergency cart with an automatic electronic defibrillator (AED), emergency drugs, and intubation equipment.

For a colonoscopy, most patients receive medication for sedation and analgesia. Because of this, additional training regarding the role of staff during administration of these medications may be required. Critical are the knowledge of correct doses, possible cumulative effects, interactions with other medications, and the role of monitoring the patient for respiratory depression. Staff should also be familiar with pharmacologic antagonists for opioids and benzodiazepines.

The patient is escorted to the procedure room by the assistant and baseline vital signs are obtained. ASGE guidelines state "the endoscopist must know the clinical parameters to be monitored during the procedure and the standards of documentation should be understood. Although the assistant plays an essential role, the ultimate responsibility for all aspects of the monitoring process rests with the endoscopist."

The licensing board or nurse practice act in the majority of states dictates that medications given by direct intravenous route can only be administered by a registered nurse or by a physician. The endoscopist should be aware of the limitations according to each staff member's licensure for their state.

The patient's vital signs will be monitored during the procedure. This monitoring should include blood pressure, pulse, and pulse oximetry, the patient's level of pain and response to the procedure. Ventilatory function should be observed visually throughout the procedure. This information should be recorded in the patient's record. Automatic monitoring devices may enhance the ability to accurately assess the patient, but are no substitute for the watchful, educated assessment by a registered nurse [5,6].

Depending on center policy, ongoing interval blood pressure measurement, and continuous heart rate and pulse oximetry readings are measured. Recommendations from the American Society of Anesthesiologists (ASA) include that the type and amount of medication administered, length of the procedure, and the general condition of the patient should be the factors to determine frequency of measurement. At a minimum, these measurements should be obtained and recorded prior to the start of the procedure, after administration of sedative/analgesic agents, completion of the procedure, during initial recovery, and at the time of discharge.

Regular readings and recording of vital signs should be incorporated into the policy of the endoscopy unit, such as: obtain blood pressure, pulse, and pulse oximetry readings before the procedure, every 5 min during the procedure, and in the immediate recovery phase. Cardiac monitoring is done if the patient has a history of cardiac disease. When the patient is transferred to the recovery area, blood pressure, pulse, and pulse oximetry should be measured on arrival and at specified intervals, such as every 15 min, for a minimum of 30 min, until discharge.

The ASA suggests that continuous electrocardiographic monitoring should be available and used selectively for patients with hypertension, significant cardiovascular disease, or dysrhythmias. A triple-lead monitor supplies adequate basic information, the assistant should be familiar with basic arrhythmias. Any changes in rate or rhythm should be immediately reported to the endoscopist.

With basic monitoring equipment in place, an observant assistant can detect early changes in the patient's heart rate and blood pressure allowing for early detection and intervention. In addition to monitoring vital signs, the patient's level of consciousness, assessment of pain, warmth, dryness, and skin color must be observed and recorded [3]. Excessive sedation may result in cardiac or respiratory depression. These symptoms must be rapidly recognized, reported to the endoscopist, and treated to avoid the risk of hypoxic brain damage, cardiac arrest, or death. The person assigned to monitor the patient should be situated facing the patient and only assist with minor interruptible tasks. A second assistant should be present for sick patients and complicated procedures [4].

The American Society of Anesthesiologists [7] recommends the use of oxygen during procedures that require sedation and analgesia.

In cases where supplemental oxygen is used, close observation of the patient is critical because the discovery of respiratory depression using pulse oximetry may be delayed. Because this delay can occur, the importance of observing the patient for effective pulmonary ventilation increases. In cases when oxygen is not initiated

before the start of the procedure appropriate equipment should be present at all times during sedation. If hypoxemia occurs during sedation, supplemental oxygen is to be administered immediately.

The use of capnography via a nasal cannula with a CO₂ sensor in addition to pulse oximetry to monitor for hypoxia appears to be superior to close observation of the patient during the procedure [8,9]. However, even with this in place, the patient must be observed to verify accuracy of placement due to the patient's position or if he/she is a mouth breather.

Despite an excellent overall safety record, cardiopulmonary complications, likely due to sedative and analgesic medications are believed to account for 50–60% of procedure-related morbidity and mortality, respectively [10].

The assistant during the procedure

Staff should be in personal protective equipment before the procedure is started. The patient is assisted to the left lateral position with knees bent for the start of the procedure. Many endoscopists find that there are benefits to repositioning the patient during the procedure. The patient may be asked to turn to supine, right lateral, and occasionally to a prone position. Although it is difficult to have an oversedated, ill, or elderly patient change position, most patients can change position with minimal assistance and verbal cues. The assistant must be aware of multiple safety issues when repositioning the patient. The patient's position in relation to the edge of the cart or table must be carefully observed. A safety belt over the patient and attached to the cart platform is available and will prevent falling off the stretcher. To prevent injury to the patient or damage to equipment, attachments such as monitoring wires, grounding pads, and oxygen tubing should be checked after any position change is made.

During the insertion of the scope, at the request of the endoscopist, the assistant may be asked to hold the scope head or secure the insertion tube of the scope at the rectum. It is the position of the SGNA that, while functioning within limitations of licensure, nurse practice act, or institutional policy, the nurse or associate educated and experienced in endoscopy may assist the endoscopist by manipulating the endoscope when required to facilitate an endoscopic procedure. Manipulation refers to the act of advancing or withdrawing the endoscope under the direct supervision of the endoscopist. The statement is clear that the nurse or associate manipulating the endoscope has full view of the lumen by way of a teaching adaptor for the fiberoptic scope, or video screen for electronic colonoscopes [11].

As the scope is advanced during the procedure, loop formation may occur. The assistant may be asked by

the endoscopist to apply external abdominal pressure. Properly applied, external abdominal pressure can reduce patient discomfort and reduce procedure time. Pressure may be given in various locations: general pressure in the left colon can be used to control the sigmoid colon. The assistant should attempt to feel for the loop made by the scope to establish position. There is no need for pressure application when the endoscopist withdraws the scope to straighten it, but pressure may be helpful to maintain the straightened position of the colon as the scope is advanced. Since every patient is unique, the assistant may need to adjust pressure several times until the most effective position is found. When the scope advances past the splenic flexure, mid-abdominal pressure may be applied in an upward motion to support the transverse colon. As the scope progresses from left to right, pressure at a specific site may become more useful. In general, the hand position of abdominal pressure is usually located by the endoscopist who may request non-specific pressure at various areas such as suprapubic (when the instrument is in the distal sigmoid) or left lower quadrant pressure when a loop is forming in the sigmoid colon. Alternatively, the endoscopist while viewing the lumen may find a specific point by abdominal palpation that aids in scope advance. When this is located, the assistant should replace the endoscopist's pressure point with his/her hand in the same position before the endoscopist removes pressure. There is rarely a need for application of sustained pressure, as the maneuver is intended to assist in advancing the tip around a fold or a bend in the colon; once that advance is accomplished (or not accomplished), the pressure may be released as another maneuver is performed, or another location for pressure is determined.

An adequate number of specimen containers and labels with appropriate patient information should be available before the start of the colonoscopy. The assistant must be observant during the procedure so that the need to remove polyps or obtain biopsies can be anticipated. Both the patient and equipment can be prepared as the procedure progresses. When a polyp requiring electrocautery is encountered, the grounding pad can be applied to the patient and an appropriate snare chosen. Biopsy forceps or other equipment can also be readied when need is anticipated.

Operation of a snare

Since there are a number of sizes and shapes of snares available, the choice is made by the endoscopist according to the size and location of the polyp in the colon. The assistant usually opens and closes the snare as requested. Snare cutting is dependent upon a combination of mechanical forces of the wire closing against the

plastic sheath and the use of high-frequency current, which is produced by an electrocautery machine. The sheath may compress during snare closure so that the tip of the snare, which withdrew into the sheath when tested outside the patient, cannot be fully withdrawn once around a polyp because the sheath has shortened with compression. This may preclude complete resection and cause an impacted snare. To avoid this problem, verify that the tip of the wire snare retracts at least 15 mm into the sheath prior to polypectomy.

The assistant should be familiar with each electro-surgical unit being used in the endoscopy center. In some cases, current output may vary according to unit or manufacturer. Instructions and use of settings specific to the units available in the department should be readily available for training and reference purposes.

If an electrical grounding pad is used, the usual placement is on the upper thigh or lower trunk, whichever is the largest tissue mass. To ensure complete contact with the patient's skin, the chosen area should be dry and as free from hair as possible. If a polyp is to be removed, a specimen trap should be placed between the scope and the suction tubing to retrieve any tissue suctioned through the scope. The active cord is connected between the snare and the electro-surgical unit and the dial is set as appropriate per manufacturer's directions, unit policy, and by the endoscopist's preference. Electrical currents that have a pure cutting effect are usually not employed for colonoscopic polypectomy. Electro-coagulation current alone may be used or a blend of cut and coagulation may be applied. The activation pedal for the unit is placed in position for ready access to the endoscopist.

During polypectomy, the endoscopist will position the sheath and give the order to open the snare. The assistant will extend the loop and the endoscopist will position the loop around the polyp. The assistant should be sure that the electrocautery unit is turned on before use and ensure that the active cord is securely connected. Upon the direction to close the snare, it is important for the assistant to close the snare slowly while maintaining continuous communication with the endoscopist. While visualizing the polyp and feeling for resistance, the assistant will close the loop on the snare slowly until tension is felt and the loop can be seen to be in the proper position. When ready for electrocautery, the endoscopist will depress the foot pedal and give the direction to close.

If saline injection is used to lift the polyp tissue from the mucosal wall, an injection needle and normal saline for should be available. One or two 10 cc syringes should be prepared depending on the size and number of polyps. The normal saline should be drawn up and, depending on the endoscopist's preference, a drop or two of methylene blue can also be drawn up in the syringe. The advantage of using the methylene blue is that the blush of the tissue as well as the translucent

color can identify the margins of the polyp. Whenever methylene blue is used during a procedure, the patient must be advised that their urine may turn green and there may be a color change in their stool as the medication is excreted. Advising them of the possible color change before discharge will prevent a panicked phone call regarding the strange color of their urine.

The severed polyp may be retrieved in several ways (see Chapter 37). If a biopsy forceps or hot biopsy forceps are used, the tissue is removed with the forceps. Small polyps can be readily retrieved by suction into a small capture bottle (trap) attached to the main suction plug of the instrument. For larger polyps removed with a snare, suction can be used to secure it to the end of the scope. The polyp can be resnared to carry it out of the colon, or an entrapment or retrieval device such as a basket or tripod grasper can be used. For multiple polyps, each polyp specimen should be placed in an individual container with the site clearly identified in addition to the patient information. The ability to keep all specimens in their proper order (size, location, method of removal) is aided by keeping a written log of each event as it occurs.

Biopsy and cytology

The removal of polyps is only one reason to obtain a specimen during a colonoscopy. Biopsies are obtained for suspected neoplasm, diagnosis and surveillance of inflammatory bowel disease, and diagnosis of chronic diarrhea. Usually multiple specimens are obtained from each site for histopathologic interpretation. Tissue obtained can be cultured to identify infectious processes including bacteria, parasites, cytomegalovirus, and herpes. These specimens must be carefully handled to ensure that they can be processed for the needed exams. Specific instructions should be obtained from the department of microbiology for processing these specimens.

If numerous specimens need to be obtained during the procedure, an additional staff member should be present and dedicated to obtaining and processing specimens. The other staff member should concentrate on monitoring the condition of the patient.

In addition to the biopsy forceps and snare to obtain a specimen, cells for cytologic analysis or cell culture can be obtained using a cytology brush or by using washing and/or aspiration techniques.

There are a number of types of biopsy forceps available for use during colonoscopy (see Chapter 27). Some are available with a central spike, which is helpful in holding tissue in place to prevent the forceps from slipping so an accurate specimen can be obtained. Jumbo forceps and those that can take up to four bites can be used to obtain larger pieces but may require larger channel instruments for them to pass freely without damage to the scope. When ready to obtain a biopsy, the

assistant should examine the forceps for any obvious defect and test them for function. The forceps should be closed when handed to the endoscopist to prevent injuries. After the biopsy, as the assistant removes the forceps from the channel he/she should also hold a cloth or gauze over the biopsy port to prevent splattering and remove secretions from the outside of the forceps.

Not all specimens are placed in a fixative such as formalin. Tissue specimens for viral, bacterial, or fungal culture are obtained and placed on gauze moistened with normal saline or on slides according to facility policy. If a frozen section is desired, the specimen should not be placed in a preservative of any kind. It is mounted and labeled as desired by the laboratory, kept moist, and transported immediately to the laboratory for immediate examination by the pathologist.

Cytologic or viral specimens can be obtained using a biopsy forceps, a brush manufactured for that purpose, by washing, or by aspiration.

For brush cytology, before insertion into the biopsy channel, the brush should be withdrawn into the sheath for protection. After the specimen has been obtained, the brush is retracted into the sheath and withdrawn from the scope. A cloth or gauze should be used to wipe the exterior of the sheath during removal to prevent splatter. The brush is extended again and thin smears of cells are placed on a microscope slide and fixative solution applied, or the brush is cut and placed in a container with cytology fixative solution. Delay in fixation should be avoided, since air drying affects the interpretation.

Endoscopic tattoo

Approximately 1–1.5 mL of the marker solution is used to flush the injection needle and sheath. While injecting into the mucosa, the assistant should state that he/she is injecting, how much resistance is felt, and how much fluid is injected by 0.5- to 1-mL increments. The amount injected should be recorded in the patient's procedure record (see Chapter 36).

Colorectal bleeding

When a bleeding site is encountered, several items of equipment must be available for immediate use. Review of skills on a regular basis is essential, especially with devices that are used on an irregular basis. Devices or instruments available include injection needles, bipolar probes, detachable snares, clip devices, argon ionized coagulator, laser and heater probes. As technology changes and advances, other instruments may be available in the future.

Epinephrine 1 : 10 000 is often the hemostatic agent of choice. Most sites are injected with 1–2 mL as instructed by the endoscopist.

A detachable snare (see Chapter 26) may be used in the event that the area bleeding is clearly identified, such as a polyp stalk following transection. The snare is tightened on the bleeding area and when secure it is detached from the device and left in place. After healing occurs, the snare sloughs off and is passed with the patient's stool.

There are several options available when using a bipolar probe. There are 7Fr and 10Fr sizes available with or without a needle for injection. Having the needle built in is helpful when that need is anticipated, but can be more difficult to deploy than a standard injection needle.

It is ideal to have an additional staff member available during and after these complex procedures to assist with equipment and disinfecting the procedure area following the procedure. This enables close monitoring of the patient and the effectiveness of interventions, as well as efficient room turnover between procedures [4].

Postprocedure or recovery care

The postprocedure phase is from the completion of the procedure until the patient is discharged from the facility [3]. The frequency of assessment is determined by institutional and/or departmental policy. There are recommendations by the US Joint Commission for Accreditation of Healthcare Organizations and requirements from Centers for Medicare and Medicaid Services. These recommendations include charting:

- the time of arrival;
- vital signs including recording of pulse oximetry until the patient has returned to preprocedure baseline;
- the patient's level of consciousness and mental status, especially if there is a change in warmth, dryness and color of skin;
- type and dose of medications including oxygen and response to intervention;
- the total amount of intravenous fluid administered and the time the intravenous access is discontinued;
- unusual events, interventions, and outcome;
- disposition of the patient (to hospital room, home, radiology, etc.);
- report that is given to any subsequent caregiver;
- mode of transportation (ambulatory, cart, wheelchair, etc.);
- the name of the person responsible for the patient at discharge if any medications are administered;
- age-specific discharge instructions, educational materials such as dietary instructions, any prescription given to the patient or responsible adult and statement of understanding;
- statement that the discharge criteria have been met;
- time of discharge.

Occupational Safety and Health Administration regulations

The US Occupational Safety and Health Administration (OSHA) has specific guidelines to ensure protection of workers from hazardous exposure or injury. Some of the items covered under these regulations are contamination by potentially infectious material and chemical exposure, which includes toxic levels of glutaraldehyde and fumes from chemicals used in the endoscopy unit. These chemicals can include, but are not limited to, formalin, high-level disinfectant concentrate, and alcohol. Proper ventilation must be provided and the air quality monitored in environments with fumes such as endoscope-cleaning areas.

Each endoscopy unit must have a listing of all hazardous substances that can be used in the area. These material safety datasheets list all relevant information about a substance and must be on file in the department, available to every employee for immediate reference. Included is everything contained in the substance, the boiling or evaporation point, fire hazard, safety warnings, exposure limitations, directions for resuscitation in the event of overexposure or overdose, and contact numbers for the company which produces the product.

Occupational exposure is defined as: "a reasonably anticipated skin, eye, mucous membrane, or parenteral contact with blood or other potentially infectious materials that may result from the performance of the employee's duties." [12]. Policies and procedures that are followed in the performance of daily duties reduce the likelihood of exposure by defining the manner in which tasks are performed. These practices include but are not limited to:

- washing hands when gloves are removed or as soon as possible after contact with potentially infectious material;
- providing an area for eye irrigation in the event of exposure;
- prohibition of eating, drinking, smoking, or applying of cosmetics in areas where occupational exposure is possible.

It is an OSHA requirement that engineering controls be in place to protect employees from hazards in the workplace. Sharp objects are used daily in the performance of duties in the endoscopy center and must be handled and disposed of with caution. Items in this category include, but are not limited to, needles, scalpels, and broken glass. Equipment used during colonoscopy may include disposable biopsy forceps with spikes, injection devices, and hemostatic clip deployment devices.

The wearing of appropriate gloves when contact with blood, mucous membranes, and potentially infectious materials is anticipated reduces the risk of exposure to blood-borne pathogens and is mandated by OSHA.

Gowns and protective apparel are worn to reduce the risk of exposure to blood-borne pathogens under specified circumstances and are mandated by the OSHA blood-borne pathogens final rule.

Each facility is responsible for implementing regulations regarding hazardous materials. Information is available listing OSHA standards, as well as publications and assistance available at www.osha.org.

Protective gear

Blood is not the only source of exposure to potentially infectious materials. Other potentially infectious materials include, but are not limited to, human body fluids such as saliva, peritoneal fluid, stool, and unfixed human tissue [12].

It is possible for almost every employee of an endoscopy center to have occupational exposure to blood or other potentially infectious material. All nurses and associates are regularly exposed to these materials and even ward clerks or secretaries may be exposed on occasion when they handle specimens.

Protective gear should be universally used to provide a physical barrier for staff during interactions with patients when there is a potential for exposure to infectious and toxic substances. Because the same measures are used in every case, body substance precautions protect the healthcare worker from unrecognized or asymptomatic cases of infectious diseases as well as recognized or symptomatic cases.

Protective gear should include a gown, eye protection, a face mask or shield if splash is anticipated, and gloves for every event which presents the possibility of exposure. Radiation and laser protection should be provided if these therapeutic measures are needed. Semipermeable gowns can be used if excessive splash is not anticipated. Non-permeable gowns in either plastic or treated fabric are available to protect staff members from any type of splash.

Eye protection, either safety goggles/glasses, or face shields should provide adequate protection without restricting movement or vision. The equipment should be provided by the employer and should be durable, easy to clean and disinfect. Staff members should keep safety equipment clean and in good repair.

Gloves should meet the need of the staff member and the patient. Any sensitivity to latex should be noted and taken seriously as anaphylaxis can occur and is a life-threatening event. Gloves should be removed immediately following the procedure or in the event there is a possibility of a break in the surface integrity. Hands should be washed immediately after gloves or personal protective equipment are removed.

In accordance with sound occupational health principles, employee training should occur prior to the time

that the employee is placed in a situation where exposure could occur. Training must be provided at the time of the initial assignment or job change that causes exposure and must be repeated annually [12].

In our experience using methylene blue tissue staining during endoscopy, the spatter of material from the endoscope and equipment is more common than generally anticipated and may occur two or more meters away from the biopsy cap.

Processing of reusable equipment

(see Chapter 28)

The Spaulding classification was developed in the 1960s to categorize equipment and patient-care items and provide appropriate levels of disinfection. The gastroenterology nurse or associate should be familiar with Spaulding's classification system to be able to sort accessory devices for reprocessing [13].

Reusable items include scopes, water supply bottles, and power wash bottles, with their tubing, connectors, and caps. This category also includes equipment carts, patient monitoring devices, intravenous pole, fixed surfaces, and the procedure table or gurney.

Standards for infection control were published jointly by the SGNA and the ASGE. Reprocessing standards endorsed by the SGNA, the ASGE, the AGA, the ACG, and the Association for Professionals in Infection Control and Epidemiology (APIC) require that manual cleaning of the endoscope, including all channels and removable parts, precede manual or automated disinfection. There must be strict adherence to these standards [13].

Reprocessing refers to the sequence of cleaning, lubricating (if necessary), and sterilizing or high-level disinfecting steps that will assure that the equipment or accessory is patient-ready. The reprocessing of a flexible endoscope is accomplished in two phases: (i) decontamination and (ii) sterilization or high-level disinfection. The objective of decontamination is to remove gross organic material and microorganisms and to prevent drying of these substances. Using instructions from the colonoscope manufacturer, the insertion tube, all channels, external surfaces, and accessories must undergo a thorough mechanical cleaning with an enzymatic detergent and an appropriate sized cleaning brush designed for endoscopic equipment. In many centers automatic washing devices are used. Automatic endoscopic reprocessors may reduce staff exposure to liquid chemical germicides. Exposure to 2% glutaraldehyde has been the cause of asthma, sinusitis, serious skin sensitivity, and conjunctivitis in staff members. The proper use of these devices as well as personal protective equipment in combination with adequate ventilation may decrease staff exposure problems (see Chapter 28).

Once decontamination is complete, the scope is placed in the reprocessor and the wash and disinfecting cycles are automatically completed. There are a number of different devices available from several manufacturers. The manufacturer's instructions must be followed completely for proper, high-level disinfection. Reprocessing should always be performed by trained and accredited personnel according to written guidelines or standards of practice as defined by professional societies. Regular monitoring of the reprocessing process is important for quality control and insuring patient's safety.

Rinsing and drying are essential steps to remove the chemical disinfection solution and this prevents bacterial colonization during storage. The exterior of the scope and accessories should be dried. Seventy per cent alcohol can be flushed through the channels followed by air (to remove residual alcohol), before hanging the scopes vertically for storage. After disinfection, all items must be rinsed with filtered or sterile water, and stored as recommended by the manufacturer without valves or devices attached.

Water supply bottles for the scope and the power wash, as well as any tubing or connectors, should be changed according to infection control guidelines, manufacturer's direction, or facility policy.

Contaminated areas where accessories and specimens are handled should be separated from clean counter areas. All contaminated areas must be cleaned and decontaminated between patients with an Environmental Protection Agency registered hospital grade disinfectant and used according to manufacturer's directions.

Disposable items

Any equipment or supplies that are labeled as non-reusable should be used once and then discarded. It is the position of the SGNA that critical medical devices such as biopsy forceps, injection needles, snare devices that are manufactured and intended for one-time use on one patient during one procedure be handled as disposable equipment. The devices labeled as single-use devices (SUDs) are not intended by the manufacturer to be reprocessed, or reused. Reprocessing refers to the sequence of cleaning, lubricating if necessary, and sterilizing or high-level disinfecting steps that assures that the accessory is patient-ready. Much equipment in this disposable category is not manufactured to enable complete disinfection or sterilization and reusing the devices may be a source of contamination or it may break or malfunction during use [14].

In August 2000, the US Federal Drug Administration (FDA) issued enforcement priorities for the regulation of third-party processors and hospitals that engage in reprocessing SUDs. The reuse of SUDs is a complex issue

that must be balanced with the assurance of patient safety and the delivery of quality healthcare. The FDA's enforcement priorities fail to include regulation of reprocessing that occurs in freestanding ambulatory surgery facilities or physician offices [15].

All items used in the performance of procedures that are to be discarded are considered to be medical waste and must be handled as potential biohazard items. These items include, but are not limited to, electrocautery grounding pads, protective pads, intravenous access catheters, and disposable personal protective equipment used by staff members. These items are to be discarded in a plastic-lined biohazard-labeled trash receptacle according to federal, state, and local regulations. The use of solidifiers in suction canisters before disposal in the waste can reduce contamination by spillage in the event of breakage of a container or the trash bag. Solidifier is a powder substance which, when added to the liquid contents of the suction container, turns the contents into a gel. Some powders are available that also provide some level of disinfection and odor control.

Ordering supplies

Ordering of supplies is best assigned to one person to prevent duplication of or overlooked orders. There should be backup personnel trained in the case of absence of the primary staff member or for emergency acquisition of equipment or supplies.

A stock level should be determined for each procedure room based on average utilization, and this should be adjusted as needed based on utilization and new product requirements. It is desirable to use a detailed checklist to stock equipment to the predetermined level. The staff member responsible for stocking that procedure room should initial the sheet indicating completion and this form should be reviewed by the supervisor (Fig. 3.1).

Generally, the most efficient time to stock the procedure room is at the end of the day or after completion of all procedures.

The control of odors in the endoscopy suite

Maintaining control of contaminated waste is the ideal way to control odors in the endoscopy suite. This includes disposal of products such as bed pads, biopsy forceps, and suction containers, reusable devices and linens.

For every procedure, there are several measures that should be taken immediately at the end of the case. The scope should be removed from the room after adequate water has been suctioned through the channel to clear solid debris. If the colonoscopy was highly odorous, the suction canister should be changed and soiled linen removed.

Inventory Check Sheet

Month:	Year:	Mon	Tues	Wed	Thurs	Fri	Mon	Tues	Wed	Thurs	Fri
Item:	Stock Level:	Date:	Date:	Date:	Date:	Date:	Date:	Date:	Date:	Date:	Date:
Alcohol wipes	1 Box										
Clips, hemostasis	4										
Emergency medications:											
atropine 0.5 mg/ml (1ml)	2										
epinephrine 1:10,000 (10 ml)	2										
flumazenil 0.1 mg/ml (5 ml)	2										
naloxone hcl 0.4 mg/ml (1 ml)	2										
Forceps, Biopsy multi bite	2										
Forceps, Biopsy w/needle	6										
Forceps, Hot biopsy	2										
Formalin bottles	15										
Gloves, Small (box)	1										
Gloves, Medium (box)	1										
Gloves, Large (box)	1										
Gloves, Non latex (box)	1										
Gowns, Disposable	20										
Grounding pads	8										
Irrigation catheter	2										
IV fluids, LR	5										
IV fluids, NS	5										
Lubricant (Jelly 4.5 oz tube)	3										
Needle, Injection	5										
Saccomono solution	4										
Safety Glasses	5										
Snare, detachable (for hemostasis)	2										
Snare, regular	4										
Snare, small	6										
Suction cannister	10										
Suction tubing	20										
Syringe 3 cc	30										
Syringe 5 cc	15										
Syringe, irrigation 60 cc	10										
Trap, Specimen	5										
Washing pipe	3										
STAFF INITIALS:											

Instructions: Check inventory daily. Put checkmark in box when supplies replaced to assigned level
 Staff signing initials assumes responsibility for completion

Fig. 3.1 Inventory check sheet.

There are general air freshener products that do little more than add another smell. Commercially available products made especially for this setting may be more effective if used properly.

Having a high-flow ventilation system in each procedure room as well as in the equipment cleaning area is ideal. This type of system provides rapid turnover of room air so odors do not linger.

Summary

The gastrointestinal assistant (GIA) is an important member of the endoscopy team. It is the responsibility of the GIA to keep the endoscopy unit running on a day-to-day basis. It is no longer acceptable for any untrained nurse to act as a GIA since the functions are so complex that special training is required to avoid errors which could result in catastrophic events to human life, such

as mistakes in setting the electrocautery unit, overly aggressive snare closure, or injection of the wrong solution. The GIA is responsible for multiple functions during the procedure in addition to monitoring the patient, and is the person who ensures a smooth and safe endoscopic experience. Ongoing communication between the endoscopist and assistant is a link which must function in both directions to ensure the greatest efficiency and safety for the patient.

Trouble-shooting tips for the assistant

Prevention and preparation

Prevention and proper preparation are the best tools to avoid problems during the procedure. Pretesting endoscope functions can prevent increased length of procedure, the need for more sedation, longer patient

recovery, possible use of a second scope, and potential compromise of patient safety.

- Patient assessment could help to circumvent beginning a procedure on a patient who knowingly did not follow prep instructions.
- Ensure the immediate availability of necessary accessories compatible with the diameter of the suction/instrumentation channel of the endoscope.
- Just prior to the procedure, the assistant must test the air/water/suction and light source/visual functions of the endoscope.
- Note the hours remaining on the light source and replace the bulb as the meter moves toward the indicator that the useful bulb life is expiring.

Air/water failure

- Check the water bottle assembly:
 - Is the cap screwed on tight?
 - Is there water in the water bottle?
 - Is there too much water in the water bottle?
 - Does the point of insertion of the connector have the necessary rubber “O” ring?
 - Does the inside top of the water bottle have the necessary “O” ring?
 - Is there a crack in the water bottle?
- If you think the water bottle is a problem, change the water bottle.
- Disconnect the water bottle insertion tube from the light source:
 - Place fingers over the air and water supply ports.
 - Depress air/water button. This maneuver may open a clogged air/water channel.
- Do not be tempted to insert the air/water adapter used for precleaning an endoscope: this may create pressures that are too high in the colon.

Suction failure

- Make sure the suction apparatus is properly assembled.
- If applicable, increase the suction from low or medium to high.
- Attempt to reposition the scope in the patient:
 - Sometimes the scope rests up against the mucosa and will not aspirate fluid or air because a piece of mucosa has been sucked into the suction port on the colonoscopy tip.
- Determine if suction still works. Remove the suction tubing from the plug-in module of the umbilicus and place a finger over the suction line to ensure that suction is being delivered to the endoscope.
- If suction apparatus is okay:
 - Flush water through the disposable rubber biopsy valve covering the suction/instrument channel.
 - Reusable metal accessory introducers make good

flush tips (they require reprocessing following each use). If stool or debris becomes attached to the tip of the scope, flushing through the rubber biopsy valve will usually clear the problem.

- Check the patency of the disposable rubber biopsy valve covering the suction/instrument channel:
 - If the seal has been compromised following multiple insertion of accessories, suction may be sluggish.
- Remove suction trumpet valve:
 - Place finger over that hole to see if suction is present.
 - If suction is not felt:
 - check to see if the suction bottle is full;
 - check to see if the pump is connected.
 - If suction is present, look at the trumpet valve to see if stool has clogged up the side hole. Insert a clean trumpet valve.
 - If no suction is felt, place the wall suction line directly over the empty valve slot and suction to remove debris clogging the instrument channel.
 - If there is still no suction, the umbilicus is plugged. Pass the cleaning brush straight down the insertion tube so it exits at the point where the suction attaches to the endoscope. This will clear the umbilicus.
- Remove the disposable biopsy valve from the instrument channel. Suction here with the wall suction line.
- Pass the biopsy forceps or cleaning brush of appropriate length through the instrument channel:
 - This often works to clear debris from the channel that does not respond to a water flush. However, by using this method, a single-use forceps may be wasted and a reusable forceps will require a steam sterilization as if it had been used to take a tissue sample.
- Back flush the suction port:
 - Remove the wall suction line from the endoscope at the plug-in module suction port.
 - Attach the catheter and tubing in its place. Attach a 7–10 cm (3–4 inch) piece of suction tubing to the tip of a 60 mL catheter tip syringe filled with water. The assistant should communicate with the physician to hold down (depress) the suction trumpet valve prior to flushing. This may result in a backflow of water. As usual, all staff should already be wearing personal protective equipment, including mask, face shield, and impervious gown.
- If flushing through the biopsy port shows free flow of fluid into the lumen, and suction is present at the trumpet valve slot (and the valve itself is not clogged), and still fluid cannot be suctioned from the colon, the block is between the trumpet valve and the disposable rubber valve over the biopsy port.
 - To clear this area:
 - Remove the suction trumpet valve.
 - Insert a cleaning brush through the trumpet valve in a direction toward the scope shaft. This should be advanced for at least 25 cm (12 inches) to ensure that

this area is unclogged. It is possible to continue to pass the brush all the way down to the tip of the instrument and out into the lumen. If passing of the cleaning brush is desired, be sure that the tip of the instrument, at the 5 o'clock position, is pointed toward the lumen so that the suction brush is not inadvertently passed completely through the channel and possibly perforate the colon wall.

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Chapter 4

Informed Consent for Colonoscopy

Andrew D. Feld

Introduction

Obtaining informed consent is a process that goes beyond the action of obtaining a signature on a standardized form. It includes assessment of the competence of the individual to process information, disclosure of appropriate information necessary to allow an informed decision, and ensuring the plan chosen by the patient is voluntary. The process involves mutual communication and decision-making, not merely the request for a signature on a standardized form that lists complications of a procedure.

The process of obtaining informed consent may appear to some to be another regulated nuisance that slows down the busy practitioner and hinders efficient medical practice. However, it could better be viewed as a basic ethical obligation in the practice of medicine, one that can be used as a communication tool cementing the provider–patient relationship [1–3]. It is also a risk management tool, transferring known standard procedural risks to the patient who has understood and accepted the premise that even competently performed colonoscopy has risks. Finally, it is a legal obligation in the practice of medicine. An understanding of the conceptual aspects of informed consent will best allow the healthcare provider to negotiate the many areas of uncertainty regarding the specifics of informed consent.

Conceptual aspects of informed consent

History of informed consent

Most healthcare providers currently accept the concept of informed consent, which is rooted in patient autonomy and self-determination. Many healthcare providers incorrectly assume this is a long-standing medical tradition. Prior to the 1950s, the focus of prominent medical personnel was to provide medical benefit and protect the patient from harm. Recall the Hippocratic Oath: first, do no harm. Protecting the patient from harm was felt to ethically justify withholding distressing information from a patient. Thus patient autonomy and decision-making took a back seat to the precept of “do no harm.” Disclosure of poor prognosis was felt associated with

harmful outcome, and little disclosure probably took place before the 19th century [4]. In fact, it was more likely that early physicians concealed their activities from their patients [5].

In the 18th and 19th centuries, some physicians were credited with enlightened views about disclosure of medical information. However, history of medicine scholars suggest that the purpose of those physicians was to educate patients to understand and follow physician recommendations rather than to allow the patient to participate in medical decision-making [4]. It was an early effort to ensure compliance with therapy, not to ensure patient autonomy.

Legal history

In 1914, the influential legal scholar Justice Cardozo wrote that “every human being of adult years and sound mind has a right to determine what shall be done with his body” [6]. This landmark case is often cited as the beginning of modern informed consent. The judicial ruling found that a person’s right of self-determination would justify imposing an obligation on the healthcare provider to obtain informed consent. The legal precedent set was that consent was necessary for medical treatment.

Further legal developments included the emphasis on the *informed* part of patient consent. This is the provider’s obligation to give sufficient information for truly informed decision-making not mere consent. In the 1950s, a patient whose translumbar aortography resulted in a rare complication of hemiplegia successfully sued on the basis that he had not been given sufficient information about the risks of the procedure. The court ruled that “a physician violates his duty to his patient and subjects himself to liability if he withholds any facts which are necessary to form the basis of an intelligent consent by the patient” [7]. Several additional cases firmly established the physician’s duty to convey adequate information regarding the nature and probable consequences of the treatment, and the potential risks involved [8].

Initially, the consent process had a *provider-based* standard. A physician was expected to disclose information

about the treatment that reasonable physicians believed relevant for the patient to know, and that reasonable physicians generally disclosed to their patients in similar circumstances. In another landmark case, the court moved toward a *patient-based* standard for what information should be disclosed in order to obtain truly informed consent [9]. The court was concerned that control of what information needed to be presented to the patient was too important to be left to physician groups, which may have too low a standard or no generally accepted standard of disclosure. The court noted: “respect for the patient’s right of self determination on particular therapy demands a standard set by law for physicians, rather than one which physicians may or may not impose upon themselves” [9]. Patient-based standard mandates that a treating physician discloses as much information as a reasonable patient would wish to know. Unfortunately, there is no comprehensive list for physicians to find out what a reasonable patient would like know in any given situation. A physician must estimate this according to the general principles of informed consent. Thus, this chapter has a conceptual approach, which allows a basic understanding in order to guide a provider’s performance of informed consent. If one goes to court, a jury will decide after the fact whether the physician met the patient’s basic standard of informed consent. The ultimate answer will come only from the jury hearing a disputed case. Some states have a physician-based standard; other states have a patient-based standard. The prudent medical provider will attempt to convey consent using a “patient-based standard,” since this appears to be the direction in which court decisions are trending.

Material risks

Not every possible risk must be disclosed, only those a reasonable patient would wish to know in order to make an appropriate decision. These have been termed “material risks” and are specific to each procedure and patient situation. However, the courts do not define these risks a priori. If the physician’s consent information is challenged and a trial results, what should have been disclosed would be decided by the jury after the fact.

There are no comprehensive legally binding lists available to the physician, although some state statutes have begun to provide some specific guidance [10]. In fact, in Louisiana a Medical Disclosure Panel has a list of material risks for over 100 medical procedures [11]. Electronic databases may aid physicians in providing information to patients; however, the physician cannot abdicate responsibility for providing the final individualized communication with the patient [5].

There are guiding principles that can be used to help determine what an average patient (and average jury!) would find significant.

The four elements of risk that physicians need to consider in providing informed consent are:

- 1 nature of the risk;
- 2 magnitude of the risk (seriousness);
- 3 probability that the risk may occur;
- 4 imminence of the risk (i.e. post procedure or decades later).

The more serious the risk, the more disclosure is warranted; the higher the probability of the risk, the more disclosure is warranted. However, deciding what is material is often not easy. An authoritative text on informed consent notes that “the physician must walk a fine line between providing pertinent risk information and overwhelming the patient with frightening statistics. Providing too much extraneous information may be as likely to impair informed decision making as providing too little” [5].

Ironically, it is often impossible to find a legal precedent that would allow the prudent physician to list specific required disclosures related to a specific procedure. Even if a legal ruling were found, medical cases may be different enough so that one judicial ruling may not apply to another case. Differing judicial districts may not follow each other’s precedents. Further, medical advances may alter “current” list expectations. The best one can do is apply the principles of informed consent and fully involve the patient in decision-making; this is likely to be sufficient. Thus it is not possible to give a brief statement that the reader can “cut and paste,” outlining the optimal risks to be disclosed for colonoscopy. However, a spectrum of medical journal articles regarding colonoscopy and gastrointestinal society information and guidelines on the use of colonoscopy provide some authoritative basic information about colonoscopic risk. To help direct thinking about informed consent for colonoscopy, consider information (material risks) an average patient may want (Table 4.1). (See

Table 4.1 Information to disclose to the average patient.

Serious and uncommon risks of colonoscopy, likely to include:

- perforation and bleeding
- could require transfusion or surgery

Serious and uncommon risks associated with colonoscopy and/or the administered anesthesia, which could include:

- cardiac or respiratory complications
- infection (arrhythmia, infarction, aspiration)

Common nonserious risks:

- gas
- bloating
- self-limited discomfort
- intravenous access site complications

Colonoscopy is an imperfect procedure:

- possibility of missing a lesion or diagnosis
 - even with technically adequate examination [17]
-

Chapter 15 on complications of colonoscopy for further thoughts on what information to disclose.)

Finally, should one mention the possibility of death as a result of the procedure? One study from England reported that a survey of barristers (the English equivalent of plaintiff's attorneys) indicated that serious risks should be mentioned even if as rare as one in a million [12]. Although it is generally legally safer to mention more risks (including very rare risks), there is a potential cost in unnecessarily frightening patients away from beneficial procedures by not adequately conveying the rarity of such an event. My own colonoscopy consent discussion does not mention death (unless specifically asked); however, readers must review the concepts of consent, and use their knowledge of colonoscopic risks to form their own opinion on this matter.

Unsettled areas

What else should be disclosed for truly informed decision-making? Although traditional informed consent doctrine has involved disclosure of medical and surgical risks of a procedure, a patient-oriented standard of disclosure allows a broader interpretation of material risk. The language of the seminal legal case, "when a reasonable person . . . would be likely to attach significance to the risk . . . in deciding whether or not to forgo the proposed therapy" [9], has allowed nontraditional interpretations of pertinent disclosure information to include the experience of the provider, and economic interests of the provider. In a legal case involving a complex and risky brain aneurysm surgery, the provider was found liable for withholding information regarding his inexperience [13,14]. While disclosing current complication rates from the medical literature for standard procedures seems appropriate, if the provider has a substantially different rate of complications, courts could find that this information should have been disclosed. With improving information systems, will provider-specific complication rates become the informed consent expectation? What about other information patients may think pertinent to their decision to proceed with a specific provider such as illness of the provider, alcoholism, social stresses such as divorce, or even lack of sleep after a rough night on call? These issues have been raised but not yet answered [15].

Issues of conflict of interest and the physician's fiduciary duties to the patient have led to an expectation of disclosure of significant financial interests. In a case where physicians had a financial interest in developing a cell culture line from a spleen resected from a patient with hairy cell leukemia, it was found that physicians must disclose economic or research interests that might affect their judgment [16]. These principles could apply to colonoscopists being either paid per case for patient

entry into a research study or receiving managed care incentives to reduce service [5].

Failure to obtain informed consent: legal consequences

Risk-management programs involve understanding the risk of malpractice by analysis and legal theory in order to develop awareness of risks pertaining to specific treatment encounters. Medical malpractice most commonly involves the tort of negligence, in which a healthcare provider is felt to have practiced below the standard of care. However, a common and independent cause of malpractice action involves failure to obtain informed consent. Of note, even if a malpractice claim fails with respect to the standard of care allegation, a healthcare provider can be liable for inadequate informed consent.

Since informed consent requires communication between provider and patient and since studies of malpractice risk note that better communication reduces malpractice risk, the process of informed consent can actually be a tool to reduce malpractice risk. Further, the process of disclosing the inherent risks of a procedure essentially asks the patient to accept that risk as part of the performance of the procedure. This transfers the risk of a nonperfect procedure from the colonoscopist to the patient, who assumes the risk with the decision to proceed despite the knowledge of procedural risks. The risk shift does not apply to substandard care, but would apply to many of the complications of colonoscopy that may occur even with appropriate technical performance of the procedure [17].

Thus the process of obtaining informed consent can positively affect malpractice risk for the following reasons.

- 1 It allows communication to occur between the healthcare provider and patient, which should strengthen the professional relationship, build trust, and demonstrate the professional's respect for the patient's autonomy.
- 2 It performs a risk-management function by decreasing the likelihood of a common malpractice claim (failure to obtain informed consent). It also shifts the liability risk of a complication toward the patient, who has accepted the procedure knowing the associated risks.
- 3 It fulfills the legal obligation to obtain consent prior to a medical procedure.

Possible malpractice actions: negligence or battery

Most malpractice claims are made under the legal theory of negligence. A healthcare provider breaches the duty of care to the patient by substandard care, or lack of informed consent, that causes harm to the patient. However lack of informed consent is an independent cause of legal action and can lead to a finding of provider

liability, even if the standard of care was met. For instance, a postpolypectomy bleed may have occurred without substandard procedure; complications can happen despite careful technique. The mere existence of a complication is not enough to find the provider liable. However, if there had been no informed consent prior to the procedure, the patient could successfully argue that if he or she had known there was a risk of bleeding, he or she would not have chosen to undergo the screening colonoscopy.

If there is absolutely no consent, a charge of battery could be brought. By definition, battery is a nonconsensual touching that is harmful or offensive. One pictures thugs rather than physicians when one hears a charge of battery. It is a currently disfavored approach in litigation of informed consent cases. However, if there is absolutely no consent (not merely a failure to obtain a signature on a form but no consent discussion about the procedure) or the procedure is well beyond the scope of consent, a claim of battery could result [13]. Battery is not covered by most malpractice insurance and thus personal liability could result (although most physicians would be more concerned about potential personal liability, many plaintiff's attorneys would prefer a negligence action in order to ensure the insurance agency remains liable). Battery can be a criminal charge that could affect future hospital credentialing. Hospital credentialing committees often have bylaws that reject physicians with a criminal record. However, this charge is rare in medical malpractice settings, where the cause of action is usually under the legal theory of negligence.

Practical aspects of informed consent

Process (elements) of consent

The colonoscopist must ensure that the patient is competent to understand the information disclosed. Note that the medical literature contains information indicating that ordinarily competent older patients may be temporarily unable to adequately comprehend information when hospitalized with a serious illness. Having a family member present may be useful to ensure adequate consent or at least reduce the likelihood of successful consent challenge later. Informational materials may be given to the patient to facilitate understanding of the procedure. Appropriate institutional forms should be signed and witnessed, and a statement written or dictated as part of the colonoscopy note indicating that informed consent has been obtained. It is best if the witness to consent is a family member or friend, since this implies that the witness believes the patient capable of consent, and is also there to help in the process. If a member of staff witnesses the consent, it is best if this is

Table 4.2 Components of the informed consent form.

Explanation of the nature and character of the procedure in nontechnical form
Material risks of the procedure
Patient's name
Date and time of consent
Disclaimer of guarantee of success
Identification of the colonoscopist
Consent to allow the physician to modify the procedure for unforeseen circumstances
Acknowledgment of opportunity to ask questions
Consent to disposal of removed tissue
Consent for transmission of results to appropriate parties

not the person obtaining the consent or helping perform the procedure. If an issue comes to trial and those in the procedure room are named as defendants, their testimony witnessing the adequacy of consent may appear biased.

Elements of consent

The standard core elements of informed consent (Table 4.2) include the nature and character of the procedure (preferably in nontechnical terms), the material risks of the procedure, the likely benefits, and the potential alternatives (including no treatment). Most consent forms will also include the patient's name, date and time of consent, disclaimer of guarantee of success, identification of staff who will perform the procedure, consent to allow the physician to modify the procedure for unforeseen circumstances, an acknowledgment that the patient has been given the opportunity to ask questions which have been answered, consent to disposal of removed organs, and, with new privacy concerns and regulations, consent for transmission of the results to appropriate parties [18].

Who gives consent?

Valid consent is given by a competent adult, by an adult for their dependent child, and by an "emancipated minor." A durable power of attorney for healthcare may give consent for the named individual. Relatives of the adult patient may give consent. The priority order is usually specified by state statute, and often has an order such as spouse, children over 18, parents, adult brothers and sisters. However, if there is no designated relative to give consent and there is obvious family disagreement, it may be prudent to attempt to achieve a degree of consensus before proceeding with an elective procedure. Also, if DNR ("do not resuscitate") orders exist, it is important to clarify whether the power of attorney or family member is willing to suspend these during the procedure. If

Table 4.3 Exceptions to informed consent.

Emergencies
Implied consent
Patient waives right to informed consent
Therapeutic privilege
Legal mandates

DNR orders is part of a living will and it is not possible to suspend them, the issues surrounding this must be clearly discussed with the individual(s) providing consent for the procedure.

Exceptions to informed consent (Table 4.3)

In an emergency situation, a healthcare provider may treat the patient without obtaining consent; consent is presumed, or “implied” in legal parlance. The definition of emergency may vary in different jurisdictions, but the principles of imminent harm by failure of prompt treatment can be applied. This issue is less likely to arise with colonoscopy. Further, attempting even a limited consent with a conscious patient is worthwhile if it will not unduly delay emergency treatment.

Implied consent has been found sufficient in non-emergency situations. An old legal case found consent had been implied by a person standing in line for a vaccine and holding out her arm [19]. With respect to colonoscopy, a patient getting up on the table with an intravenous line in place would likely lead a jury to find enough implied consent to exclude a charge of battery. However, without adequate disclosure and opportunity to ask questions, a modern jury would be unlikely to find that true informed consent had taken place.

Patients are able to waive their right to informed consent. However, they must know they have the right to information necessary to make an informed decision. Thus when a colonoscopy patient says “You’re the doctor, you decide what is best,” the careful doctor may accept that responsibility but will first inform the patient of the right to information and decision-making.

Therapeutic privilege allows physicians to withhold information they generally must disclose, based upon the physician’s perception that disclosure will be harmful to the patient [20]. However, this is a disfavored exception; there is concern that it may be used as an excuse for not informing patients. Unless there is clear and convincing evidence of psychologic fragility, it would be best to ignore this exception.

Finally, a legal mandate supersedes a patient’s decision regarding a course of treatment. Thus a patient with infectious tuberculosis or dangerous mental illness may be required by court order to undergo medical treatment.

Scope of consent

The patient consents to a specific treatment course. If an unforeseen problem arises during the course of treatment and the patient is unable to consent to further needed treatment, the physician may undertake the needed treatment, thus “expanding” the scope of the original consent [13]. However, events that should have been foreseeable should be included in the original consent. Thus, if perforation is a known possible complication of colonoscopy, it is best to inform the patient in advance of the colonoscopy that surgery could be necessary to correct such a complication.

Informed refusal

An unusual correlate of informed consent is informed refusal. It is clear that patients have the right to refuse treatment. However, it remains the obligation of the physician to educate the patient sufficiently as to the nature and need for the treatment so that refusal is based upon a clear understanding of what has been proposed. In an old but often-cited legal case, the patient’s chart documented repeated refusal of a pelvic examination. In the lawsuit after the development of cervical cancer, the patient successfully argued that she had never been told why the test had been recommended. She contended she would have undergone the pelvic examination if she had known that this was a cancer screening test [21]. With modern communication and abundant public health messages, it may be harder to convince a jury that the patient did not know the rationale for the refused colonoscopy. However, the prudent physician documenting the refusal of a recommended examination is best protected by noting the patient had been told the purpose of the examination included cancer screening.

Documentation

An oft-quoted malpractice maxim is “if it isn’t written in the chart, it didn’t happen.” Informed consent is a process, more than a signature on a standardized form. While many hospitals and institutions require specific forms be signed, it may be even more helpful in the event of litigation to also have a note in the chart documenting consent. However, that note does not need to be a verbatim or encyclopedic recitation of the consent discussion. A mere statement that risks, benefits, and alternatives were discussed and informed consent obtained will document that the process occurred. It is impossible to predict what any particular jury would want discussed. One study from England noted that plaintiff’s attorneys felt risks as rare as one in a million should be mentioned [12]. One scholar has suggested tape recording the informed consent discussion, which in my view seems

both impractical and detrimental to the doctor–patient relationship. Further, a study of taped physician–patient treatment interactions later analyzed for elements of consent discussed revealed a poor performance [22]; unless carefully done, it is unclear if a taped conversation would help or hurt the physician in court. It also seems impractical to list all items discussed and statistics mentioned in the documentation. However, a brief mention in the dictated colonoscopy note stating “the nature and character of the procedure, as well as risks, benefits and alternatives were discussed” may be beneficial. Citing materials given to the patient (e.g. American Society for Gastrointestinal Endoscopy patient education materials) allows these to be introduced as evidence of education and disclosure. It is important to note that no procedure is perfect, and the physician should raise the concept that even competently performed colonoscopy can miss a lesion [17,23]. Further, if one dictates specific complications or statistics, it may be helpful to note that this was not the complete discussion (e.g. “complications were said to *include* perforation, bleeding, cardiac and respiratory complications, infection and missed diagnosis”).

Documentation includes far more than consent issues. Physicians notoriously do more than they document. This can be problematic in litigation, billing issues, and quality assurance reviews. Documentation should include the reasons for the procedure, a comprehensive procedure report, any complications and corrective action. State laws specify record retention times. Additional information about documentation specific to gastrointestinal endoscopy can be found in the manual, *Risk Management for the GI Endoscopist* [18], which can be requested from the American Society for Gastrointestinal Endoscopy.

Special situations and problem areas for informed consent with respect to colonoscopy

When the patient says “Stop!”

What should the conscientious gastroenterologist do when, during a colonoscopy, the sedated patient rouses from the conscious sedation haze and says “Stop!” A British survey demonstrated uncertainty among gastroenterologists [12]. The nature of conscious sedation is such that a patient may perceive but not be aware of the context and surroundings to sufficiently understand the implications of a demand to stop the procedure, e.g. a lesser procedure without therapeutic capacity, or a repeat colonoscopy after a repeat colon preparation. The discomfort is likely to be short-lived and the procedure safe and successful, and often the patient has no recall of difficulty or any request to stop the procedure.

Additional medication and gentler techniques may allow a more comfortable completion of the colonoscopy. Indeed, the patient may wish the discomfort to stop, not the procedure.

However, the colonoscopist and staff must be aware that consent can be withdrawn (by a competent patient). If a physician were to persist after consent was revoked by a competent patient, the physician is then proceeding without consent and could be accused of battery. Consider a patient who is not in the sedated–amnesic state of conscious sedation but alert enough to intend to revoke consent, and remembers staff holding him down while he is screaming “Stop!” Consider him describing that scene to a jury.

On the basis of conversations with experienced colonoscopists, I surmise that most requests to stop are not true withdrawal of consent but an artifact of sedation causing misperception of the context of procedural activity. However, the prudent colonoscopist will carefully evaluate a request to stop and be as certain as possible that it is not true withdrawal of consent for the procedure, which would mandate withdrawal of the instrument. The colonoscopist may temporarily cease insertion and converse with the patient. This may establish that the patient does wish to proceed or is no longer conscious enough to continue to request stopping the procedure. On the one hand, if a very sedated patient rouses briefly to semicoherently mumble “Stop!” and the physician aborts the procedure, she may have to explain to the unhappy patient, who remembers nothing about a request to stop, about the need for a repeat colonoscopy and the obligatory repeat preparation. On the other hand, picture a lightly sedated patient (perhaps coaxed into the examination by a concerned spouse) who experiences difficulty with the procedure, who truly changes his/her mind about the procedure and repeatedly asserts that the procedure should stop. If the colonoscopist ignores this request, serious consequences could result. There are no easy answers. Listen carefully to the patient and to the endoscopy nursing staff. If experienced nursing staff are uncomfortable continuing, this is important information for the colonoscopist. Also, these are the individuals who, if the procedure should come to trial, would be asked to testify about exactly what the patient said and their perception of whether this was a revoked consent. Good judgment, prudence, and discretion will keep the colonoscopist out of trouble.

Open-access colonoscopy

There are strong practical, efficiency, and business arguments to support open-access colonoscopy. In a public health sense, this may help make a scarce resource more accessible, more convenient, and less expensive.

However, the very nature of its efficiency, in which a patient comes already prepared for the procedure, poses problems with respect to informed decision-making [24]. As previously noted, consent is a mutual process, which occurs after appropriate disclosure, with time for answering questions, in an uncoerced process. In open-access colonoscopy, the patient has not met the colonoscopist prior to the decision to proceed with colonoscopy, prior to having undergone preparation for the procedure, or in some cases prior to arriving in the procedure room with an intravenous line in place! The issue is whether truly informed consent can be obtained in this setting or whether there will be a perceived coercion. Consent must be voluntary as well as informed. If the patient is learning about the procedural risks and alternatives after having been prepared, with an intravenous line running, with the physician and nursing staff impatiently waiting to begin, is that patient in a position to ask questions and make a voluntary decision to proceed? Could a skilled plaintiff's attorney make a case that the complication that occurred, though perhaps within the technical standard of care, is malpractice because of faulty consent? I am not aware of any litigation that addresses this issue. The concept of open-access colonoscopy remains attractive. If gastroenterologists and medical institutions wish to pursue open-access colonoscopy, then some attempts to ameliorate consent issues may be warranted. These may include developing processes that show effort to present adequate information in advance, with opportunity to ask further questions in a noncoerced manner. The following suggestions are meant to offer one example, by no means necessary, or even tested and necessarily sufficient, but at least an attempt to incorporate the principles of informed consent.

- 1 Have the patient receive oral and/or written information specific for colonoscopy and screening from the primary care office at the time of referral, and/or from the gastrointestinal staff who call the patient to schedule colonoscopy and discuss preparation instructions.
- 2 Ask patients to call the gastrointestinal office if, after reviewing the materials/information received, they feel that more information is needed prior to agreeing to undergo the procedure. Document this instruction.
- 3 On the day of the procedure, have the patient greeted by the office staff (or physician) before starting the intravenous line. At this time, disclosure information can be reviewed and the patient asked if there are any questions remaining that need the physician's input.

Transmission of data

Obtaining photographic or video documentation at the time of colonoscopy may be considered a part of the procedure. Privacy and confidentiality of medical informa-

tion has long been an expectation of medical care [15]. However, the revolution in electronic information technology has heightened privacy concerns. The electronic transfer of information has important business purposes, but also the potential for problems with respect to the privacy and confidentiality of health information. The Health Insurance Portability and Accountability Act (HIPAA) became law in 1996 and underwent extensive comment and revision periods, with final privacy regulations established in 2002 [25]. Many healthcare entities are still digesting the required regulations and formulating compliance protocols. It is beyond the scope of this chapter to address those regulations. Suffice to say that in general consent will be required for the transmission of colonoscopy reports, photographs or videotapes, and biopsy results to other entities. Office personnel will need to be trained in matters of confidentiality, and office systems will need to be designed in ways that insure confidentiality. Providers using email should be certain that they can maintain the level of confidentiality required for transmission of medical data and that they have warned their patients about email confidentiality problems [26]. Many mass-market email vendors, designed for home use, will likely not meet these privacy standards. Failure to comply with HIPAA regulations may result in civil or criminal penalties, fines, or even incarceration.

Summary

The ethical and legal requirement to obtain informed consent prior to performing colonoscopy derives from the concept of personal (patient) autonomy. The competent patient, after receiving appropriate disclosure of the material risks of the procedure, understanding those risks, the benefits, and the alternative approaches, makes a voluntary and uncoerced informed decision to proceed. This is a basic ethical obligation in the practice of medicine. It should be a communication tool that cements the provider-patient relationship. It functions as a risk-management tool, transferring known standard procedural risks to the patient who has understood and accepted the premise that even competently performed colonoscopy has risks. The procedural elements involved in obtaining consent include a discussion of material risks, a knowledge of who gives and obtains consent, the scope of consent, exceptions to consent, witnessing and documentation of consent, and the use of educational materials and consent forms.

Specific areas of legal uncertainty with regard to disclosure include whether it is necessary to discuss certain provider attributes (such as level of experience) or how to disclose economic interests of the provider/researcher. Special situations or problem areas, such as how to obtain valid consent for open-access colonoscopy,

what to do when a sedated patient requests halting the procedure, and privacy/confidentiality issues regarding the transmission of patient reports to other providers, have been reviewed. Knowledge of informed consent theory will help the provider to address the specific consent issues for an individual patient.

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Chapter 5

Training in Colonoscopy

Martin L. Freeman

Introduction

Colonoscopy is a potentially complex endoscopic procedure that often involves therapeutic maneuvers such as polypectomy. Colonoscopy has significant potential not only to benefit patients but also to cause adverse outcomes due to missed diagnoses, incomplete or failed therapies, and complications. More than 4 million colonoscopies are performed annually in the USA by a variety of practitioners including gastroenterologists, surgeons, primary care physicians, physicians' assistants, and nurse practitioners, with more than half of colonoscopies performed by nongastroenterologists. These practitioners have levels of training varying from formal training programs such as gastrointestinal or colorectal surgery fellowships to self-teaching in practice or short courses. There are no established national standards for granting hospital privileges to perform any specific endoscopic procedure. The American Society for Gastrointestinal Endoscopy (ASGE) and the American Gastroenterological Association (AGA) have issued suggested guidelines for granting privileges that include warnings about the medicolegal consequences of granting privileges to undertrained physicians [1,2]. Neither the ASGE nor any other organization accredits or certifies the endoscopic training of individuals or institutions [3]. Certification of procedural competence is generally provided by endoscopy training directors or more broadly through board certification by appropriate examining bodies, such as the American Board of Internal Medicine (ABIM) or the American Board of Surgery. There is no nationally established mechanism to recertify competence in the practice of previously performed procedures or to establish competence in new procedures learned after training is completed. Although most endoscopists become more adept with continued experience after training, maintenance of expert performance cannot be assumed. As new technologies and techniques emerge, most established practitioners endeavor to enhance and expand their own capabilities. It is rarely feasible for training programs to accommodate the retraining needs of past trainees. Such individuals would ideally consider the option of pursuing advanced endoscopic training fellowship positions. In practice, this rarely happens.

Definition and assessment of competence

Definition of competence in gastrointestinal endoscopy has been an elusive goal [3–10]. Competence has been defined as “the minimum level of skill, knowledge, and/or experience required to safely and proficiently perform a task or procedure” [3]. It is widely recognized that competence in endoscopy or any other procedure involves a combination of technical and cognitive skills. Specific components, as detailed by the ASGE, include:

- 1 ability to integrate gastrointestinal endoscopy into the overall clinical evaluation of the patient;
- 2 sound general medical or surgical training;
- 3 thorough understanding of indications, contraindications, risk factors, and benefit–risk considerations for the individual patient;
- 4 ability to describe the procedure clearly and obtain informed consent;
- 5 knowledge of endoscopic anatomy, technical features of equipment, accessory endoscopic techniques, and therapies;
- 6 ability to identify and interpret endoscopic findings accurately;
- 7 understanding of principles, pharmacology, and risks of sedation and analgesia;
- 8 ability to document findings;
- 9 competent performance of the procedure [1].

Traditionally, the assessment of competence has relied on tallying total numbers of procedures performed or subjective evaluation by a proctor. The use of threshold procedure numbers at which competence may be globally assessed provides only a rough guide for evaluation of competence. Increasingly, the importance of objective assessment of endoscopic performance has been recognized [1,3]. A variety of methods for monitoring performance during training or in practice have been suggested (Table 5.1). Suggested objective performance criteria for the evaluation of technical skills in gastrointestinal endoscopy are listed in Table 5.2 [3]. It has been proposed that expert endoscopists should be expected to perform at a technical success level of 95–100% [3]. The available data support as reasonable the standard

Table 5.1 Strategies for objective assessment of competence in trainees or in practice.

Self-reporting of performance parameters in log book
Selective observation by a designated evaluator
Recording of performance data by supervising endoscopic trainers
Incorporating performance data into an electronically generated endoscopic report

Table 5.2 Suggested objective performance criteria for the evaluation of technical skills in gastrointestinal endoscopy as proposed by the American Society for Gastrointestinal Endoscopy [3].

Procedure	Performance criteria
Colonoscopy	Intubation of splenic flexure Intubation of cecum Intubation of terminal ileum (desirable skill)
Polypectomy	Successful performance
All procedures	Accurate recognition of normal and abnormal findings Development of appropriate endoscopic/medical treatment in response to endoscopic findings

of 80–90% technical success before trainees are deemed competent in a specific skill.

Recommendations of various organizations on minimum numbers of procedures required to achieve competence

Medical societies have issued position papers regarding how much training is required to achieve competence in colonoscopy. In the absence of data, expert opinion has

Source	Year	Colonoscopies
<i>Expert opinion</i>		
Internists [12]	1989	25
Internal medicine directors [13]	1989	25
Gastroenterologists [14]	1990	88
Gastrointestinal training directors [15]	1990	75
<i>Professional societies</i>		
Society of American Gastrointestinal Endoscopic Surgery [19]	1991	25
European Diploma of Gastroenterology [18]	1995	100
British Society of Gastroenterology [16]	1996	100
American Society for Gastrointestinal Endoscopy [1]	1998	100
Conjoint Committee (Australia) [17]	1999	100
American Academy of Family Practice [20]	2000	~10 (short course)
<i>Data-derived</i>	—	>340

Table 5.4 Recommendations of the American Society for Gastrointestinal Endoscopy for minimum number of procedures before competency can be assessed [1].

Standard procedure	Number of cases required
Total colonoscopy	100
Snare polypectomy	20*
Flexible sigmoidoscopy	25

* Included in total number.

generally been relied upon (Table 5.3). The Federation of Digestive Disease Societies has recommended 50–100 procedures for competence in esophagogastroduodenoscopy (EGD) or colonoscopy [11]. Wigton obtained estimates from internists, internal medicine residency directors, and gastroenterologists of the numbers of procedures thought necessary to achieve competence [12–14]. The first two groups thought a median of 25 colonoscopies was sufficient, whereas gastroenterologists thought a median of 88 colonoscopies was needed. The ABIM surveyed gastroenterology fellowship directors and found that a median 75 colonoscopies was considered adequate [15]. Official recommendations of organizations (Table 5.3) have included those of the ASGE, which recommends a minimum of 100 colonoscopies to achieve competence [1] (Table 5.4); the British Society of Gastroenterology, which recommends 100 colonoscopies [16]; the Conjoint Committee for Recognition of Training in Gastrointestinal Endoscopy of Australia, which recommends 100 colonoscopies [17]; and the European Diploma of Gastroenterology, which suggests 100 colonoscopies [18]. In contrast to gastroenterology-oriented societies, other specialties have often suggested that much lower numbers would be adequate; for example, the Society of American Gastrointestinal Endoscopic Surgery (SAGES) has recommended 25

Table 5.3 Minimum number of procedures to achieve competency at colonoscopy according to expert opinion, society recommendations, and as summary of available data.

procedures [19]. Recently, at the urging of the ASGE, SAGES has agreed to eliminate suggested numbers of procedures (personal communication from ASGE). The American Academy of Family Practice has endorsed “short courses” during which trainees perform an average of less than 10 supervised procedures [20].

Acquisition of competency in colonoscopy

Data have gradually emerged to shed some light on the rate at which endoscopists acquire objective skills in gastrointestinal endoscopy. In an early study, Hawes and colleagues showed that 24–30 procedures were required for the average trainee to achieve an acceptable level of competence in flexible sigmoidoscopy, based on a 6-point subjective scale [21]. It has become apparent from a series of subsequent studies based on objective evaluation of skills in a variety of endoscopic procedures that learning curves are substantially longer than previously suspected, and that the number of procedures required to achieve competency is substantially higher than generally thought [22].

An increasing body of work suggests that there is substantial variation in outcomes of endoscopy in clinical practice. These variations relate to both technical success and complications, and result from a number of factors. Factors that contribute to the overall outcomes of endoscopy include the physician’s specialty background and endoscopic training, ongoing case volume and, to a certain degree, the cumulative case volume of the center in which the endoscopist works [23]. For a specific procedure, the endoscopist’s total experience or ongoing volume of analogous cases may be the most relevant factor, for example with more specialized therapeutic procedures such as complex saline-lift polypectomy of sessile polyps. Finally, it is recognized that there is substantial variation in the innate ability of each endoscopist.

In the USA and other countries, colonoscopy is performed by gastroenterologists and nongastroenterologists, including general surgeons, colorectal surgeons, internists, family practitioners, and even radiologists. Most likely the specialty background of endoscopists is not as important as the experience and case volume of endoscopy performed. In practice in the USA, however, there are relatively few nongastroenterologists who devote major portions of their training or practice to endoscopy. Some family practitioners receive their entire endoscopic training during “short courses” over a single weekend involving 10 or fewer supervised procedures [24]. Data would suggest that it is impossible to achieve a reasonable level of competence with this sort of training. In one study, Schauer and colleagues found that surgical residents had completed an average of 75 upper endoscopies and 75 colonoscopies [25]. In con-

trast, gastroenterology fellows typically complete more than 400–500 EGDs and 200–600 colonoscopies during training.

Because the entire colon must be examined to be confident that lesions have not been missed, reaching the cecum has become a surrogate marker for basic technical competence in diagnostic colonoscopy. As a “gold standard,” expert endoscopists are able to reach the cecum in more than 95% of cases. For example, in a recent prospective multicenter study from 13 Veterans Affairs medical centers involving screening colonoscopy in 3196 patients, the cecum was reached in 97.7% of examinations [26]. In a recent large prospective survey, practicing German gastroenterologists reached the cecum in 97% of cases [27]. This result validates the ASGE recommendations of a goal of technical success of greater than 95% for experts and 80–90% for trainees [3].

A number of studies have evaluated the acquisition of competency at colonoscopy during training. Parry, a practicing surgeon in New Zealand, kept records concerning consecutive colonoscopies that he performed [28]. At 305 procedures, he reached the cecum only 91% of the time. Marshall followed nine gastroenterology fellows and measured their success in reaching the cecum during the last 7 months of the first and second years [29]. He found a success rate of only 86% for cecal intubation after trainees had performed a mean of 328 procedures. Chak and colleagues followed five first-year and seven second-year gastroenterology fellows during a 4-month period of a 2-year fellowship program and observed their performance [30]. They found that after 123 colonoscopies, trainees reached the cecum in only 64% of cases. Church followed 10 surgical residents and reported on their first 125 procedures [31]. By the last 25 procedures, the cecum was reached only 72% of the time.

The largest body of data on learning curves of colonoscopy comes from Cass and colleagues in two sequential studies. In an initial study using a computer program to evaluate simple measures of competence at colonoscopy by seven gastroenterology fellows and five fourth-year surgical residents, cecal intubation remained at 84% after 100 procedures [7] (Fig. 5.1). In the most comprehensive study of endoscopic learning curves to date, which has so far been published in abstract form only, Cass and colleagues evaluated learning curves of 135 gastroenterologists performing 8349 colonoscopies throughout their 3-year fellowships at 14 gastroenterology training programs in the USA [23]. Competence at colonoscopy was objectively assessed by a proctor and was defined as successful completion of four criteria: traversing the splenic flexure, intubating the cecum, recognizing abnormalities, and correctly identifying abnormalities. A subjective assessment of competence was also performed using a 5-point scale, competency being indicated by a score of 4 (competent) or 5

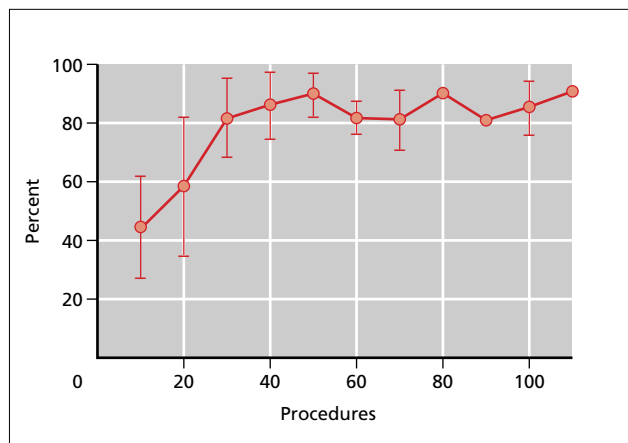


Fig. 5.1 Success at cecal intubation during colonoscopy by gastrointestinal fellows and surgical residents as a function of total number of procedures performed. (From Cass *et al.* [7] with permission.)

(competent and expedient). A success rate of 90% for unaided intubation of the splenic flexure and cecum was achieved at a mean of 195 procedures, but there were too few fellows exceeding that number of procedures to achieve statistical certainty. Conclusions were that for the average fellow, more than 200 colonoscopies would be necessary to achieve competence at basic diagnostic colonoscopy. This study if anything underestimated the numbers of procedures required to perform competent colonoscopy because (i) some procedures were missed, (ii) the fellows were simultaneously learning EGD, (iii) fellows were not graded on “censored” cases (i.e. cases in which the proctor did not allow the fellow to attempt colonoscopy), and (iv) competence in polypectomy was not assessed. Cass also found that while subjective assessments of technical competency were accurate in

upper gastrointestinal endoscopy, they overestimated technical competence at colonoscopy. The proctors assessed the fellows as being competent by subjective criteria after a median of 60 procedures while, by objective criteria, they achieved competence only after approximately 200 procedures. The observed gulf between subjective and objective assessment of competency points out the pitfalls of the traditional certification by proctors and emphasizes the need for objective assessment of performance. Another conclusion from this study was that fewer procedures would be missed when data-gathering was linked to production of an endoscopic report. In Cass’s first study [7], which was performed at a single institution using a computerized database, no report could be printed that included a fellow until a grade had been entered.

Cass has summarized the available literature concerning cecal intubation rates during colonoscopy as a function of the cumulative experience of the endoscopist [32] (Table 5.5). He then calculated a least-squares regression of logarithmic curve based on these data to determine the mean number of colonoscopies necessary to achieve a 90% cecal intubation rate (Fig. 5.2). Considering all the data, the calculated mean number of procedures to achieve a 90% success rate was 341 colonoscopies. Interestingly, this number exceeds the recommendations of any professional society and is more than 10 times higher than the numbers previously recommended by organizations such as SAGES. Furthermore, these numbers represent only the ability to advance the colonoscope to the cecum and do not include recognition and identification of abnormalities or the ability to remove polyps. It would seem to be clear from the above data that recommendations of most professional societies regarding the number of colonoscopies required to achieve competence are too low.

Table 5.5 Studies of acquisition of technical competence at colonoscopy during training: cecal intubation rate after performance of the stated number of procedures. (Adapted from Cass [32].)

Reference	Date	Specialty	Trainees	Procedures	Cecal intubation rate (%)	Estimated 90% success
Parry & Williams [28]	1991	Surgeon	1	305	91	261
Godreau [36]	1992	Family practitioner	1	157	83	—
Cass <i>et al.</i> [7]	1993	Gastroenterologists/surgeons	12	100	84	97
Church [43]	1993	Surgeons	8	100	62	—
Rodney <i>et al.</i> [35]	1993	Family practitioner	1	100	52	551
Church [31]	1995	Surgeons	10	125	72	376
Marshall [29]	1995	Gastroenterologists	6	328	86	—
Cass <i>et al.</i> [23]	1996	Gastroenterologists	35	200	90	200
Chak <i>et al.</i> [30]	1996	Gastroenterologists	7	123	64	—
Hopper <i>et al.</i> [37]	1996	Family practitioner	1	1048	75	—
Tassios <i>et al.</i> [44]	1999	Gastroenterologists	8	180	77	188

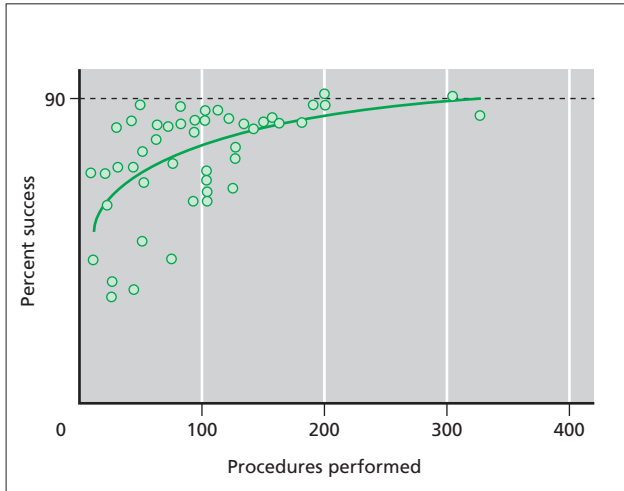


Fig. 5.2 Success at cecal intubation during colonoscopy by total number of procedures performed: summary of all published literature. The curve is a least-squares fit of a logarithmic function. (Adapted from Cass [32] with permission.)

Colonoscopy by nongastroenterologists

The available data suggest that there is substantial variation in outcomes of colonoscopy between different subspecialties. Rex and colleagues examined consecutive cases of colon cancer in a region of Indiana and showed that colonoscopy performed by gastroenterologists was significantly more sensitive (97.3%) for cancer than colonoscopy by nongastroenterologists (87%) [33]. The odds ratio for nongastroenterologists (family physicians, internists, or general surgeons) missing a cancer compared with gastroenterologists was 5.36. In a subsequent evaluation of reasons for failure of colonoscopy to detect 47 missed cases of colon cancer, it was found that nearly half of missed cases were the result of failure to reach the cecum, whereas the remainder were presumably reached but not recognized [34].

A prospective survey of colonoscopy in Germany showed substantial differences in cecal intubation rate between gastroenterologists (97%) and internists (91%), as well as differences in complication rates (1 per 5155 procedures vs. 1 per 1539 procedures) [27].

Performance of colonoscopy by family physicians has been reported in several studies, with surprisingly low cecal intubation rates despite presentation as an apparent endorsement. Rodney and colleagues reported on the initial 293 colonoscopies performed by family physicians in a rural practice [35]. They found that the physicians' cecal intubation rate for the 293 examinations was 54% among the 87% of patients who were sedated, the implication being that the cecal intubation rate would have been even lower if unsedated examinations were excluded. These authors reported a cecal intubation rate

of 52% in the first 100 cases, with no improvement after the first 50 procedures. Failure to reach the cecum resulted in the need for air-contrast barium enema examinations in 74 (24%) of the patients.

Godreau and Hopper also reported their experiences of carrying out colonoscopy after training in short courses during brief preceptorships or after learning on the job [36,37]. They reported 83% and 75% success rates at intubating the cecum in 157 and 1048 procedures, respectively. Unfortunately in Hopper's very large series, cases were not analyzed according to consecutive procedures but rather by the type of sedation used. With sedation, the cecum was reached in more than 90% of cases. Harper and colleagues reported that their family practice service performed colonoscopy with similar outcomes for the gastroenterology and general surgery services, with a cecal intubation rate of 87% in all services, and with significantly more cancers found by the family practice service [38]. The disconcerting finding of this study is the low 87% cecal intubation rate achieved by the specialty services, suggesting poor performance by the gastroenterologists and general surgeons rather than adequate performance by the family practice service.

These reports raise serious concerns about the quality of colonoscopy with inadequate training. There are obvious concerns about the consequences of incomplete colonoscopy, including the cost, risk, and inconvenience of a second bowel preparation and colonoscopy, insensitivity to right colonic lesions, the need for subsequent barium enemas, and the adverse consequences to patients and society of undiagnosed and untreated disease [39]. As already emphasized, however, subspecialty background does not necessarily imply or preclude excellence. Wexner and colleagues reported on the abilities of four nationally recognized surgical colonoscopists to perform colonoscopy in practice. They reported a cecal intubation rate of 96.5%, which is comparable to that of expert gastroenterologists [40].

Strategies for assessing competence in training and practice

It is clear from the above data that performance of a minimum number of procedures, although a prerequisite for acquiring skill, does not guarantee competence. Based on the available data regarding number of procedures required, it does not seem feasible or likely that training to the point of competence is possible outside a structured gastrointestinal fellowship or surgery residency, and especially not with brief training available through short courses [41]. Nonetheless, there is a strong feeling among physicians in other subspecialties, such as family practice, that they should be allowed to perform these procedures [42]. The increased demand for screening

colonoscopy, combined with the decrease in number of gastrointestinal fellowship positions, will no doubt increase the pressure for inadequately trained practitioners to perform colonoscopy.

Because subjective assessment of competence by a proctor is often inaccurate, objective assessment of performance at endoscopy is necessary to assess accurately the competence of an individual. Such objective performance data are useful not only in training but also for credentialing, obtaining hospital privileges, and perhaps even allowing patients and healthcare providers to choose their physicians. Of available strategies to assess competence objectively, self-reporting of performance parameters in trainee or practice logs is obviously flawed by selectivity and lack of objectivity. Observation of trainees by a designated evaluator is a better option but suffers from similar problems. Continuous recording of performance data by a third party, such as supervising endoscopic trainers or gastrointestinal unit coordinators, would be more accurate but does not seem universally feasible because experience has shown that compliance is poor. Ultimately, incorporating performance data into an electronically generated endoscopic report seems to be the only feasible and reliable method of assessing endoscopic performance on a widespread basis.

Currently, a number of software applications are available for routine endoscopic report generation, including CORI and cMORE. Only when endoscopists routinely enter their results into computer-generated reports can all their consecutive cases be systematically analyzed for simple benchmarks, such as documentation of cecal intubation for colonoscopy. Ultimately, for the protection of patients, healthcare providers, and physicians themselves, it will be desirable for endoscopists to produce a "practice summary" in which they document their past experience, their ongoing experience, and outcomes with simple benchmarks for their previous years' cases.

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Chapter 6

Teaching Aids in Colonoscopy

Melvin Schapiro

Introduction

The performance of endoscopy requires both cognitive and technical skills. The American Society for Gastrointestinal Endoscopy (ASGE) and other organizations have prepared guidelines for training in endoscopic procedures for a variety of gastrointestinal diseases [1–3]. These and other guidelines, as well as the assessment of competency of training, credentialing of training, and methods of training (including use of ancillary tools such as simulators), are all discussed in other chapters. This chapter reviews the use and availability of teaching aids both for the learning process and for updating cognitive and technical skills. Three formats of teaching aids are considered:

- 1 text with photographic images;
- 2 electronic media;
- 3 teaching courses.

Role of teaching aids

The question of minimal numbers of previously performed procedures has generated much controversy. It is well known that technical competency is very difficult to achieve for many procedures, particularly those that involve therapy. Nearly all individuals require considerably more cases than stated in the guidelines in order to achieve acceptable standards. A large volume of endoscopic procedures is not practical in all training programs and therefore many endoscopists add skills themselves after becoming facultative in basic procedures. It is important that the basic training in endoscopy be undertaken in conjunction with an experienced endoscopist.

Teaching aids for endoscopy are intended to enable endoscopists to perform their work more productively. The variety of available formats is meant to provide individuals with alternative means to visualize the techniques of procedure performance. These methods of observing the experts “in action” have gained utilization for both initial learning and for the upgrading of endoscopic techniques. Each of the formats has its advantages and drawbacks.

Text with photographic images

The use of the slide or photographic endoscopic image has definite value for learning the cognitive aspects of endoscopy. However, these images have little if any value in the development of technical skills. Multiple textbooks are available [4–7] that contain both detailed descriptions of the performance of gastrointestinal endoscopy and high-quality photographic images of both normal and pathologic endoscopic anatomy. In addition to the classical texts, a variety of atlases of endoscopic findings are available [8–11]. These compilations enable the reader to upgrade cognitive skills but are not useful for self-development of the manipulative aspects of endoscopic procedures.

Electronic media

The “live” patient situation cannot be fully duplicated by modern training models and video formats, although current and developing electronic video formats do offer a substantial library of high-quality images allowing close-up observation of the “expert” and ancillary personnel in the performance of specific procedures. The advantages provided by these technologies include user interactivity, random access to content, and low cost. These formats are available as videotape, CD-ROM, DVD and the Internet. Exchange of electronic endoscopic video images may be made via floppy, zip or CD-ROM disks, computer-to-computer transfer via modem, downloading from the Internet, and directly by satellite transmission. Each of the formats has its own advantages and drawbacks.

Videotape

There is a large library of videotape material available in both PAL and NTSC formats. These formats vary in their use throughout the world. Users must determine the format of their video recorder and order the videocassette accordingly. The endoscopic content from the World Organization of Digestive Endoscopy (OMED) post-graduate courses are available in both PAL and NTSC.

These courses were held at the World Congresses of Gastroenterology in 1990, 1994, and 1998 and are all available from the OMED offices at nominal cost (<http://www.omed.org>). The content includes a large cross-section of diagnostic and therapeutic endoscopic cases with a prominent inclusion of colonoscopic case material. The ASGE library of most of the materials presented at the learning centers held at the annual Digestive Disease Week in the USA (<http://www.asge.org>) are available for purchase through the firm of Milner-Fenwick (<http://www.milnerfenwick.com>). Other sources are available and one can check with a regional society for gastroenterology and endoscopy to inquire about a resource.

Videotapes provide the largest number of topics. They are sometimes directed to the learning endoscopist with minimal experience but most are oriented toward the experienced endoscopist in order to review the performance of highly technical cases or topic-oriented material. Most importantly, these are playable on VHS hardware available to nearly everyone.

The major drawback of the use of videotapes is that they are cumbersome with regard to random access. Forwarding and rewind functions take time and are not accurate. The "pause" image that is desirable for individual frame analysis is usually of poor quality. "Book marking" for return to an image or section to allow repeat or rapid review is not possible. The slow-motion function is not precise for individual frames and the resolution quality of both the video and still images are not as good as other formats (see DVD). Since detailed analysis may be a desirable part of the viewing process, the videotape format is best used for overall observation of a story or case review, to watch an expert, or for receiving ancillary directions and "tricks" of procedure performance.

CD-ROM

A variety of video endoscopic materials have become available from both the endoscopic and pharmaceutical industry, primarily for promotional purposes. Many of these are of good quality and offer the advantage of interactivity that is not available with videotapes. The interactive environment and the ability to use these disks on portable computers has brought another dimension to the learning process. The viewer can navigate through the "menu," selecting the location for review and re-review quickly. Sections can be eliminated from view thereby conserving and optimizing viewing time. Study of disk content can be carried out in airplanes, on vacation, or at the office; in effect anywhere that the personal or portable computer can be taken.

Other valuable features that can be incorporated include (i) the ability to download slide material or video segments for teaching purposes; and (ii) interactive quizzes.

The limitations of the CD-ROM format are its small picture size and relatively inferior resolution. Motion flaws are common occurrences and the limited capacity of the disk does not allow a large number of video cases or additional video material to be included. The disk must be prepared in advance to play on the commonly available hardware platforms. For a variety of reasons, usually related to production costs, not all disks are designed to play on Macintosh computers. This media is satisfactory but has not progressed as the most desirable format for teaching or self-learning.

DVD

The cutting-edge technology is the digital videodisk (DVD). A few years ago DVDs and their players were not much more than toys but have now become the main video delivery format. The advantages of DVDs compared with videotapes and CD-ROMs are listed in Tables 6.1 and 6.2. This format offers full-motion high-resolution video with interactive user interfaces (Fig. 6.1) at far greater storage capacity than the CD-ROM. The disks are compatible with personal computer CD and DVD drives and some are available in multiple language tracks. They offer advantages for medical education such as ultra slow motion, accurate freeze frame, and enhanced audio. Alternate angles of view can be incorporated that will allow ancillary personnel to study the same material from the perspective of the endoscopic

Table 6.1 DVD is superior to videotape.

-
- Full-motion, high-resolution video
 - Interactive user interface
 - Rapid reverse and fast forward
 - Slow motion and accurate freeze frame
 - Random access to specific segments
 - Compatibility with PCs with DVD drives
 - Multiple language tracks
 - Convenient storage and transport
-

Table 6.2 DVD is superior to CD-ROM.

-
- Full-screen broadcast-quality video
 - Multi-platform compatibility
 - Computers with DVD drives
 - Television sets
 - Increased storage capacity
 - Hollywood and computer industry standard
 - Enhanced audio
-

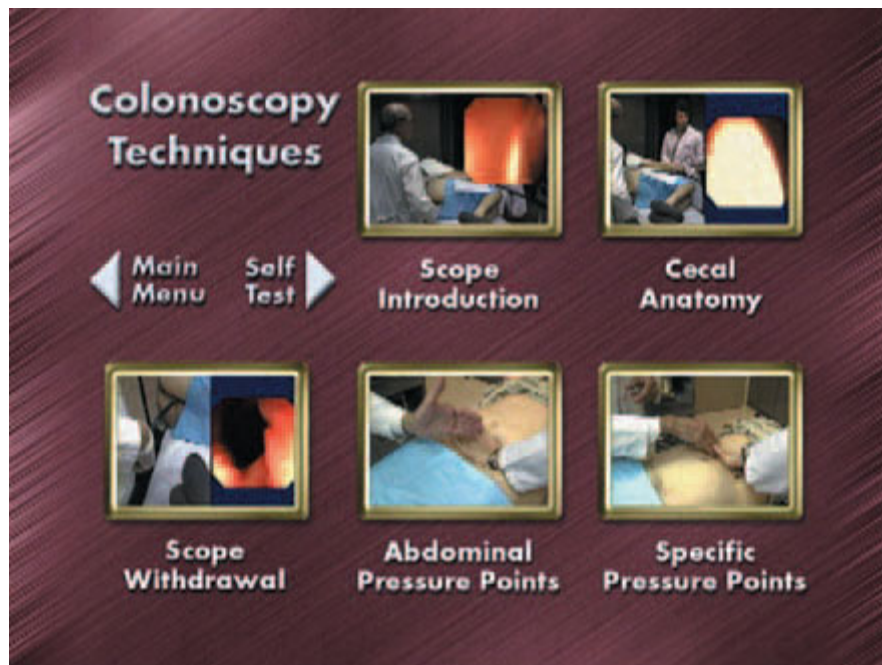


Fig. 6.1 DVD sub-menu.

assistant. DVDs are available on diagnostic and therapeutic topics in extended therapeutic areas with self-study quiz sections, and also on specific topics comprising shorter “experts” series. Both CDs and DVDs allow the technical and cognitive aspects of each case performance to be studied, with narration by the performing endoscopist. The endoscopic, fluoroscopic, and ultrasound images are coordinated with the visual technical aspects of procedure performance by the endoscopist and ancillary personnel.

The most important drawback to the DVD technology has been the lack of widespread availability of the hardware. Retailers are undertaking the permanent shift to DVDs from videocassettes, much as they did when CDs superseded vinyl records. Some commercial electronic chains have announced that they intend to stop selling videotapes, and it may be that in a few years videotapes will disappear from stores altogether. Early estimates were that it would take longer for this format to assert itself, but Hollywood studios moved quickly to record their libraries on disk and the price of DVD players dropped rapidly. Adding to the popularity of DVDs is that computers now play them. This means viewers are no longer chained to their television sets; they can watch DVDs in the car, on the train, even at work using a laptop computer or a small portable DVD player. Making the shift from videotapes to DVDs more appealing is the cost of manufacturing, which is less than half that for a cassette.

DVDs are a vast improvement in quality over cassettes and have many more features. They are changing the way individuals watch movies at home. The enhanced

video and audio qualities allow elaborate home-theater systems. The digital nature of DVD allows viewers to watch only one or two important moments instead of a whole film, much like a favorite track on a CD. This changes video from a linear experience to a more interactive one. It is anticipated that study habits of endoscopic material will follow the same trends.

Though the cost of DVD players has diminished markedly, many in the world’s audience have not yet replaced their VHS or CD-ROM hardware. It is expected that there will be a worldwide trend toward acceptance of DVD for “ordinary” consumption. The costs of conversion are minimal when viewed in comparison to other available formats for endoscopic learning.

Internet

It is anticipated that in the near future the Internet will be the universal broadcast medium. There is an increasing volume of publications concerning the use of the Web to improve education in medicine [12]. The advantages of streaming media include (i) immediate broadcast of the latest innovations, (ii) the presentation of synchronized lecture slides with digitally recorded narration, (iii) high-quality moving endoscopic images, and (iv) accessibility around the world and around the clock. For teaching or learning purposes (e-learning) this format provides fast access to any content from any location, and there is a growing on-demand archive of diverse multimedia presentations.

The ultimate purpose of e-learning is to provide a highly accessible educational opportunity equivalent to

the live experience. Advances in electronic technology have provided a degree of interactivity. It is known that most users prefer not to “surf the Web” and spend time on the printed or slide format. Reference source and the ability to print content are recognized advantages of many sites; however, for e-learning of technical concepts video is required. If the Internet is to be a successful format for e-learning in endoscopy, surgery, and other technical disciplines, it must allow the viewer to use the content for practical purposes. Interactive sites allow the participant to manipulate the content (fast forward, slow and stop motion, alternative angles, replay, and download). Many sites allow the participant to contact the site and participate in discussion.

The Internet is presently available for limited video e-learning in multiple endoscopic areas including colonoscopy. Interactive cases combining written, slide, and video materials are available. The Internet is becoming more like television and the streaming media market is rapidly growing.

In comparison with DVD and videotape formats, standard Internet access (compared with broadband) provides a picture quality of small size and resolution with a significant delay in access time that can discourage the viewer. Surfing the Web and downloading large files is usually too slow to allow e-learning to be practical. Internet “glitches” often occur and can provoke the viewer into giving up. This impedes the delivery of e-learning content since high-speed connections are not yet available to a wide audience. Rapid and higher resolution formats depend on the availability of high-speed technology (broadband). These are available as the digital subscriber line (DSL), cable and, in very limited use, wireless and fiberoptic options. The DSL option uses the existing phone structure and may be more secure than cable, whereas cable has a large television user base and offers the lower cost-speed ratio. Though both wireless and fiberoptic technologies are extremely fast, their costs are presently prohibitive for general application.

The average user connects to the Internet at speeds up to 56 kilobytes per second (kbps). This is often slower than a page of text about every 0.5 s. This speed does not support an enjoyable and instructive activity because skipping and broadcast breaks commonly occur with speeds less than 128 kbps. Quality streaming media requires 128 kbps, which is twice that of a 56-kbps dial-up modem. In fact, the fluid transmission of high-definition video often requires up to 20 megabytes per second (Mbps). The high-speed technologies that are presently available allow e-learning via the Internet for basic concepts and technology review. Current video quality is low even when the skips are removed. The greater bandwidths will allow high-definition video. The development and large-scale supply of 100 Mbps is

the goal at which fast upload and skip-free digital video will allow the Internet to realize its potential and provide a technical experience approaching that currently contained in the DVD format.

The main problem for large-scale rapid utilization of broadband technology is the cost. The majority of users still rely on dial-up connections through their telephone lines and do not find available content to justify the increased cost. The user does not have a good reason to upgrade and providers do not have a significantly large audience to supply the incentive (i.e. content). As the high-speed technology advances (and become more cost-effective) it will allow full-screen interactive selection for more detailed study.

Internet 2 [13] is a consortium of providers that intends to construct a smarter and faster technology for education. It is composed of universities, industry, and government agencies committed to developing the provision and delivery of high-speed, high-quality educational content throughout the world (<http://www.internet2.edu>). Its goals are to:

- create a leading-edge network capability for the national research community;
- enable revolutionary Internet applications;
- ensure the rapid transfer of new network services and applications to the broader Internet community.

Networking centers have been established that allow high-speed communication through fiberoptic lines. It is anticipated that high-definition videostreams can be available on Internet 2. The breakthroughs already demonstrated with this technology gives hope that the Internet will realize its potential as the universal medium for e-learning.

Home television

One of the incentives of Internet e-learning is to transform the learning experience from being computer-oriented and make it a part of the home entertainment center. The technology available in game consoles and set-top boxes allows broadband connections, with subsequent downloading of video. It is anticipated that just as we have witnessed the emergence of topic-specific television channels for food and sport, the future of e-learning will allow the audience to “tune in” to a variety of technical video e-learning materials through a menu-on-demand system. The interactivity presently available in the DVD and Internet formats is just one step in that direction.

Teaching courses

Teaching courses exist in a variety of formats that include the use of electronic video media, small group observation of live cases in the endoscopy suite, and live

transmission by satellite or telephone lines to remote locations. These “programs” have proliferated throughout the world and are mainly attended by endoscopists wishing to upgrade their skills by observing experts in the performance of live cases. The discussions that have emerged as to which is the best method for upgrading skills is superfluous as these programs are complementary and synergistic. They should not be taken as the ultimate or only methods to gain the desired result. Each format has its advantages and drawbacks.

Video-based courses

The format that uses playback of highly edited video media (videotapes, CD-ROMs, DVDs) has been termed a “simulcast” production [14]. At present, videotapes are most commonly used for playback. These are usually professionally produced, allow selective views of both the endoscopist and ancillary personnel, and provide split-screen format for simultaneous endoscopic, fluoroscopic and endosonographic imaging. The “simulcast,” or attempted recreation of the live environment, is further enhanced by the presence of the endoscopist that performed the procedure. The on-disk narration by the endoscopist explains the procedure and is recorded at the time the procedure was performed. This narration is interrupted “live” by the endoscopist on site to emphasize, explain, or comment on a point. In addition, a “facilitator,” acting as a moderator and familiar with the tape, will interrupt the endoscopist at predetermined “stop points.” This allows a live interaction for both pre-selected and spontaneous questions in order to discuss an issue that is important to the procedure. The addition of “telestrator” technology allows the presenting (performing) endoscopist the opportunity to draw over the image for emphasis and to sketch diagrams over the image or on to a blank screen. The use of digital technology for filming and playback has further enhanced image resolution. When the program venue is provided with multiple high-resolution video monitors, the attendee experiences a “workshop” atmosphere that is intended to afford a detailed focus on the case performance. This atmosphere more closely simulates small group sessions.

Though video playback courses are highly technique focused, they do not fully reproduce the actual case. The editing procedure emphasizes what the medical editor wishes the audience to see and often leaves out decision-making concepts, technical troubles, or patient difficulties. Though a successful conclusion to a case is expected, some of the videotape material has been constructed to emphasize complications and technical difficulties. The “simulcast” production is an effective learning tool and should be considered synergistic to the “live” course format.

Live courses

The format for “live” courses ranges from small group teaching in the endoscopy room to programs involving hundreds of attendees in large auditoriums. Present technology allows simultaneous transmission to multiple environments of endoscopic and related images along with live video of the endoscopy suite and procedure performance. The intention is to allow the attendee access to the sounds and images of the local live environment coupled to the voiced instructional comments of the performing endoscopist, the ancillary personnel, and any added expert or moderator instructors. Expert-attendee interaction is stressed during the live procedure.

Small group sessions

This method is the traditional and logically the best method for learning from an expert. It provides an excellent opportunity for direct student-expert interaction as well as for observation of the assistants, room set-up, and use of the ancillary equipment. Its limitation is audience size. Expanding small group sessions to 10–20 attendees progressively dilutes the aims of small sessions. The logistics of space, access to video screens, and ability to provide one-on-one interaction dictates the size of the session.

Live transmission to remote sites

Many large, live video-transmitted courses exist throughout the world. The aim of this format is the same as for the others: to provide exposure of the technical and cognitive aspects of the endoscopic procedure in a learning manner. The success of these programs is measured primarily by the size of the audience in attendance and audience feedback. There have been no studies conducted attesting to their learning value compared with other formats. These programs are useful in introducing new techniques rapidly to large audiences and, like all the ancillary modalities, are not intended to replace one-on-one training.

One of the main advantages of the large group format is that it allows the gathering of multiple experts to share their knowledge and expertise both between themselves and with the audience. There is opportunity to see and compare individual nuances as well as discuss alternative approaches with the audience and assembled experts. These programs offer the best opportunity for participation in problem-solving, although the downtime for procedure performance often requires switching to another procedure, while decisions and techniques are made away from the audiences’ view.

Compared with the small group format, the audience is usually blocked from observation of the total case

experience. Interaction is decreased and downtime for set-up, procedure difficulty, and technical transmission problems can impose restrictions on the amount and quality of the educational experience.

The logistical and ethical aspects of this format have been questioned [15]. Opinions on the appropriate considerations in the use of all these formats for learning have been presented [14] and the ASGE has published a "white paper" addressing guidelines for the development of large courses [16].

It is important that issues concerning patient ethics and the performing endoscopist are addressed, e.g. patient safety, informed consent, use of cases within the expertise of the performing endoscopist, and demonstration of the highest standard of care. The educational goals and relevancy to practice should be reviewed before case selection. The technical arrangements for these programs should include multiple camera angles for transmission of the performance of the live procedure. Highly professional video teams are necessary for on-site presentation of both video images and case performance.

The costs of the presentation of large-scale remote transmissions are considerable. Whether these costs equal or exceed the cost of the edited video media format is unknown. The costs of participation are usually high to the attendee and often require additional expense such as transportation and hotel accommodation.

Telemedicine centers

A limited number of telemedicine centers have been developed that are involved in training and assisting in procedure performance or interpretation, usually within their own units. The outreach intramural technology has been demonstrated to be effective and to provide image and communication of adequate resolution for quality care and monitoring. Numerous improvements are certain to occur.

The problems of the telemedicine approach where real-time presentations can be sent to remote locations include the high costs of equipment, ancillary personnel, and communication time. There are medicolegal issues that need to be addressed and a multitude of technical issues yet to be resolved.

Summary

The cost-effectiveness of the electronic media is obvious. Though unreported as yet, it is hoped that these will be

an efficient method of upgrading learning while decreasing the high costs of producing live symposia and eliminating travel costs for conference attendees. The "live" endoscopic demonstration and the "edited" case version are not competitive but synergistic. The "live by simulcast" environment has its advantages particularly as an ancillary learning experience to on-site demonstrations, live conferences, and Internet streaming.

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Chapter 7

Teaching Colonoscopy

Robin H. Teague and Roger J. Leicester

Introduction

The first generation of colonoscopists were essentially self-taught. At that time there existed no guidelines as to how the technique should be carried out and most gained expertise by a process of trial and error. Learning under these circumstances required time, dedication, and immense enthusiasm to maintain improvement and exchange of technical information was essential. In this way the best practice of a small group of "experts" was disseminated among a select few and the technique gradually evolved.

The advent of population screening for colorectal cancer will mean an explosion in the number of colonoscopists required to meet the demands of this screening program. Our challenge for the 21st century is to fulfill the ongoing and increasing need to teach safe, accurate, and complete colonoscopy and accomplish this within a reasonable time limit by methods that involve structured and motivational training. The objective of any colonoscopy training course fellowship or program is to help doctors (or nurses) achieve a sustainable, greater than 90% cecal intubation rate combined with a careful inspection of as much colonic mucosa as possible. This has to be achieved in the context of patient comfort and the consideration of all aspects of safety and sedation. The initial training should be motivational and viewed as a springboard to the lifelong and sustained challenge of expertise [1].

Training units

The enthusiasm for structured training in colonoscopy is growing, but in order to be effective the units offering training must fulfill some basic criteria so that the standard of the finished product, i.e. the trainee, is uniformly acceptable and sustainable. In the early days of fiberoptic colonoscopy, teaching was performed via the lecture scope, which was difficult and cumbersome and often unacceptable to the trainer in terms of image and light quality. Televised endoscopy soon began to rectify these deficiencies, and modern-day video systems offer excellent image quality for all. We would recommend therefore that any unit considering offering training in

colonoscopy should be equipped with a video system and some method of video recording. Models and simulators are helpful in the early stages of the learning process and enable supervised and later unsupervised training to take place.

In order to maintain continuity of training the unit will require two or more trainers. Traditional training took place during service lists on the basis of "see one, do one, and teach one." This practice is now totally unacceptable and contemporary teaching demands that the trainer has one or two weekly sessions dedicated to the training process. Initially these training sessions will contain few patients, but as the trainee's experience increases, the number of patients can be expanded. Each unit should undertake at least 300 and preferably more colonoscopies annually, with an annual exposure of a minimum of 100 procedures per trainee and at least 200 colonoscopies performed in the first 2 years of training. Large units with more trainees will need multiples of these figures and shorter training programs will necessitate an increased annual exposure.

The teaching of any practical skill is heavily reliant on the team approach within the training unit. It is important to have at least one medical and one nursing leader who are the champions and advocates of the team. It is their responsibility to create shared values and a common purpose and to generate trust and respect both on an interpersonal basis and for evidence-based practice. The team needs to be flexible and able to embrace change to new practices seamlessly. There must be a commitment to the creation of a teaching and learning environment at every level, with routine feedback and appraisal. When these requirements are met, a palpable atmosphere of encouragement and expectation of success is generated and the training process becomes enjoyable and successful. Free exchange of faculty and staff between units will inevitably lead to an increase in the standard not only of training but of all aspects of colonoscopic practice within the region.

Trainees

Trainees in colonoscopy will come from different backgrounds, including physician gastroenterologists, in

surgeons, radiologists, and nurses. There will obviously be a wide spectrum of expertise, expectation, and motivation but it is most important that the individual trainee can demonstrate an ongoing commitment to lifelong colonoscopic expertise and that it is not seen as an amusing diversion on the way to some higher training in a different aspect of gastroenterology. There is no evidence in the literature that admitting trainees into colonoscopic training based on preselected criteria of aptitude has ever been attempted or evaluated. However, there is extensive literature involving medical and surgical trainees which indicates that complicated testing based on intellect, dexterity, motivation, stress tolerance and teamwork does not identify those who will become experts or those who will fail [2–5].

In every group of trainees there will be a minority who appear to be “natural” endoscopists and who learn quickly, but given time, almost all the group will arrive at an acceptable level of expertise with a very small percentage of failures.

It is important that, whenever possible, training is continuous as there is good evidence that failure or lack of opportunity to practice endoscopic skills soon results in their loss, so that breaks in training and practice should be minimized [6]. Motivation to gain expertise is obviously a very important factor in learning. It is most valuable when it is intrinsic (based on curiosity and a desire to meet challenges) rather than when it is extrinsic (driven by competition, examinations, or grades) when material retention is often short-lived. The challenge therefore is to make learning interesting and keep it relevant to the trainee’s needs.

Many training units will begin upper and lower endoscopic training concomitantly but others only embark on colonoscopic training after expertise in upper endoscopy has been acquired. There is no evidence that either method is particularly advantageous, although initial colonoscopic training is certainly much easier if basic instrument handling skills are already in place.

Basic Skills Colonoscopy Course

The UK Basic Skills Colonoscopy Course is a 3-day course with four sessions of one-to-one hands-on training. This special course was developed by gastroenterologists to increase the level of expertise and is provided in five centers across the country. There is a fee charged for all participants. The course is taught by a core group of volunteers, and is open to consultants and trainees in the greater community of gastroenterology, which includes colorectal surgeons, radiologists, and nurses. Four candidates are enrolled in each course and they each perform four colonoscopies over the four sessions with 1 h allowed for each colonoscopy on the training schedule. The first morning is devoted to instruction

in instrument anatomy, function, and decontamination and includes the indications, contraindications, and complications of colonoscopic technique and selected topics from the course handbook. The last session of the course is devoted to the organization of the endoscopy team and gives some insight into how an endoscopy unit can be run successfully. The trainees are recruited irrespective of previous experience during the obligatory 5-year training program for gastroenterology in the course of which they may attend the course more than once. We have found that the course benefits all levels of trainee expertise and the practical instruction is tailored in some part to the needs of each individual. The overall aim of the course is to introduce the candidates to a safe method of achieving a 90% cecal intubation rate. A predictable finding has been that trainees with the least experience make the most progress. Trainers are selected on the basis of enthusiasm to teach and teaching ability. All the trainers involved have attended specific “Training the Trainers” courses where there is intensive instruction in practical skills teaching. The trainers are then progressively assimilated into the program, initially attending the course as observers and then as occasional faculty. As occasional faculty they are observed by multilayer teaching, i.e. their training technique is observed by an experienced trainer and they take part in the debriefing process after each colonoscopy. Finally they are enrolled as faculty but remain under the guidance of the course director. In this way the initially small number of trainers has increased substantially over the past 2 years.

A course handbook is provided for each trainee and is sent out several weeks before the beginning of the course. Included in this package is a database diskette so that candidates can examine their cusum performance (see later) before and after completion of the course. Initial examination of cusum scores before and after the course has indicated a marked and sustained improvement in cecal intubation rates. There is no reason why generic introductory skills courses cannot be given “in house” at the start of the training program.

Basic information

Whichever way it is given, basic information and training should include the principles of safe sedation, indications for antibiotic prophylaxis, informed consent, and the theory and practice of diathermy. It is important that basic handling skills are taught and not acquired as this can lead to the development of poor technique at the inception of training. Once basic handling skills are in place the trainee can practice on simple models. Formal lectures and videos may have some value at this stage but the information is often delivered more poignantly (and better retained) as “mini” tutorials during the

course of practical teaching. This is especially true of therapeutic procedures such as biopsy, hot biopsy, and polypectomy, and the use of a video recording of the event allows focused reflection after the practical session [2].

It is a simple matter to record interesting pathology or complicated therapeutic techniques on video when the trainee is not physically present and then to review the procedure later within a dedicated session. If this culture is adopted by all colonoscopists within a unit, trainees soon become familiar with all the common and most of the uncommon findings and procedures. These home-made videos can be supplemented with examples of very unusual pathology/techniques derived from other centers or via the Internet. It is extremely important that trainee fellows keep a detailed log of their colonoscopic experience, which should include cecal and terminal ileum intubation rates, pathology encountered, and therapeutic procedures carried out. This provides a permanent record of their increasing expertise and experience.

Completion rates and cusums

As far as completion rates are concerned, we recommend that trainees keep a cusum-based record of their experience [7–9]. Successful completion can be assessed on an intention-to-treat basis but this is a harsh regime for the trainee and it may be reasonable to exclude “failures” in which an obstruction/lesion prevented cecal intubation. It may also be reasonable to claim that poor preparation was the reason for an incomplete examination, but all too often a less than optimal preparation is blamed when really the true culprit was poor technique. Whatever exclusions are made, the trainee should aspire to a sustained 90% completion rate. In order to chart this

as a cusum graph at a 90% level, each success is given a negative value of 0.1 and each failure a positive value of 0.9. The cusum is then plotted using the cumulative sum of successes and failures as the ordinate and the number of procedures as the abscissa. A more demanding graph can be plotted using a 95% completion rate, where each success is given a negative value of 0.05 and each failure a positive value of 0.95.

Depending on the intensity and expertise of the training provided, the novice's 90% cusum will usually rise steeply and then level out at between 50 and 100 examinations (Fig. 7.1). Steep rises indicate successive failures. Figure 7.1 shows that the first success occurred after 21 examinations and followed extra structured training given by an expert trainer. Thereafter there is an obvious improvement, with a plateau being reached after 54 examinations. A sustained plateau indicates that the cecum has been reached in 90% of cases, and failure to level out before 100 examinations usually suggests a need for more intense or more structured training. Rises subsequent to the plateau level being achieved may also require specific intervention with different training methods. The cusum is a valuable indicator of performance at all levels of colonoscopic expertise, and it is essential that all trainers keep their own cusum and examine it critically on a regular basis [10].

Trainers

Colonoscopy trainers should have expert knowledge of the technical and practical aspects of diagnostic and therapeutic colonoscopy. However, there are many expert colonoscopists who cannot teach and many mediocre colonoscopists who are expert teachers. This means that all aspiring trainers should be familiar with modern teaching methods and their applications. Just to

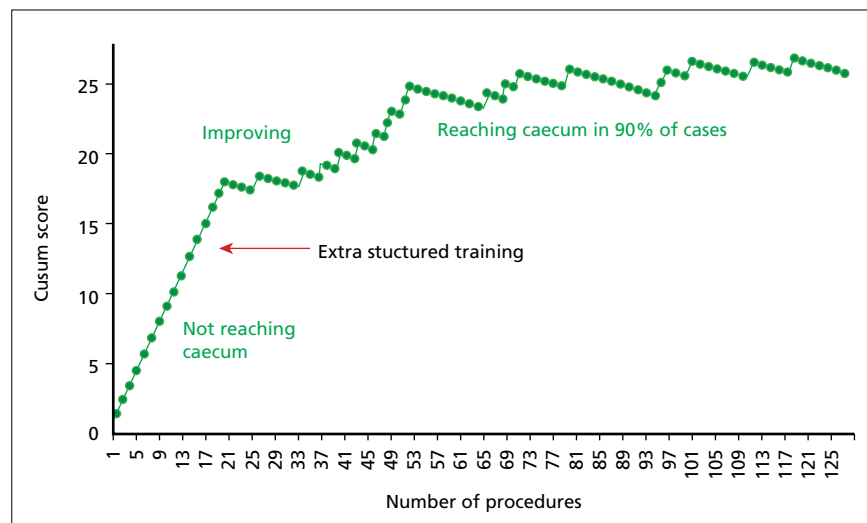


Fig. 7.1 Cusum plot of successive progress in colonoscopy completion rate. This provides a graphic representation of experience and can be constructed at any level of expertise.

have taught it “my way” for the last 15 years is simply not a good enough qualification for the 21st century. Many of these so-called expert teachers have never been subject to either peer review or trainee feedback, so that the value of their highly personalized methods has never been brought into question. We feel it is important that all trainers should at least have attended a “Train the Trainers” course and, better still, should have achieved some form of educational qualification.

It is relatively easy to describe the qualities that make a good teacher. First and foremost, teachers must have an intense desire to help their pupils learn whatever they are teaching. Secondly, they will adhere to basic principles and set specific objectives, especially in the early stages of training. Thirdly, they realize that endoscopic skills are multidimensional and must be patient and positive at all times. Lastly, and most importantly, they will give positive feedback and structured assessment.

It is essential that teachers are friendly and enthusiastic and that they are just as delighted as their pupils in the completion of a colonoscopy or a particular aspect of colonoscopic technique. Good teachers are team players and value their nursing and ancillary staff, often soliciting their opinions on particular aspects of the training process. It is important that the teachers themselves are subjected to regular and rigorous audit of their performance, which will include completion rates and time taken, patient comfort and complications, and the success or otherwise of their training methods.

It is recognized that not all endoscopists within a unit will want to be teachers but those that do should be encouraged to embrace modern teaching methods and their enthusiasm used for the good of all the trainees.

Almost all colonoscopy teachers will be experts and are therefore unconsciously competent (UC), whereas most trainees will be unconsciously incompetent (UI) (Fig. 7.2) [11]. Trainers must therefore retrace the steps of

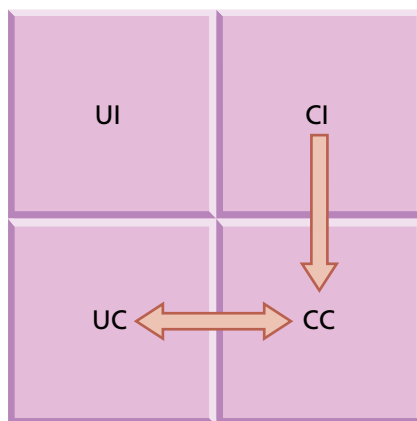


Fig. 7.2 Bridging the learning cycle. CC, conscious competence; CI, conscious incompetence; UC, unconscious competence; UI, unconscious incompetence.

their own expertise and become consciously competent (CC) in order to bring the trainee from conscious incompetence (CI) to conscious competence. This is a fundamental step in the teaching of practical skills. Trainers must ask themselves what they did to achieve a particular aspect of technique and what problems and alternatives there were that they took into account during their reasoning. They must then be able to verbalize the steps taken in order to communicate these to the trainee effectively. This requires practice and the teacher will recognize that there are some aspects of technique, particularly those where tactile recognition is paramount, that do not readily translate into verbal instructions.

Teaching methods

Basic instrument-handling skills can be taught on simple models or simulators. The increasing sophistication and realism of electronic simulators means that soon we will be able to teach rudimentary colonoscopic techniques without early recourse to patients. Simulators involving animals and animal viscera (realistic but perishable) are rapidly being overtaken by their computerized counterparts. Modern simulators may spare patients prolonged and painful procedures during early training and reduce the number of patient procedures during the learning process. They certainly allow reproducible practice and exploration of alternative approaches; with suitable software, sedation problems, pathology recognition, and therapeutic techniques can be added. The new generation of simulators can easily estimate the percentage of mucosa examined and the number of missed lesions, and if they achieve little else they teach the trainee to be cautious and assiduous on instrument withdrawal.

It must be recognized that whether the basic skills training is carried out on models, simulators, or patients, this must be on a one-to-one basis with the trainer. Letting a new trainee loose unsupervised with an expensive colonoscope on a sophisticated simulator or an unsuspecting patient is analogous to giving a 10-year-old child the keys to a new automobile.

Training sessions must be allocated dedicated time and freedom from service commitments. Interruptions must be kept to a minimum and sessions where either of the two parties is tired avoided. Idle conversation and irrelevant remarks that may be de rigueur when the trainer is endoscoping must be excluded when the trainee is under instruction. Acquisition of practical skills requires intense concentration for long periods so short breaks for coffee are essential and both parties must recognize the endpoint of fatigue and should not persist beyond this. When patients are involved, their comfort and dignity are of paramount importance and good communication with the patient will allay anxiety and minimize discomfort. We should all aspire to teach a

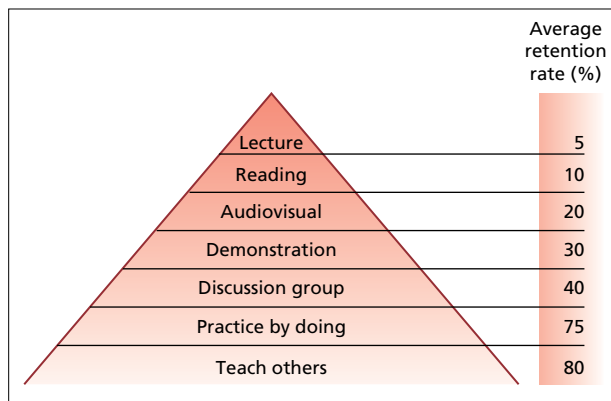


Fig. 7.3 The learning pyramid.

technique that provokes minimal discomfort so light sedation should be the order of the day, and under these circumstances the patient will often make a sensible and valuable contribution to the training process. The patient should understand that the procedure is to be used for training and specific consent must be obtained for this and for video recording.

Practice on models or simulators should have taught the novice torque steering and its importance in minimizing sigmoid looping. If the student is fortunate enough to have access to a modern simulator, some experience of the tactile recognition of loops may also have been gained, but from this point onwards most of the training will be carried out on patients.

The basis of any good coaching technique is the relationship between teacher and learner. The emphasis is on the expectation and encouragement of success, which is defined as reaching and exceeding personal objectives rather than competing with the peer group. Demonstration by the trainer with commentary is an invaluable introduction to the learning process. However, the retention rate is low (approximately 30%) (Fig. 7.3) and after the initial stages it should be used sparingly and for specific aspects of technique.

A tried and tested method in surgical practice over many years involves a four-part teaching process [11].

1 Demonstration by the trainer of the procedure at normal speed.

2 Demonstration by the trainer with full explanation and questions from the trainee.

3 Demonstration by the trainer with trainee describing each step and being questioned on key issues. The trainer provides any necessary correction and each step is continued until the trainer is satisfied that the trainee fully understands the procedure.

4 The trainee now carries out the procedure under close supervision, describing each key step *before* it is taken.

This method can be used in many situations during colonoscopic teaching, including torque steering, loop

reduction, cannulation of the ileocecal valve, and whenever the trainee encounters difficulty during the examination.

Attempting and completing a total colonoscopy is a source of considerable satisfaction to trainee and trainer alike. The trainer should give close support and advice but should avoid taking over the procedure if at all possible, the so-called “hands in pockets” philosophy. Fear of failure and humiliation, which is very common in novices and often accentuated by the presence of peers, is avoided by the behavior of the trainer and the unhurried atmosphere, together with the presence of experienced nursing and technical staff skilled in the support of trainees. The trainer offers frequent and prompt feedback, praising good technique and reiterating the correct procedure if the trainee errs.

If the trainee is unable to make progress, the trainer encourages a review of options, offering a choice of the most appropriate action rather than telling the trainee what to do. When the trainer requires a specific maneuver to be performed that the trainee finds difficult, the endoscope is withdrawn sufficiently for the trainee to attempt the move again after instruction, provided that the patient is not in excessive discomfort. Far too often the examination is carried beyond the point of difficulty by the trainer and the trainee takes over again without learning how to overcome the problem.

Inevitably, there will occasionally arise a situation where the trainee is totally unable to make further progress around the colon despite expert tuition. This is usually due to excessive patient discomfort, as in irritable bowel, or unexpected anatomic abnormalities, and the trainer has to take over and complete the examination. It is imperative that this is viewed not as failure but as part of the ongoing learning process and that the trainee is positively critiqued up to that point in the examination.

In the initial stages of training the use of the magnetic positional imager may be very helpful [12]. The imager allows trainees to make an association between what they feel on advancing or withdrawing the instrument and its actual configuration on the screen. The development of tactile discrimination is of vital importance in the recognition of loops and their avoidance and management. This experience cannot be imparted by verbal instruction and is wholly reliant on learned responses over many cases. Unfortunately the imager is not yet available for the vast majority of clinical practice, which means that teaching must still stress the need for an orderly pragmatic series of maneuvers to recognize and correct loops and to pass the colonoscope.

Although the tactile feel of looping cannot be verbalized, the end results of loop formation can. The trainee will learn to recognize that lack of one-to-one instrument advance, paradoxical movement, and patient discomfort

all signify that loops are present and that steps must be taken to reduce or avoid them. Maneuvers that accomplish this include torque steering, withdrawal with clockwise or counterclockwise rotation to straighten loops, changes of position of the patient, and abdominal compression. With increasing experience the trainee learns to recognize the feel of the instrument throughout these maneuvers and knows when and how to apply them.

Patient selection in the initial stages of training is extremely important in order to avoid the risk of failure as much as possible. Preassessment of patients is highly recommended to ensure that difficult cases do not slip through the net. This does not mean that only patients with sigmoid resection should be examined; but apprehensive patients and patients with previous abdominal and pelvic surgery or previously failed colonoscopy would also be sensible exclusions.

Postcolonoscopy discussion

Debriefing should take place immediately after each endoscopy and should adhere to the principles of positive critiquing. The trainee enumerates what went well and this is followed by the trainer's perception of the good points of the endoscopy. The trainee is then asked what could be improved and further commentary is added by the trainer. The importance of this 5–10 min interview immediately after the colonoscopy cannot be overstressed. Initially, almost all trainees are extremely self-critical and preoccupied with their failures, but the sensitive approach of positive critiquing means that they soon recognize that the trainer is sympathetic and working toward a common goal. In this way a close and valuable relationship is built up between the trainer and trainee, with feedback given on a regular basis and anticipated and welcomed [13].

During the initial stages of training, novices often benefit by watching their peers being taught on video link and may pick up valuable information that was not experienced during their own endoscopies. At the end of the session a group debriefing often encourages in-depth discussion of colonoscopic technique and does much to encourage group participation during a teaching course. There is increasing evidence that videoing the performance of trainees and subsequent playback and reflection may be extremely helpful in advancing the acquisition of practical skills. However, the process seems to have increased value when cueings are used at key points of the procedure by the trainer [2].

As a learner's experience increases, they can be exposed to the full range of diagnostic and therapeutic colonoscopy but the basic teaching principles will remain the same. Teaching is stimulating and provokes reflection on one's own practice and standards. If the

training ethos is accepted and welcomed throughout a region, standards of practice and training are invariably high.

Completion of training

Early recommendations for the completion of colonoscopic training involved only the number of procedures carried out. Fortunately, numbers are now recognized to be a fatuous indicator of colonoscopic competence and our recommendation is that trainees can be considered competent when they have carried out 100 consecutive procedures with a cecal intubation rate of 90% or more. This is easy to calculate using the cusum of their accumulated log of procedures [8]. However, it is worth noting that this may take some trainees as many as 400 or more procedures to achieve and a small proportion never manage it. Even when this level of competence has been achieved, we would recommend that teaching support should be withdrawn gradually (and not abruptly, which can have disastrous effects on the learning process). Trainers should therefore be present initially in an adjacent room, then within the hospital, and finally available by telephone. Difficult (and new to the trainee) therapeutic procedures require the trainer to be present at all times.

Completion of the examination to the cecal pole or terminal ileum is only one aspect of the acquisition of colonoscopic expertise. It must be stressed to the trainee that they should spend at least as long withdrawing the instrument as they did inserting it and that they should carry out a careful and as complete as possible examination of the mucosa. All too often after a difficult colonoscopy the time taken and relief at arriving at the cecum conspires to provoke a hurried and less than adequate inspection on the way out. All other members of the unit present during the procedure and who are not immediately concerned with the well-being of the patient (other doctors, nurses, etc.) should be encouraged to watch the procedure and comment critically on missed pathology or areas of mucosa that were not adequately examined. Nobody is perfect and four pairs of eyes are always better than one. Safe and comfortable endoscopy must be taught hand in hand with high completion and accuracy rates so that at the end of training the new colonoscopist has a sensible and comprehensive knowledge of the technique and its advantages and shortcomings.

Assessment

Assessment and feedback are inseparable and are applied from the outset in the initial stages of colonoscopic training. Selected and agreed criteria can be used at any stage, i.e. at the end of a training session, at the

ASSESSMENT FORM FOR THE BASIC SKILLS IN COLONOSCOPY COURSE		
Trainee: Course dates: Centre: Scale: 3–no errors observed; 2–occasional errors, but corrected by the participant; 1–frequent errors or occasional errors uncorrected by the participant; 0–persistently unsatisfactory performance		
Criteria	Grading	Comment
Endoscope handling <ul style="list-style-type: none"> • Correct position of the left hand and appropriate use of air/water and suction valves. • Appropriate use of the angulation control knobs. • Understands the principles of torque steering. • Uses correct procedure to check the endoscope function before intubation. 		
Patient communication <ul style="list-style-type: none"> • Obtains informed consent using a structured approach. • Demonstrates awareness of patient's consciousness during the procedure. • Demonstrates awareness of patient pain. • Communicates results of the procedure to the patient clearly. 		
Safety and sedation <ul style="list-style-type: none"> • Gives appropriate dose of analgesia and sedation. • Ensures adequate oxygenation and monitoring of patient. • Demonstrates awareness of endoscopy assistant's concerns and recognition of their roles as team members. • Demonstrates awareness of safety issues in relation to sedation and endoscopic procedures. 		
Specific skills <ul style="list-style-type: none"> • Gentle insertion of colonoscope. • Recognition of luminal direction. • Torque steering. • Uses appropriate inflation of the colon. • Uses suction appropriately. • Recognises loop formation. • Performs logical approach to loop resolution. • Achieves caecal intubation. 		
<p style="text-align: center;"><i>Please note that this form is designed to provide trainees and their endoscopy tutors with feedback on individual performance and guidance for future practice. Signed;</i></p>		
Trainee		Date
Clinical supervisor/trainer.....		Date.....

Fig. 7.4 Assessment form for Basic Skills in Colonoscopy Course.

end of a skills course, or at the completion of training. The UK Basic Skills Colonoscopy Course applies 21 criteria within four domains (Fig. 7.4), with a scale of competence from 0 to 3. A score of 0 indicates persistently unsatisfactory performance, a score of 1 indicates frequent errors or occasional errors uncorrected by the participant, a score of 2 indicates occasional errors cor-

rected by the participant, and a score of 3 means no errors observed, giving a possible maximum score of 63. The four domains are those of endoscope handling, patient communication, safety and sedation, and specific skills. These can be discussed and agreed before the start of any course or session so that the trainee shares and owns the criteria for their own assessment. On the basic skills course we are, at present, using the assessment form after the first and the last case so that improvement, or lack of, can be demonstrated to the candidates.

Summary

Using structured criteria for assessment means that trainees can readily see their advancement (or lack of) within the technique and, in conjunction with the trainer, can identify and correct deficiencies almost as they occur. The method also enables a very small minority of trainees who are unable to complete successful training to be identified early and excluded with mutual agreement.

In this chapter we have attempted to describe how a novice can be taught to perform the technique safely, accurately, and comfortably with a high rate of cecal intubation. This sensible and structured approach to the problem should ensure that we are ready and able to meet the challenges of the 21st century.

Remember that today's trainees are tomorrow's colonoscopists and today's trainers may be tomorrow's patients, so take training seriously and do it properly.

Acknowledgments

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Chapter 8

Role of Simulators in Endoscopy

Simon Bar-Meir

Introduction

The concept of a simulator as a training tool is well established, notably in aviation training [1]. Simulators are being used to train new pilots and for the annual accreditation of experienced pilots. Training pilots on simulators is both safe and inexpensive, providing the ability to react quickly and precisely in a safe environment in order to avoid errors in actual flight that may be critical and cost lives. It is increasingly feasible for simulators to be used for training in the medical field as well. Advanced simulation technology has been introduced into medicine in several fields, such as laparoscopy [2], cardiology [3,4], and anesthesiology [5,6].

Performing an endoscopy requires skill and training. For each procedure there is a minimum number needed to achieve competence, ranging from 100 to 300 procedures for esophagogastroduodenoscopy, colonoscopy, and endoscopic retrograde cholangiopancreatography (ERCP) [7–10]. Tassios and colleagues showed that between 100 and 180 procedures had to be performed for the learning curve of colonoscopy performance to reach a plateau [9]. Cass and colleagues reported that 140 colonoscopies are required in order to achieve a 90% success rate of cecal intubation [10]. In another regression analysis of all studies that reported the success rate of cecal intubation as a function of the number of colonoscopies performed, it was determined that 341 colonoscopies were needed to reach a 90% success rate of cecal intubation [11]. It is clear that a long period of supervision is required before the trainee achieves an acceptable level of competence. However, in this period of increasing colonoscopic utilization, many supervising endoscopists find that they have insufficient time to properly proctor trainees. An endoscopic simulator that partially decreases the need for hours of one-on-one teaching would therefore be of value.

Types of simulators

Historically, the first endoscopic simulators were mechanical and designed for use with the semirigid upper intestinal gastroscopes. Particular interest has currently focused on flexible sigmoidoscopy and colonoscopy

[12,13]. The various models have ranged from a simple slide projection system to rubber models of the colon. In 1974 Classen and Ruppin [14] developed an anatomically shaped plastic dummy of the gastrointestinal tract. About the same time, Williams and associates [15] used the spiral metal reinforced tube of a hair dryer for colonic simulation (Fig. 8.1). None of these mechanical simulators gained popularity and all have been abandoned. The most advanced mechanical model available at the present time has been developed by the University Hospital of Tübingen [16]. This simulator consists of a realistic anatomically correct phantom in dimension, color, structure, and sensation (Fig. 8.2). It permits the simulation of all diagnostic and most of the therapeutic endoscopic interventions. The acceptability of this

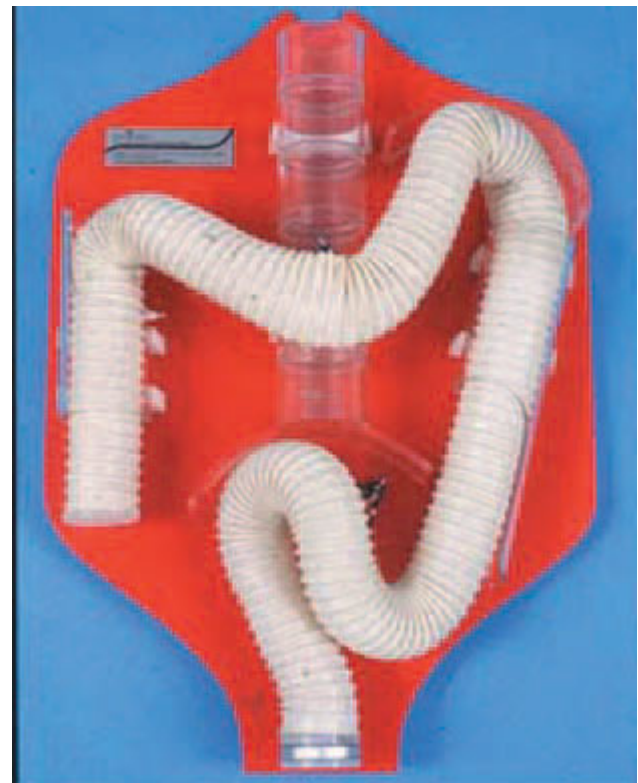


Fig. 8.1 Mechanical simulator for colonoscopy. (Courtesy of Dr Christopher Williams.)



Fig. 8.2 Tübingen model.

model is related to an artificial tissue, Artitex, which has a wax-like consistency and can be shaped as needed. It can be manipulated and molded to resemble various pathologies such as strictures, polyps, and tumors. It is also possible to perform electrosurgical interventions such as polypectomy, ablation of a tumor with either laser or argon plasma coagulator, and stent deployment. Modules for upper gastrointestinal endoscopy and ERCP together with sphincterotomy are also available. The characteristics of the artificial tissue and its behavior under electrosurgical energy make it an ideal model for therapeutic procedures. In this simulator, the force feedback during endoscopy and the behavior of the gastrointestinal tract during insertion of an upper endoscope or colonoscope are different from that experienced during a real procedure on a human patient, which makes it less valuable for training in diagnostic procedures or for practice of technique. There is no interaction between the trainee and the simulator so the presence of a supervisor is required. The Tübingen simulator is not for sale and current policy is to make it available for workshops only. The cost of such a workshop is about \$7000; for workshops outside the University of Tübingen, a technical team accompanies the model.

Animal models are the most realistic simulations but require continuous search for animals and ethical objection is likely to limit their availability. For these reasons models such as the exteriorized dog colon, used for colonoscopy [17], failed to gain popularity. Exceptions are the two Erlangen models (Fig. 8.3) known as EASIE (Erlangen Active Simulator for Interventional Endoscopy) and the Erlangen Endo-Trainer, in both of which the gastrointestinal tract and pancreaticobiliary system are obtained from slaughtered pigs [18–20]. The ethical issue is eliminated because the pig's gastrointestinal tract is obtained from the slaughterhouse, where the animal is killed for the supply of meat. In the Erlangen

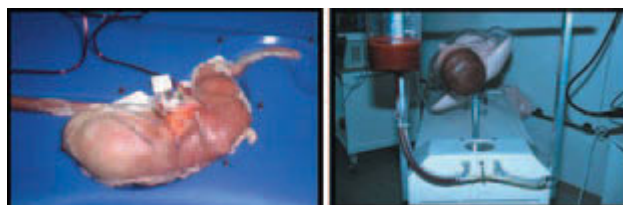


Fig. 8.3 Erlangen models.

Endo-Trainer, the upper or lower gastrointestinal tract is installed on a plastic structure shaped like the human organ. An ingenious perfusion system generates realistic bleeding episodes that respond to therapeutic intervention. Both Erlangen models allow the performance of most of the gastrointestinal procedures in a realistic fashion, very similar to the human environment. They are more adequate for training on therapeutic procedures than for endoscopic intubation or practice of technique. Procedures such as polypectomy and hemostatic procedures (coagulation and clips) are easily performed.

The Endo-Trainer can be purchased for about \$5500, whereas EASIE is not available for sale but can be used in courses conducted in Erlangen for \$300 per person, with a firm recommendation to have both the physician and nurse undergo training at the same time. Gastrointestinal organs such as stomach and colon (with the appropriate connections to blood vessels, for bleeding episodes) are for sale at approximately \$100–200. The organs are prepared and shipped frozen and can be kept for long periods before being used.

More recently, computer-based simulators have become available [21,22]. Their biggest advantage is their availability for training with no need for previous preparation. Once activated, training may start immediately. Computer-based simulators are constructed as a three-dimensional geometric model. Texture of the gastrointestinal tract is transferred via videotape from a real endoscopic procedure as one of a variety of computer manipulations. Built into the systems are both global and local deformity, i.e. a change in the configuration of either the entire gastrointestinal tract due to insertion of

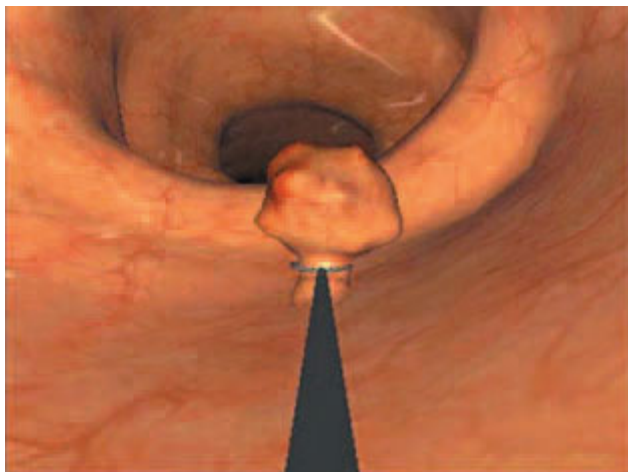


Fig. 8.4 A snared polyp of the colon as seen on the GI-Mentor.

the endoscope or only the gastrointestinal wall due to local pressure by an endoscope or accessories. Sensors on the endoscope continuously transmit its location to a computer, which displays the information on a monitor. Insertion of the endoscope is associated with a sensation of resistance (force feedback) in an attempt to resemble the tactile experience of intubating a human subject.

Presently, there are two computer-based simulators of the gastrointestinal tract: the GI-Mentor, which was developed by Sionix (Tel-Hashomer, Israel), and the AccuTouch, which was developed by Immersion Medical (Gaithersburg, Maryland, USA). Both companies use real endoscopes; Sionix uses a modified Pentax endoscope whereas Immersion Medical has spe-

cially designed an endoscope very similar to a real one. Both of these simulators allow steering and torque of the endoscope, which also has suction and inflation buttons. Both devices provide trainees with sensations that mimic an actual endoscopic examination, using modules for sigmoidoscopy, colonoscopy, and ERCP (Figs 8.4 & 8.5). Each module contains several cases that start with a history, including laboratory work-up and imaging studies, to allow the trainee to assess the appropriate management of the condition prior to practicing the endoscopic procedure. Upon completion of a tutorial session, instructors can view the recorded events. Comments can be entered in the trainee file and special notes can be sent to the trainee using a message facility. An optional Internet connection allows instructors to connect to the simulator from any remote location and assign programs or send messages in real time from any location in the world.

The Sionix basic platform costs \$15 000, with an additional \$5000 for either a straight-view endoscope or a side-view endoscope. There is an additional cost of approximately \$10 000 for each of the modules consisting of 20 cases. Immersion Medical charges \$30 000 for the platform and the endoscope and approximately \$20 000 for the lower gastrointestinal endoscopy module. Both simulators are continuously updated and new modules are being added.

There is a need to prove that learning to perform endoscopy on simulators will decrease patient discomfort and increase safety. At present, the value of teaching on simulators is based on impressions gained during workshops and on some very preliminary studies. These

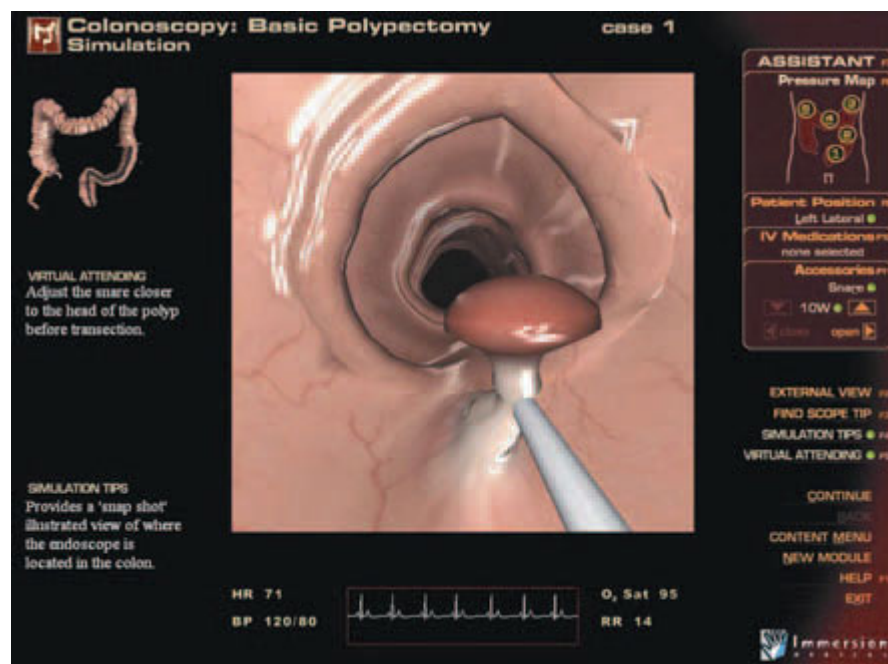


Fig. 8.5 Polyp of the colon as seen on the Immersion Medical simulator. The polyp is snared and ready to be resected.

studies have insufficient trainee enrolment and the evaluation of skill is performed on a simulator rather than on patients.

An initial impression of the GI-Mentor was obtained during two workshops held in 2000 in Nice and Hamburg [21], where 71 gastroenterologists with experience in performing endoscopy for more than 1 year worked on the GI-Mentor and answered an evaluation questionnaire. The responses showed that 96% felt that the simulator met their expectations and 83% considered that it would be advantageous to train in an institution where such a simulator exists; 81% would use the simulator in their next training program, if available, and 90% felt that prior training on the GI-Mentor would reduce the potential risk of complications to patients. The simulator was considered friendly by 97%, and 88% will recommend it to others. Similar results were reported by Aabakken and colleagues [23] from the annual SADE course, where the usefulness of the simulator was rated highest by the least experienced participants.

The first study to assess the value of a simulator in teaching endoscopy compared the performance of five residents in a control group and another five who served as an experimental group [24]. The latter group trained on a simulator for 6–10 h before performing their first sigmoidoscopies on volunteers. The experimental group achieved significantly faster insertion time (211 vs. 518 s) and a shorter mean length of examination (323 vs. 654 s) and visualized a higher percentage of colon (79 vs. 45%).

In another study [25], fellows were divided into two groups of 11 each. The first group served as a control and the second group had 10 h training on a simulator. All fellows were asked to perform 20 upper gastrointestinal endoscopies on patients under tutoring. The group trained on the simulator required 18% less time to perform the procedure, 30% less assistance by the tutor, and missed 8% less lesions.

Ferlitsch and colleagues [26] compared the performance of beginners and experts using the GI-Mentor. Without prior simulator training, experts performed better during an upper gastrointestinal endoscopy with regard to insertion time, correct identification of pathology, less adverse events, and better retroflexion. Training on the simulator for 3 weeks abolished the difference between beginners and experts. The conclusion to this study was that the simulator is able to identify experts and to improve the performance of trainees. Sedlack and Kolars [27] showed similar findings using the Immersion Medical simulator. Scores obtained on the simulator permitted differentiation between the performance of staff, fellows, and residents, with better results (less time to perform the procedure and more of the surface visualized) by those with more experience. Datta and colleagues [28] confirmed previous findings and showed that the Immersion Medical simulator was

a valid discriminator of flexible sigmoidoscopy experience, permitting numerical distinction between novice, intermediate (5–50 examinations), and trained (> 200 examinations) endoscopists.

In a controlled trial on five patients performed by Gerson and Van Dam [29], the traditional bedside teaching method turned out to be superior to training on the simulator. This study evaluated the performance of flexible sigmoidoscopy by trainees trained only on the simulator compared with a group instructed in the traditional fashion. Subjects in the simulator arm had more difficulty with initial scope insertion and negotiation of the rectosigmoid junction. The splenic flexure was reached by 87% in the traditional arm compared with 62% in the simulator arm ($P = 0.02$). The average time per procedure was 24 min in both groups. Patient satisfaction and discomfort associated with the procedure did not differ between the two groups. Although the teaching group achieved better results, it is not clear whether a combination of traditional and computer simulation training would reduce teaching time and improve performance.

The Mayo Clinic in Rochester, Minnesota has established a first-year training program based on the computer-controlled colonoscopy simulator [30]. Performance variables measured by the simulator include time to complete the procedure, distance the scope was advanced, degree to which the mucosa was adequately visualized, possible complications such as perforation, and level of pain experienced by the simulated patient. Based on calculation of the average performance of novice, partially trained, and “expert” faculty colonoscopists, the researchers were able to estimate the minimal performance standards for new trainees. The curriculum consists of a 1-h multimedia tutorial, followed by 9 h of simulator training (to include 25 colonoscopies). Performance of patient-based colonoscopy as well as surveys of patient satisfaction will be measured and analyzed to determine what, if any, benefits are provided by the simulator.

Summary

The introduction of endoscopy simulators will change the preliminary aspects of endoscopy training. This is due to multiple factors, including the limited time of supervising physicians, but most important is the ability to gain familiarity with the basic steps of the endoscopic procedure without inconveniencing a human subject. Training on simulators can facilitate the required eye–hand coordination, the repetitive steps necessary to learn the technique, and the acquisition of knowledge about some of the decision processes needed to perform colonoscopy. Simulation teaching has advanced considerably in the past decade, but more sophisticated

apparatus will further enhance the attractiveness of this emerging field. In addition to basic training, simulators may be useful in credentialing and re-credentialing endoscopists at intervals during their career. Based on simulators already available, the increased public awareness of medicolegal aspects, and the limited time of supervising physicians, endoscopic training will be changed. Trainees will start their training on a computer-based simulator. More advanced training in therapeutic procedures will be obtained with the computer-based simulator first and the Erlangen and Tübingen models later. Such training will most probably be integrated into large training centers.

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Chapter 9

Continuous Quality Improvement in Colonoscopy

John B. Marshall

Introduction

One of the most important movements in American healthcare delivery in recent years has been the emphasis on measuring and improving the quality of patient care. In 1988, Arnold Relman, editor of the *New England Journal of Medicine*, stated that the American medical care system was entering a new era of assessment and accountability that he predicted would be the “third revolution in medical care” [1]. A number of factors have helped to drive this movement: (i) concerns about rapidly escalating healthcare costs; (ii) increased competition among healthcare providers; (iii) concerns about regional variation in the use of procedures without discernible differences in health outcome; (iv) concerns about the quality of care by healthcare payers, accrediting agencies, and consumers in an era of cost control; and (v) the incorporation of information systems into clinical medicine [2–8]. To help address these various concerns, the outcomes movement emerged as a way to measure the quality of patient care and to improve quality by identifying the most effective and efficient use of limited resources and integrating these into practice guidelines [2,6,9,10].

In the clinical practice setting, the quality and appropriateness of care are now routinely evaluated objectively and systematically to detect areas in need of improvement (“opportunities”). The intent is to then identify measures to correct problems and concerns, and finally to reevaluate the issue to determine objectively if the desired results have been achieved. This process is called “continuous quality improvement” (often abbreviated CQI); the ultimate purpose of this process is to continuously improve patient care.

The CQI model differs from another approach that has been commonly used as a means of improving American healthcare, which primarily focuses on inspecting, making measurements, and then attempting to identify outliers (“bad apples”). This second approach was the basis of many of the “quality assurance” (QA) programs in the 1980s and early 1990s of which physicians were a part. As stated by Berwick, “when quality is pursued in the form of a search for deficient people, those being surveyed play defense” [11]. The improvements in quality

which can be expected from this system of “surveillance and discipline” (or “surveillance and judgment”) appear to be modest [11]. In contrast, with a CQI model the emphasis is on learning, improving processes, and cooperating with workers. One authority summarized the difference between the two approaches to improving quality by this statement: “The emphasis of QA seems to be on dealing with outliers rather than on changing the process [the CQI approach]” [12].

Quality improvement studies can provide risk-adjusted outcomes that permit physicians, practices, and hospitals to compare their performances with their peers. This is not to punish poor performers but rather to provide the data necessary for quality improvement [13]. In addition, in the CQI model, all the steps in providing a particular kind of care can potentially be studied in detail to look for problems and areas needing improvement. The CQI approach does not seek to identify errors and problems in order to assign blame, but realizes that faulty systems of care are more often responsible for problems. It is believed that fixing systems is usually more effective in correcting problems than punishing people [13].

Given the high volume and cost of gastrointestinal endoscopic procedures in the USA, it should not be surprising that this field has come under the scrutiny of the quality and outcomes assessment movement. An estimated 4.3 million colonoscopies were performed in the USA in 1999 [14], making it one of the most commonly performed medical procedures. This number is expected to increase rapidly given the increasing awareness of colorectal cancer as a public health problem, and the availability of reimbursement for screening colonoscopy for Medicare beneficiaries since July 1, 2001 [14]. Though research in this field is limited, there is also increasing evidence to suggest that the quality of performance of colonoscopy varies in clinical practice [14]. A few examples include the varying rates of total colonoscopy based on type of training and experience, differing sensitivity of colonoscopy for the detection of colorectal cancer between gastroenterologists and nongastroenterologists, varying sensitivities between gastroenterologists for detecting colonic adenomas, and differing miss rates for adenoma detection

depending on the technique of colonoscopic withdrawal [14–19].

Why is it important for the practicing endoscopist to have some understanding regarding the outcomes movement and CQI? While acknowledging that these are fields about which we have much to learn, the most important reason is that these tools can be useful in promoting high-quality endoscopic practice and care, and to see that we are getting the “most bang for the buck” from our limited healthcare dollars. In addition, accrediting agencies require demonstration of properly functioning CQI programs in their evaluation of hospitals and ambulatory endoscopy centers. It is important for practicing endoscopists to be in the forefront in the development of practice guidelines and in the process of CQI. A recent American Society for Gastrointestinal Endoscopy (ASGE) clinical practice guideline stated that the

attention to quality must extend to the individual practitioner to ensure that patients’ interests are preserved. As providers of health care, practicing gastroenterologists need to take an active role in these efforts in both understanding and implementing the techniques of outcomes and quality assessment into their practices . . . If gastroenterologists are not actively involved in data collection and measurement to improve the quality and value of their own work, it is likely that someone else will assume this role [8].

Another author stated: “Although health plans and insurers may emphasize lowering costs, physicians are in the best position to make the case for improving quality” [13].

In the USA, the ASGE has taken a leading role in advancing the field of outcomes research relating to gastrointestinal endoscopic procedures, such as the development of specific quality indicators relating to endoscopy [8], the development of numerous practice guidelines, and the creation of the Clinical Outcomes Research Initiative (CORI), which systematically collects endoscopic data from diverse practice sites in the USA [20,21]. The ASGE has also prepared several important documents to specifically assist hospitals, outpatient endoscopy centers, and endoscopists in establishing a process for quality improvement in endoscopic practice [8,22,23]. Another important article for the practicing colonoscopist is a 2002 publication on the topic of quality in the technical performance of colonoscopy and the CQI process for colonoscopy [14]. It was developed and written by the US Multi-Society Task Force on Colorectal Cancer, comprised of representatives of the American College of Gastroenterology, the American College of Physicians–American Society of Internal Medicine, the American Gastroenterological Association, and the ASGE. But let it also be stated that the outcomes move-

ment relating to endoscopy is certainly not limited to the USA, with numerous important contributions coming from elsewhere, particularly western European countries, Canada, and Australia.

This chapter includes an overview of quality, outcomes research, outcomes management, and CQI; a detailed treatment of CQI relating to gastrointestinal endoscopy practice, including practical suggestions for implementing such a program; and a discussion of quality indicators and targets specific to colonoscopy that can be incorporated into a CQI program.

Overview of quality, outcomes research, outcomes management, and CQI

It is important that endoscopists are familiar with the concepts of quality, outcomes research, outcomes management, and CQI. A brief overview is provided here.

The Institute of Medicine’s definition of quality of healthcare is that it is the “degree to which health services for individuals and populations increase the likelihood of desired health outcomes and are consistent with current professional knowledge” [24]. As has been emphasized by the Joint Commission on Accreditation of Healthcare Organizations (JCAHO) and others, there are two dimensions to quality: first, “doing the right thing” and, second, “doing the right thing well” [5,10,25]. The former refers to high-quality decision-making (e.g. the appropriateness of the services provided), the latter to high-quality performance (e.g. skill, timeliness, safety, respect, and caring).

While quality has traditionally been defined simply in terms of care provided by practitioners and received by patients, modern perspectives acknowledge that quality of care must be responsive to the preferences and values of the consumers of healthcare services, particularly patients, but also including healthcare organizations and plans as well as organized purchasers of healthcare services [24]. In addition, patients and purchasers of healthcare want to know more about the quality of care available to them [26]. The quality of care can be measured at various levels, from the care provided by doctors and nurses to the care provided by a healthcare plan. One of the challenges we face in this regard is finding the best ways to measure quality of care. Brook and colleagues [26] have stressed that we must only use indicators “for which we have sound scientific evidence or a formal consensus of experts that the criteria we are using do indeed, when applied, lead to an improvement in health.”

Outcomes research can be defined as the systematic study of the effectiveness of medical interventions in everyday clinical practice [3,7,9]. In addition to measuring clinical endpoints, outcomes studies may also assess the effects of interventions on quality of life, func-

tional status, patient satisfaction, and costs of medical care.

While outcomes research may ask many of the same questions and employ similar research methods as traditional clinical research, there are important differences as well. For example, outcomes research is often observational and only occasionally uses randomized controlled trials. Observational studies often involve the use of large computerized administrative databases involving thousands (or even hundreds of thousands) of patients, which can provide data on parameters such as mortality, length of hospital stay, resource utilization, and costs. Not infrequently, the data were collected for purposes other than research, though this is not always the case. For instance, with the ASGE's CORI project, endoscopic procedure report data from diverse practice settings are sent to a central data repository for later research analysis. Several western European countries have remarkable country-wide databases that monitor many facets of healthcare and which are well suited to outcomes research.

In addition, outcomes studies, including those that involve controlled trials, have less strict entry criteria and involve patients with a wider spectrum and severity of illness than in traditional clinical research. When using such nonrandomized study designs, consideration must be given to the influence of patient factors, such as the severity of illness and presence of comorbid illness.

Also, importantly, outcomes studies generally examine issues of effectiveness (whether an intervention works in real practice settings) and efficiency (whether an intervention is worth the cost), rather than efficacy (impact of an intervention tested in a strictly controlled research protocol). It has become apparent over time that efficacy does not always equate with effectiveness and, further, that an intervention that is effective is not always worth the cost.

As the field of outcomes research evolves and becomes more sophisticated, more scientifically rigorous trials are being conducted, although they are called "effectiveness trials" [10]. In contrast to the classic randomized controlled trial, effectiveness trials are less restrictive in terms of the practice setting in which the study is carried out and involve a more heterogeneous study population. This can help to make the results more applicable to community hospitals and physicians.

The explosion of scientific information in medicine has necessitated new approaches to collecting and analyzing these data, and synthesizing them with expert clinical judgment, in order to give clinicians useful advice [13]. One of the most important aspects of outcomes research is the development of clinical practice guidelines that help define optimal patient management strategies [6,9,10]. Other terms for practice guidelines

found in the literature include standards of practice, standards of care, and clinical pathways [25]. This "evidence-based approach" involves a careful review of the scientific literature, including the results of available outcomes studies. The steps involved in the development of an evidence-based practice guideline have been outlined by Johanson [9]. Practice guidelines have been shown in randomized trials to improve the process and outcomes of patient care, especially when combined with other methods of communication, such as feedback on performance and education by respected peers [13].

Outcomes management can be defined as the use of disease guidelines in routine clinical practice [10]. Guidelines can be applied to large patient populations or individual patients or physicians. In either case, the outcomes of specific interventions can be studied by the CQI process. The guidelines themselves will be refined over time as more data become available. The interrelationship between outcomes research, outcomes management, and CQI is illustrated in Fig. 9.1 [4].

The concepts of CQI, initially developed by Shewhart, Deming, Juran, and others, were first successfully applied to the Japanese manufacturing sector after World War II [11,27–29]. According to the theory of CQI, "real improvement in quality depends on understanding and revising the production processes on the basis of data about the processes themselves . . . [It is] the continuous search for opportunities for all processes to get better" [11].

In essence, the process of CQI first identifies (diagnoses) a problem. It then gathers data about the problem and the processes, which are then analyzed to suggest what caused the problem. A corrective intervention (treatment) is planned and performed. One then goes back and assesses whether the intervention was effective [28]. This cycle, illustrated in Fig. 9.2, is repeated as necessary. An important element of a successful CQI program is "a managerial philosophy that favors a supportive organizational structure and culture and the widespread use of scientific methods of process understanding and enhancement" [30]. This process improvement model has now been applied to the healthcare industry and is an integral part of the "third revolution in medical care" described by Relman [1].

The continuous cycle of steps in continuous performance (quality) improvement as defined by the JCAHO can be summarized as follows [25].

- 1 Leaders of organizations should establish a planned, systematic, organizational-wide approach to process design and performance measurement, analysis, and improvement. Collaborative, interdisciplinary planning of activities is encouraged.

- 2 Data are collected to monitor performance and to identify opportunities for improvement.

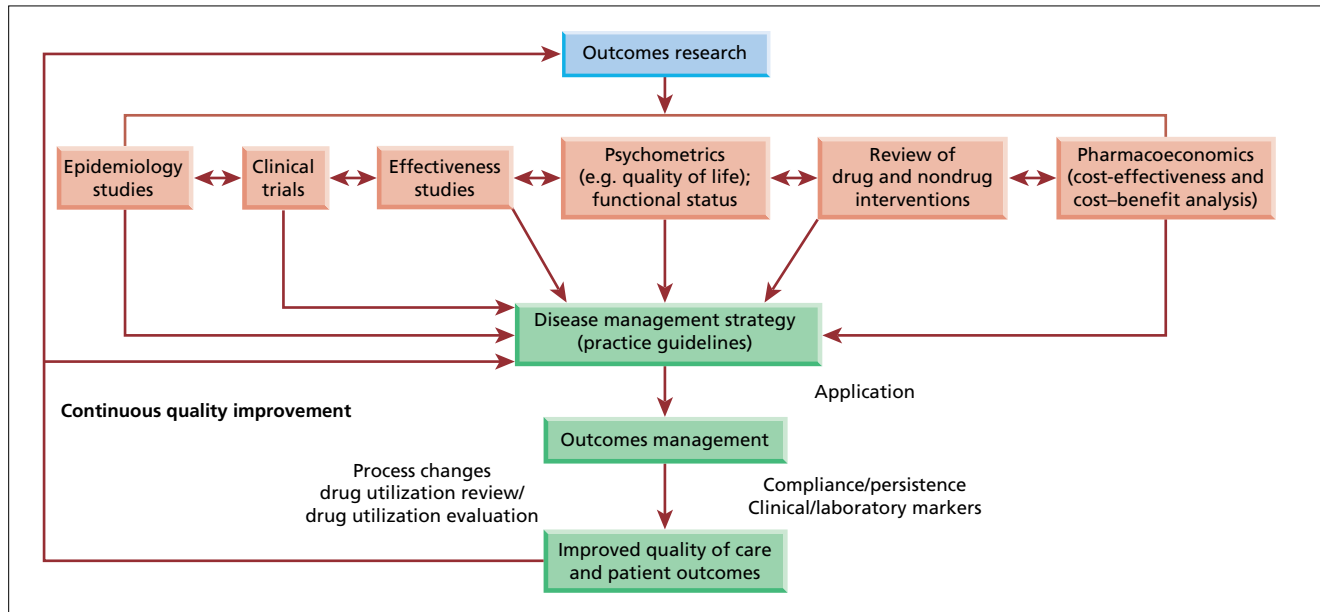


Fig. 9.1 Interrelationship between outcomes research, outcomes management, and continuous quality improvement. (From Epstein and Sherwood [4].)

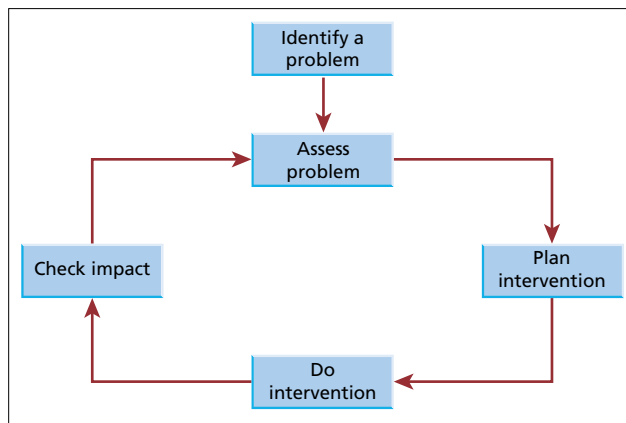


Fig. 9.2 Process improvement cycle. (From Champion and Rosenblatt [28].)

3 The information is analyzed and used to draw conclusions about outcomes. The organization should compare its performance over time and with other sources of information. Undesirable patterns of performance and sentinel events are analyzed intensively. (The JCAHO defines a sentinel event as “an unexpected occurrence involving death or serious physical or psychological injury, or the risk thereof. The event is called sentinel because it should send a signal or sound a warning that requires immediate attention” (25).)

4 Changes are identified and implemented that will lead to improved outcomes.

5 Performance is remeasured to help determine the effectiveness of the change and whether additional

changes are needed. Improved performance should be achieved and sustained.

There is widespread enthusiasm for CQI in the health-care field. A fundamental question is whether and how it works. A recent review of the topic cogently summarized the theoretical arguments and empirical evidence for it as follows:

There is no certainty that a continuous improvement program at a given institution will enhance quality for the patient and the providers and reduce costs for all concerned. If CQI is managed properly, however, it can and will provide such benefits. The challenge is to design, implement, and lead a CQI effort that is successful for a given institution. It also is clear that such a program is essential to survival in the current regulatory and competitive climate [31].

CQI of gastrointestinal endoscopy

The ultimate goal of an endoscopic unit’s performance is to continuously improve patient health outcomes. An important and expected element for maintaining and improving endoscopic practice entails an active program of CQI. Such a program should objectively and systematically evaluate and monitor the quality and appropriateness of care, identify opportunities to improve care, institute a corrective plan, and then remeasure quality indicators to show that outcomes are in fact improved [23]. Programs are expected to have written plans that describe their objectives, organization, governance, responsibilities, activities, and the processes they use [23]. Increasingly, endoscopists and endoscopic practices are being expected to provide documentation to patients and other purchasers of healthcare services of

the quality they provide [8,26]. Cotton [32] has forcefully argued that we owe our patients this documentation and that it is “really only an extension of truly informed consent.”

The goal in this section is to suggest an approach to CQI based largely on practice guidelines developed by the ASGE [8,23]. Three basic elements of any CQI program in a gastrointestinal endoscopic practice will first be discussed: (i) procedure reports, (ii) endoscopic unit record, and (iii) a regular systematic multidisciplinary peer-review process [23]. An overview of quality indicators, both physician-specific and those not physician-specific, follows. Discussion of various colonoscopic-specific quality indicators and targets is given in a subsequent section. This is a rapidly evolving field and, in the years to come, we can expect changes in the way we approach CQI.

Procedure reports

All endoscopic procedures should be systematically and carefully documented with a complete, legible, and timely procedure report. The ASGE recommends that the following elements be included in all reports [23]:

- patient identification information;
- date of procedure;
- endoscopic procedure performed;
- endoscopist(s);
- assistant(s);
- indication(s) for the procedure;
- documentation of relevant patient history and physical examination;
- indication of informed consent;
- type of endoscopic instrument used;
- medication(s) administered, including reversal agents;
- anatomic extent of the examination;
- quality of the bowel preparation (for colonoscopy);
- limitations of the examination;
- tissue or other samples obtained;
- findings;
- diagnostic impressions;
- results of therapeutic interventions (if any);
- complications (if any);
- disposition and recommendations for subsequent care.

Other useful demographic information that is helpful to include in the report includes the age, gender, and American Society of Anesthesiologists (ASA) classification of patients. Such parameters can help in comparisons of outcomes data.

The ASGE guidelines advise that written documentation of the pertinent procedure information listed above should be available in the patient’s record at the time of their discharge from the endoscopic unit, either in the form of the final endoscopy report or an abbreviated

note with relevant information that will ensure the patient’s continuity of care [23].

In today’s era of computer sophistication, the system for preparing procedure reports (containing all this information and even endoscopic images) can be coupled to other records generated in the endoscopy unit, to a hospital’s electronic medical record system, and to a database to facilitate CQI activities and clinical research. The ideal system would be “user-friendly,” allow rapid entries, have the ability to store multiple layers of information, and be affordable. A recent commentary noted that such an ideal report generator and database have not yet been achieved but that we are getting much closer [33].

Endoscopic unit record

Endoscopy units are expected to maintain a record of all endoscopic procedures. At present, there is no uniformity as to how this record should be kept: it could be in a log book, mostly in the medical record, or entered into a computer database. In the future, we can increasingly expect to see the latter approach being used. The information contained in the endoscopic unit record can play an important role in the CQI process, for instance by serving as an index for the selection of procedures for review, by providing actual data for quality improvement studies, and by serving as a record of complications. The ASGE recommends that the following information be maintained in this record [23]:

- patient identification information;
- date of procedure;
- endoscopic procedure performed;
- endoscopist(s);
- assistant(s);
- anatomic extent of the procedure;
- duration of the procedure;
- findings;
- notation of tissue sampling;
- therapeutic interventions (if any);
- complications;
- limitations of the examination;
- informed consent documentation;
- nursing notes relating to the procedure, including the preprocedural evaluation, postprocedure notes, and medication record;
- procedure report (detailed above).

The ASGE defines complications as “adverse events which necessitate intervention” [8]. Complications may be further characterized by when they occur in relationship to the procedure (immediate vs. delayed) and by their severity. Attempts are underway to standardize definitions, classification, and grading of endoscopic complications [34]. While the frequency of immediate complications associated with colonoscopy and other

endoscopic procedures is generally well defined, the incidence of late complications (occurring up to 30 days after the procedure) is probably underestimated [35]. The ASGE recommends that procedure complications be tracked, although the specific method of tracking late complications remains controversial [8].

Over time, we may also want to routinely track other pieces of information in the endoscopic unit record. One example relating to colonoscopy might be to record the time devoted to colonoscopic withdrawal as a potential measure of the thoroughness of inspection of the colon for polyps.

Endoscopy review process

Endoscopy units, be they hospital-based or ambulatory care centers, should have a formal multidisciplinary committee that meets at regular intervals to oversee performance and quality improvement activities as they relate to endoscopic practice.

The composition of this quality improvement committee generally consists of a medical director, other endoscopists privileged to perform gastrointestinal endoscopy at the institution, the nurse manager, an administrative manager, and a quality improvement representative for the hospital or ambulatory care center. In addition, the committee may seek input or assistance from other physicians, outside consultants, endoscopy assistants, and representatives from other groups, such as infection control, risk management, safety committee, and other quality improvement committees of the organization. The quality improvement committee would report to the appropriate supervisory committees or departments.

One of the basic functions of the quality improvement committee is to identify clinical indicators that can be used to measure the performance of the unit and of endoscopists. This information ultimately can be used to identify areas which need improvement. Quality indicators relating to endoscopy, and to colonoscopy in particular, are discussed more fully below. As part of the committee's regular review process, it is important that all complications be routinely reviewed. Sentinel events (defined earlier) always require timely review.

The process of CQI can be expensive and time-consuming for healthcare organizations and clinicians. Given limitations in resources, it is obviously impossible to monitor every clinical indicator and process. The JCAHO and other accrediting bodies give hospitals and ambulatory care centers considerable flexibility in selecting which processes to monitor and which data to collect. However, the JCAHO does provide general advice about prioritization, stating that data collection should focus on

processes, particularly those that are high-risk, high-volume, or problem-prone; outcomes; targeted areas of study; comprehensive performance measures (indicators); other gauges of performance (such as patients' and others' needs, expectations, and feedback; results of on-going infection-control activities; safety; quality-control and risk-management findings); and the dimensions of performance (such as efficiency and timeliness) that are important to a process or an outcome [25].

Endoscopy programs should prioritize which indicators are most suitable for initial review based on their own perceived needs, and then extend the monitoring process to other indicators over time as feasible. The indicators that the ASGE recommends be routinely tracked are listed and discussed later.

Another basic function of the quality improvement committee is to develop a mechanism for data collection. The collection of data and screening of cases and indicators can often be accomplished by nonphysician personnel. Once collected, data must be analyzed and discussed in order to draw conclusions about performance and to identify problem areas. When available, performance measures should be compared with national standards and tracked over time; this will become increasingly possible. Nelson and colleagues [36] have offered some practical advice on ways to help build measurement and data collection into medical practice.

When a problem area is discovered, the committee must discuss it and identify the cause, formulate a plan of action to improve the problem and the systems in which it resides, and then implement the actions needed to fix the immediate problem and address any factors that caused the problem. After allowing an appropriate time for changes to be made, monitoring should be done to ensure that performance has improved, leading to a second cycle if necessary [27].

One other responsibility of the quality improvement committee relates to documentation. As mentioned earlier, accrediting agencies expect every endoscopy unit to have a written plan that describes the objectives, organization, governance, responsibilities, and activities and processes of the committee. Documentation is also needed to show evidence of ongoing improvement activities, documentation of reviews, and meeting minutes. An ASGE document, *The Development of an Ambulatory Endoscopy Center: A Primer*, contains practical information that can assist endoscopists and endoscopy units to implement programs of CQI [22,37]. Particularly helpful in this regard is the sample document describing a quality improvement program, as well as an example of a quality improvement committee periodic report [37].

Table 9.1 Colonoscopy-specific quality indicators that the American Society for Gastrointestinal Endoscopy (ASGE) recommends should be routinely tracked.

Demographics	Age, gender, ASA status
Indications	ASGE approved indications Appropriate use of screening and surveillance intervals
Complications	Both immediate and delayed
Patient satisfaction	Survey information
Procedure success	Rate of cecal intubation Prevalence of colonic adenomas on screening examinations

ASA, American Society of Anesthesiologists.

Physician-specific quality indicators and activities

Some indicators that the committee will monitor will be physician-specific. Table 9.1 lists the colonoscopy-specific quality indicators that the ASGE recommends that every endoscopist track on their patients [8]. These indicators are discussed in more detail in the next section, with proposed targets given. Some indicators, such as complications, should be tracked on all patients. For other indicators, such as patient satisfaction and measures of procedure success, using just a random sample (e.g. quarterly) may be appropriate. The ASGE recommends that these quality indicators be tracked over time and that results be compared to benchmark data as they become available. Eventually, as sufficient data accumulate, it should be possible to stratify outcomes by patient populations and practice settings.

There are also other physician-specific quality indicators that a CQI program may also want to track. Examples include adequacy of procedure documentation, ensuring that patients and referring physicians receive adequate feedback regarding procedure and biopsy results, and dealing with complaints.

Dealing with peer-review issues can at times prove challenging. At our institution, they are discussed just among the physician members of the endoscopy unit’s quality improvement committee. It needs to be remembered that the basic purpose of the CQI process is an educational one, with the ultimate goal being to improve patient outcomes. Recommendations for punitive action should only be made when measures to correct deviations from practice are ignored or unsuccessful [37].

Also, the ASGE states that while the information garnered by the quality improvement committee can be considered for reprivileging and reappointment, this committee should not be the same one responsible for the granting of privileges and reappointment [23].

Other indicators and activities that are not physician-specific

Other indicators and activities of the quality improvement committee will relate to a wide spectrum of endoscopy unit activity, essential for maintaining high-quality gastrointestinal endoscopic performance. Examples include:

- scheduling mechanisms/delays;
- equipment maintenance/failure;
- adequacy of nursing and gastrointestinal assistant support during endoscopic procedures;
- adequacy of patient monitoring during and after procedures;
- adequacy of colonoscopy preparation;
- processing and transportation of tissue and microbiology specimens;
- infection control/reprocessing issues;
- ensuring adequacy of instructions at dismissal (e.g. risks, precautions about driving, verifying that appropriate follow-up has been arranged);
- patient satisfaction [37,38].

While the issue of patient satisfaction is listed last, it is a quality issue of increasing importance to patients, buyers of healthcare services, and accreditation agencies. Additional discussion of patient satisfaction is given in the next section. CQI programs should prioritize and select those indicators it is believed will meet the needs of the institution.

Specific quality indicators and targets for colonoscopy

This section focuses on specific quality indicators about which the ASGE and/or the US Multi-Society Task Force on Colorectal Cancer have recommended evidence-based or consensus-based standards [8,14]. Some of the indicators will require validation as to the feasibility of their achievement and whether they truly result in improved patient outcomes. The targets discussed are to be considered as starting points to assist endoscopists and endoscopy units in tracking their own outcomes. As data from CQI programs are reported, true benchmark data should become available that permit accurate comparison at national and regional levels. It should also eventually become possible to stratify these benchmark standards by patient population, taking into account such factors as age, gender, other demographic factors, procedure risk, and comorbid illnesses. It is logical to assume that outcomes will vary depending upon the patient population and practice setting.

The discussion of specific quality indicators that follows is limited, since most of the topics are reviewed more fully elsewhere in this book. It is also suggested

that the reader examine the two references that underlie the recommendations given here [8,14].

Procedure indication and intervals

The ASGE has provided a list of indications for colonoscopy, circumstances in which colonoscopy is generally not indicated, and the various contraindications to colonoscopy [39]. These guidelines are certainly reasonable starting points for assisting endoscopy units in determining the appropriateness of procedures. However, it is also clear that these guidelines are in need of continuing refinement. For instance, investigators from Switzerland (Chapter 11) have provided evidence that more detailed and explicit appropriateness criteria improve the diagnostic yield of colonoscopy [40,41]. Hematochezia, which is listed as an indication for colonoscopy by the ASGE, can be used as an example in this regard. There is increasing evidence that not every patient with hematochezia needs full colonoscopy and that the age of the patient, nature of the bleeding, and presence of risk factors for colorectal cancer may make anoscopy and flexible proctosigmoidoscopy a reasonable option in certain circumstances [41–44].

The US Multi-Society Task Force on Colorectal Cancer recently published its recommended intervals for colonoscopy when used as a screening and surveillance tool for the detection and prevention of colorectal cancer. This information is presented in Table 9.2. These guidelines represent reasonable CQI targets. The American

College of Gastroenterology has also provided practice guidelines relating to colorectal cancer screening and polyp surveillance [45,46].

Two other discussion points regarding appropriateness of colonoscopy are worth mentioning. First, there is generally a higher frequency of inappropriate colonoscopy (and other endoscopic procedures) in patients undergoing their procedures by open-access referral compared with patients who are first seen by a gastroenterologist in clinic [47–51]. Given the common use of open-access endoscopy in parts of the USA and the world, refinements in open-access practice will be needed. A quality improvement committee can provide valuable help in this regard. Second, the medical records and information systems that different centers employ and the difficulty in obtaining medical records from other centers can pose challenges in ensuring that colonoscopy is performed at appropriate intervals. Postpolypectomy surveillance can be taken as an example. The gastroenterologist seeing a patient in clinic, or the nongastroenterologist physician wanting to refer a patient for open-access colonoscopy, may not have access to a patient's complete medical record that indicates when previous colonoscopies were performed or what the endoscopic and histologic findings were. This can sometimes be caused by the inadequacies of that practitioner's own medical records system. Also, if the patient's previous procedure(s) was done at another hospital or center, it can be difficult to obtain the records in a timely fashion. Hopefully, advances in

Table 9.2 Appropriate age of onset and intervals for colonoscopy relating to screening and surveillance indications. (Adapted from Rex *et al.* [14].)

Indications	Interval*
<i>Screening</i>	
Average risk	10 years (begin at age 50)
Single FDR with cancer (or adenomas) at age 60 or older	10 years (begin at age 40)
Two or more FDRs with cancer (or adenomas) or 1 FDR diagnosed at younger than age 60	5 years (begin at age 40 or 10 years younger, whichever is earlier)
Prior endometrial or ovarian cancer diagnosed at younger than age 50	5 years
<i>Hereditary nonpolyposis colorectal cancer</i>	1–2 years (begin at ages 20–25)
<i>Postadenoma resection</i>	
One to two tubular adenomas of < 1 cm	5 years
Normal follow-up examination or only hyperplastic polyps at follow-up	5 years
Three or more adenomas or adenoma with villous features, ≥ 1 cm or with HGD	3 years
Numerous adenomas or sessile adenoma > 2 cm, removed piecemeal†	Short interval based on clinical judgment
<i>Postcancer resection</i>	Clear colon, in 3 years, then as per adenoma recommendations
<i>Ulcerative colitis and Crohn's disease</i>	
Surveillance after 8 years of pancolitis or 15 years of left-sided colitis	2–3 years until 20 years after onset of symptoms, then 1 year

FDR, first-degree relative; HGD, high-grade dysplasia.

* Interval recommendations assume adequate preparation and cecal intubation.

† The goal is to reexamine the site for residual polyp; repeating a flexible sigmoidoscopy is adequate for a distal polyp.

information technology and systems will eventually solve such problems.

Precautions

The risk of colonoscopy and polypectomy is increased in various preexisting conditions. Patients in whom conscious sedation is planned should routinely undergo a preprocedure history, focused physical examination, and be given an ASA class designation (which serves as an estimate of their sedation risk). The US Multi-Society Task Force on Colorectal Cancer has recommended that these be routinely performed and documented in the medical record, with a goal of 100% compliance [14]. Patients with a higher ASA classification and with serious cardiopulmonary disease may require reduction in their sedation doses and increased frequency of intra-procedure monitoring.

Diagnostic colonoscopy, with or without biopsy, is considered a low-risk procedure in terms of bleeding in patients who are receiving warfarin and who are in the therapeutic range. In contrast, colonoscopic polypectomy is a high-risk condition. The ASGE has published practice guidelines that offer recommendations for endoscopic procedures as they relate to anticoagulation [52]. The goal for the identification of patients receiving anticoagulation and appropriate actions taken on the basis of this information should be 100% [14]. For endoscopy units offering open-access colonoscopy, a mechanism should be in place whereby patients who are receiving warfarin are identified in advance of their procedures so that appropriate actions can be taken.

The risk of bacterial endocarditis as a result of colonoscopy, mucosal biopsy, and polypectomy is very low. Based on published ASGE practice guidelines, the only valvular heart conditions for which antibiotic prophylaxis might be considered are patients with prosthetic heart valves, a history of endocarditis, or surgically constructed systemic-pulmonary shunts [53]. However, the ASGE guidelines state that there are insufficient data to recommend routine antibiotic prophylaxis in such "high-risk" conditions but that the endoscopist may consider prophylaxis on a case-by-case basis. The goal recommended by the US Multi-Society Task Force on Colorectal Cancer for the identification of patients with these high-risk conditions should be 100%, and that appropriate action be taken on the basis of this information [14].

Technical measures

Reports from the 1990s indicate that competent colonoscopists should be able to intubate the cecum in excess of 90% of cases [54–56]. Even higher rates appear to be achievable in screening cases [57,58]. The US Multi-Society Task Force on Colorectal Cancer set a target of at

least 90% for all colonoscopy cases, and 95% for screening cases [14]. These cecal intubation rates assume accurate self-reporting. Examinations aborted because of inadequate preparation, severe colitis, and obstruction can be excluded when calculating cecal intubation rates. In an adequately cleansed colon, a competent colonoscopist should be able to accurately identify cecal landmarks in essentially all cases. Cecal intubation can be assured with certainty by observing the lips of the ileocecal valve and the appendiceal orifice [14]. Identification of the "crow's foot" (also called "Y-fold") of the cecal base is also helpful but considered unreliable as a single marker of cecal intubation. Intubating the terminal ileum is also helpful in documenting cecal intubation but is unnecessary unless clinically indicated. Endoscopy reports should routinely document the extent of colonoscopy and describe the landmarks used to verify cecal intubation. The goal of such procedure report documentation should be 100%.

Obtaining a combination of still photographs of the cecal landmarks is a useful adjunct to documenting complete colonoscopy, although such photographs do not provide absolute documentation in all cases [59,60]. The US Multi-Society Task Force on Colorectal Cancer stated that routine cecal photography is advisable even if imperfect [14]; the European Society of Gastrointestinal Endoscopy also recommends routine photographic documentation of cecal intubation [61]. ASGE guidelines offer no recommendations regarding documentation of cecal landmarks. Given that cecal intubation is self-reported, the use of still photography seems appropriate for providing some measure (albeit imperfect) of documentation. Videotaping of the cecum is consistently convincing but not practical for routine use [60]. However, videotaping can be used to document cecal intubation rates as part of credentialing and to evaluate an endoscopist whose claimed rate of cecal intubation has been questioned [14,60].

Many colonoscopists take considerable pride in the rapidity with which they can reach the cecum and the shortness of their overall colonoscopy procedure times. However, every bit as important as insertion is the technique and thoroughness of colonoscopic withdrawal, since for most colonoscopists the withdrawal phase allows careful inspection of the colon for neoplasms. Detection rates for adenomas correlate with such factors as (i) thoroughness of inspection of the back-side of folds, ileocecal valve, and rectal valves; (ii) careful inspection of flexures; (iii) maintaining adequate colonic distension; (iv) adequate washing; (v) adequate suctioning; and (vi) overall time spent inspecting [19]. Miss rates should be low for adenomas 1 cm and larger in size, but are considerably higher for smaller polyps [15]. The US Multi-Society Task Force on Colorectal Cancer has proposed that the withdrawal time for colonoscopy should

average at least 6–10 min, exclusive of time for biopsy and polypectomy [14]. Further study of withdrawal techniques and time is needed.

The adenoma prevalence rate in an endoscopist's practice depends on the quality of the colonoscopist's withdrawal technique, the quality of bowel preparation, and the demographics of the patient population (e.g. older age, male gender, and family history of colorectal cancer are all associated with higher rates). Based on current information, it is estimated that 25–40% of asymptomatic Americans older than 50 years have one or more adenomas [14]. So-called "advanced adenomas" are the ones clinically most important and at risk of becoming malignant. An advanced adenoma is one that is 1 cm or larger in size, contains villous elements, or contains high-grade dysplasia [46]. The prevalence of advanced adenomas in the American population over 50 years is estimated to be 3–10% [14]. CQI programs can potentially track the overall likelihood of finding all adenomas, advanced adenomas, and cancer. However, for estimating the quality of colonoscopic withdrawal, the US Multi-Society Task Force on Colorectal Cancer has proposed that programs focus on overall adenoma detection rates [14]. Their suggested adenoma prevalence target rates for persons undergoing first-time colonoscopy are 25% or more in males 50 years and older, and 15% in females of similar age. Their arguments for selecting overall adenoma detection include:

- 1 complete clearing of adenomas from the colon is still considered a desirable outcome;
- 2 it is reasonable to assume that satisfactory technique to detect small adenomas will also detect advanced adenomas;
- 3 it should be easier to detect variations in colonoscopists' performance by consideration of overall adenoma detection rates, since they are higher than advanced adenoma prevalence rates.

Both the ASGE and the US Multi-Society Task Force on Colorectal Cancer recommend that all colonoscopy procedure notes document the quality of bowel preparation. A satisfactory preparation is one that "allows confidence that mass lesions other than small (5 mm or less) polyps were generally not obscured by the preparation" [14]. Recommended intervals for colonoscopic screening and surveillance assume satisfactory preparation. It is reasonable for endoscopy units to track the adequacy of bowel preparation in their patients, although there is currently no consensus on how best to describe the quality of bowel preparation or what the target for satisfactory bowel preparation in a unit should be [62,63].

Issues relating to biopsy and polypectomy provide yet other measures of the technical success of colonoscopy. It is generally recommended that all polyps found at colonoscopy be removed, except possibly when there are

numerous small polyps (usually 1–5 mm). In this situation, representative biopsies should at least be taken [14,46]. The US Multi-Society Task Force on Colorectal Cancer states that skilled endoscopists should be able to retrieve at least 95% of polyps for pathologic examination [14].

Trained endoscopists can now remove almost any mucosally based pedunculated polyp, regardless of size. Advances in polypectomy techniques and ablative tools, such as argon plasma coagulation, are now facilitating removal of larger sessile polyps that previously were sent for surgical resection [14]. The US Multi-Society Task Force on Colorectal Cancer has recommended as a quality goal that mucosally based pedunculated polyps and sessile polyps less than 2 cm in size should not be sent for surgery without an attempt at endoscopic resection or that there be documentation of endoscopic inaccessibility [14]. If the original colonoscopist is unable to offer this service and the polyp appears endoscopically resectable, consideration should be given to referral to a more experienced endoscopist.

One other colonoscopic biopsy issue that the US Multi-Society Task Force on Colorectal Cancer has addressed relates to the number and distribution of biopsies taken for dysplasia surveillance in ulcerative colitis and Crohn's disease. Here, the goal should be to take biopsies from all four quadrants from each 10-cm segment of colon, or approximately 30 total biopsies in cases of ulcerative pancolitis [14]. The protocol followed should also be documented in the report. Procedure reports in ulcerative colitis should also describe and give the location of any mass or suspicious polypoid lesions, which should also be biopsied or removed as feasible [14].

Complications

All endoscopists and endoscopy units should routinely track procedure-related complications. As stated earlier, the specific way of tracking delayed complications (those occurring up to 30 days after the procedure) remains a subject of debate. The US Multi-Society Task Force on Colorectal Cancer has recommended several specific CQI targets and goals. First, a goal of 100% is recommended for cases in which informed consent is obtained prior to the procedure [14]. Further, it is suggested that in 100% of cases the following four principal complications be specifically listed on the consent form or in an accompanying procedure or progress note: perforation (and the probable need for surgery if it occurs), postpolypectomy bleeding, adverse cardiopulmonary reactions (usually related to sedation), and missing a significant neoplasm.

The unplanned need for reversal agents (e.g. naloxone or flumazenil) should be low and the need for

ventilatory support even lower. The US Multi-Society Task Force on Colorectal Cancer gives a goal for the need of unplanned reversal of sedation as less than 1 in 100 colonoscopy procedures [14]. The suggested goal for the need for mask ventilation or endotracheal intubation is less than 1 in 300 procedures. Colonoscopists should be competent to manage oversedation and other adverse cardiopulmonary events.

Colonic perforations can occur by several mechanisms. The US Multi-Society Task Force on Colorectal Cancer gives goals for the incidence of colonoscopic perforation as less than 1 in 1000 procedures overall and less than 1 in 2000 for screening procedures [14].

Significant bleeding following colonoscopic mucosal biopsy is very rare, even in patients on anticoagulants who are in the therapeutic range [52]. Postpolypectomy bleeding is a much more important complication and may occur immediately or be delayed. Its incidence depends on a number of factors, such as polyp size and configuration, type of device(s) and technique used to remove the polyp, type of current employed when electrosurgical techniques are used, and use of anticoagulants after polypectomy. The US Multi-Society Task Force on Colorectal Cancer gives a goal for the incidence of postpolypectomy bleeding (immediate and delayed) as less than 1 in 100 cases [14]. The rate may be higher in practices that remove large polyps and much lower in practices that refer large polyps to others.

Patient satisfaction

The use of a well-designed patient satisfaction measurement system can potentially be used to help establish performance standards, increase accountability of physicians and staff, improve risk management, and improve the quality of care [64]. The ASGE has recommended that a modified GHAA-9 patient satisfaction survey be used to assess patient satisfaction in endoscopic practices [8]. The survey and its nine questions are listed in Table 9.3. Some of the reasons that the ASGE advocated this survey are that it has been in use for many years, has been validated in many patient populations, is accepted by managed care organizations, and there is a significant quantity of benchmark data available for comparative purposes. However, a recent study has suggested that the survey may be deficient in that it does not specifically assess pain control during procedures [64]. Efforts are underway to develop an endoscopy-specific patient satisfaction survey tool.

Summary

The field of outcomes research and CQI as applied to healthcare is still young and in a rapid state of evolution. Integrating thoughtful outcomes research, clinical

Table 9.3 American Society for Gastrointestinal Endoscopy Patient Satisfaction Survey [8].

A number of questions are listed below regarding the visit you made

The possible responses for questions 1–7 are: excellent, very good, good, fair, poor

The possible responses for questions 8 and 9 are: yes, no

In terms of your satisfaction, how would you rate each of the following.

- 1 How long you waited
- 2 Length of time spent waiting at the office for the procedure
- 3 The personal manner (courtesy, respect, sensitivity, friendliness) of the physician who performed your procedure
- 4 The technical skills (thoroughness, carefulness, competence) of the physician who performed your procedure
- 5 The personal manner (courtesy, respect, sensitivity, friendliness) of the nurses and other support staff
- 6 Adequacy of explanation of what was done for you (all your questions answered)
- 7 Overall rating of the visit
- 8 Would you have the procedure done again by this physician?
- 9 Would you consider having this procedure done again at this facility?

guidelines, and better approaches to CQI into a cooperative learning clinical environment to truly improve patient health outcomes while controlling their associated costs remains a major challenge. With careful development, however, the outcomes (quality) movement has the potential to accomplish this. The words of Relman in 1988 are as appropriate now as they were then: “To achieve these objectives will require much new financial support and unprecedented cooperation among physicians, government, private insurers, and employers. No one should underestimate the size or difficulty of the task” [1].

Individual endoscopy units may embark on programs of CQI for different reasons. Some may do it just as a means of gaining or maintaining their accreditation status, doing just the minimum necessary. The best units will do it out of a genuine desire to maximize the quality of care they provide. Increasingly, patients and buyers of healthcare services expect to see our performance outcomes and will compare them to benchmarks. Cotton [32] has persuasively argued that providing such information is “really only an extension of truly informed consent.”

Increasingly, endoscopists will be expected to participate in CQI. The ASGE already recommends that individual endoscopists systematically track their practice performance. However, this should be part of a more global CQI program for the endoscopy unit or practice that is used to monitor both the performance of individual endoscopists and of a variety of other performance measures for the unit. Such data can then be

analyzed and used to improve patient care. Endoscopy units will need to be creative in determining how best to accomplish these goals for their institution, recognizing that implementing such plans requires a significant commitment of the organization in terms of time, money, and desire.

The evidence- and consensus-based quality target goals currently available, and reviewed in this chapter, must be looked at as starting points in our quest to improve outcomes. As data on these indicators accumulate, improved benchmark information should become available to permit accurate comparisons at national and regional levels, and among different patient populations and practice settings. Advances in computerized information technology at all levels will facilitate this process.

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Chapter 10

Indications and Contraindications

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Introduction

In general, the indications for colonoscopy have expanded since its inception. In recent years, the largest growth in the use of colonoscopy in the USA has resulted from acceptance of average-risk colorectal cancer screening as a valid indication. The first mention of colonoscopy for average-risk screening appeared in the literature in 1988 [1], the first studies of colonoscopy for average-risk screening in 1990 [2,3], and the first appearance in a guideline appeared from the GI Consortium in 1997 [4] and was followed very closely by the American Cancer Society that same year [5]. In 2000, the American College of Gastroenterology recommended colonoscopy as the preferred colorectal cancer screening strategy, whenever the expertise, resources, and reimbursement for the procedure were available [6]. In many countries, colonoscopy is not used as a colorectal cancer screening test and the substantial cost outlays associated with its use for this indication are unacceptable or the manpower and facilities to provide the service are unavailable. Thus, indications for colonoscopy are likely to differ between countries, depending on the resources available to supply the service of colonoscopy and the perceptions of healthcare experts in that country regarding the benefits, costs, and risks of colonoscopy relative to other diagnostic strategies that are available for both symptomatic and asymptomatic (screening) patients. The concept of limiting the indications for colonoscopy according to the feasibility of supplying the service can be readily extended beyond the decision about whether to provide the service for screening. Thus, within the symptomatic population and the surveillance population, there is a very large range of yield for cancer that can be determined by indication [7]. When resources are limited, it may be appropriate to confine the use of colonoscopy to indications with a higher yield for cancer and to use other diagnostic strategies, such as barium enema, for lower-yield indications.

This chapter assumes that the resources are available to provide colonoscopy for a broad range of indications. However, emphasis is placed on the relative yields of different indications for both cancers and adenomas.

These comparisons are of value in determining what indications are most appropriate when resources are limited. Even in the USA, where resources and personnel are very widely available to provide colonoscopy services, patients in whom colonoscopy is inappropriate are well recognized. Factors that may suggest when colonoscopy would be inappropriate include the indication, age and gender of the patient, and the presence or absence of various other risk factors for disease.

Classification of indications

Diagnostic vs. therapeutic

A common classification of colonoscopic indications is diagnostic vs. therapeutic (Table 10.1). In many instances the indications for therapeutic procedures are often more fully accepted since the alternative treatment in many cases is surgery, which is generally associated with greater morbidity, mortality, and cost than colonoscopy. Colonoscopy provides an excellent view of the mucosal surface from the anal canal to the terminal ileum. Almost any intraluminal lesion can be detected and biopsied. For any diagnostic procedure that does not involve biopsy, there is usually an available alternative, either barium enema or, in a few centers, virtual colonoscopy. The distinction between diagnostic and therapeutic colonoscopy also has value in understanding complication rates, since these are expected to be higher in therapeutic compared with diagnostic procedures. From one perspective the distinction between diagnostic and therapeutic lacks relevance, since in most therapeutic procedures, particularly polypectomy, the presence of polyps and therefore the need for polypectomy is unknown to the colonoscopist prior to the procedure. Therefore, the designation "diagnostic" or "therapeutic" can only be assigned after the procedure. Furthermore, it is generally unacceptable to perform diagnostic procedures without the skill to perform therapeutic maneuvers that are likely to be indicated. All colonoscopists must be trained in polypectomy and must generally perform colonoscopy with intent to clear the colon of polyps on the initial examination.

Table 10.1 Diagnostic and therapeutic indications for colonoscopy.*Diagnostic indications*

Evaluation of an abnormality on barium enema (or virtual colonoscopy) such as a filling defect or stricture

Evaluation of unexplained gastrointestinal bleeding

Hematochezia in absence of convincing anorectal source

Melena after an upper gastrointestinal source has been excluded

Presence of fecal occult blood

Unexplained iron-deficiency anemia

Surveillance after removal of adenomas (see Table 10.3)

Surveillance after resection of colorectal cancer

After identification of adenomas during sigmoidoscopy or for clearing the colon of synchronous neoplasia in patients with colorectal cancer

In patients with ulcerative pancolitis or Crohn's colitis of 8 or more years' duration or left-sided colitis of 15 or more years' duration

Colorectal cancer screening (see Table 10.4)

Chronic inflammatory bowel disease of the colon, if more precise diagnosis or determination of the extent of activity of disease will influence management

Clinically significant diarrhea of unexplained origin

Intraoperative identification of a lesion not apparent at surgery (e.g., polypectomy site, location of a bleeding site)

Miscellaneous therapeutic indications (from American Society for Gastrointestinal Endoscopy guideline)

Treatment of bleeding from such lesions as vascular malformation, ulceration, neoplasia, polypectomy site (e.g. electrocoagulation, heater probe, laser or injection therapy)

Foreign body removal

Excision of colonic polyp

Decompression of acute nontoxic megacolon or sigmoid volvulus

Balloon dilation of stenotic lesions (e.g. anastomotic strictures)

Palliative treatment of stenosing or bleeding neoplasms (e.g. laser, electrocoagulation, stenting)

Marking a neoplasm for localization

High-risk vs. low-risk

A second classification of indications is by risk. Not all factors that increase the risk for colonoscopy are well defined. However, indications generally associated with high risk include decompression of acute colonic pseudo-obstruction, polypectomy of large polyps, stricture dilation, and stent placement. Preexisting conditions associated with high risk include acute colonic pseudo-obstruction, sigmoid volvulus, cecal volvulus, prior radiation therapy, chronic steroid use, colonic strictures, extensive pelvic adhesions, severe diverticular disease, and severe colitis. Patients with cardiac or pulmonary disease graded 3 or higher on the American Society of Anesthesiologists (ASA) scale are at risk for cardiopulmonary compromise with sedation. The same patients, plus patients with severe liver or kidney disease, often do not tolerate any surgery required for management of colonoscopic complications. Specific procedures that are associated with risk follow closely the high-risk indications, including removal of large polyps (particularly sessile lesions in the right colon), stricture dilation (particularly if the etiology is nonanastomotic Crohn's strictures or radiation strictures), stent placement, and tumor ablation. The potential benefits of the procedure vs. the risks should always be taken into account in determining whether the indication is valid in a given patient.

Screening procedures, which are generally performed in asymptomatic persons who are healthy or relatively healthy, have thus far been associated with a very low risk of perforation. In more than 6000 reported screening colonoscopies in average-risk persons, no perforations have yet occurred [8–10].

High-yield vs. low-yield

A final method of classifying diagnostic indications for colonoscopy is by their expected yield for disease, particularly neoplasia (see Chapter 11). The yield of colonoscopy for cancer is highly dependent on indication. For example, bleeding indications consistently have the highest yield for cancer (Table 10.2). The lowest-yield indications for cancer are postpolypectomy surveillance and ulcerative colitis surveillance. Within many indications, the yield of cancer increases substantially according to patient age. For example, an 80-year-old patient with rectal bleeding or with a positive fecal occult blood test is many times more likely to have colorectal cancer than a 30-year-old patient with the same findings. The yield of adenomas and advanced adenomas is largely independent of indication, although bleeding indications have an increased predictive value for large adenomas. To a substantial extent, the prevalence of adenomas is independent of indication; rather the prevalence reflects

Indication	Procedures to detect one cancer
Two consecutive positive FOBT, neither rehydrated	2.7
Rectal bleeding: nonemergency	8.9
Positive FOBT: nonrehydrated	9.8
Melena with negative EGD	9.9
Acute lower gastrointestinal hemorrhage	11.8
Iron-deficiency anemia	13
Colonic symptoms without bleeding	36
Screening Lynch syndromes	39
Positive FOBT: rehydrated	45
Screening average-risk males \geq 60 years	64
Surveillance after cancer resection: anastomotic recurrence	74
Surveillance after cancer resection: metachronous cancer	82
Colonic symptoms without bleeding	109
Screening positive family history; non-Lynch kindred	141
Screening average-risk persons \geq 50 years	143
Screening positive family history; prospective studies only	286
Postpolypectomy surveillance	317
Prospective UC surveillance	360

Table 10.2 Yield of colonoscopy by indication. (From Rex [7] with permission.)

EGD, esophagogastroduodenoscopy; FOBT, fecal occult blood test.

demographic features, including age and gender and to some extent family history of colorectal cancer or adenomas [7]. Age is the most powerful predictor but male gender is a consistent predictor of both adenomas and advanced adenomas [8,10].

In the absence of bleeding (no report of hematochezia, negative stool tests for occult blood, and normal hemoglobin level), symptoms such as abdominal pain and altered bowel habit have no predictive value for colorectal cancer [9,11]. In these persons, the yield of colonoscopy for neoplasia essentially reflects the age, gender, and family history of the patient. This observation becomes the justification for making a positive diagnosis of irritable bowel syndrome in many women aged less than 50 years with nonbleeding colonic symptoms. On the other hand, colonoscopy in persons aged 50 years and older with only nonbleeding colonic symptoms is justified based on age, rather than the presence of nonbleeding symptoms.

To summarize, the decision about whether to proceed with colonoscopy should take into account the anticipated risk and potential benefit of the procedure. The potential for benefit can be approximated by estimating the potential yield for neoplasia, which is a function of the indication (with regard to cancer) and the patient's age, gender, and family history (with regard to adenomas).

Alternatives to colonoscopy

The decision about whether colonoscopy is indicated must also take into account the cost, risk, and accuracy of

diagnostic alternatives. Double-contrast barium enema (DCBE) is several times more likely than colonoscopy to miss colorectal cancer [12,13] and has a sensitivity of only about 50% for large adenomas. Although these recent studies have clearly established the superiority of colonoscopy over DCBE for detection of both cancer and adenomas, reviews of earlier studies by independent groups clearly indicated that barium enema had limited effectiveness [14]. Similarly, computed tomography (CT) colonography (virtual colonoscopy) has had marked variability in results when all reported studies are considered [15]. Because of its high cost, virtual colonoscopy is still a research tool with regard to colorectal cancer screening. DCBE and virtual colonoscopy are most appropriate for low prevalence populations and indications. Thus, patients under 50 years old, particularly females without a family history of colorectal cancer, who present with nonbleeding symptoms would be appropriate candidates for DCBE (or virtual colonoscopy if it is available and is demonstrated to have high quality locally) if imaging the colon is necessary. The ability of barium enema to detect mucosal lesions is extremely dependent on the quality of the double-contrast technique, which is very variable among services and hospitals.

The relative use of colonoscopy vs. radiographic colon imaging tests (which are only diagnostic) should take into account local expertise with both colonoscopy and the radiographic methods. Virtual colonoscopy is available in very few centers and of these, only a limited number have proven their ability to achieve adequate sensitivity for colon neoplasms. DCBE sensitivity varies

markedly between hospitals and may be a function of the interest and training of radiologists. Colonoscopy effectiveness and risks also vary between examiners. Ideally, one would like to know the local effectiveness and safety of colonoscopy and radiographic imaging studies and take these factors into account, combined with the anticipated risk and yield of colonoscopy, in deciding the best diagnostic approach to an individual patient.

Specific indications

Bleeding

Bleeding indications have the highest yield of neoplasia of any indication for colonoscopy. Positive fecal occult blood test is perhaps the single best indication for colonoscopy, since it is associated not only with a high prevalence of cancer (2–12%) [16–18] but also cancers tend to be early stage (80% Stage I or II) and therefore associated with high survival rates. Hematochezia, iron-deficiency anemia, and melena with a negative upper endoscopy are all associated with a substantial prevalence of colon cancer [7], although the positive predictive value of each of these findings increases with age [19]. A report of blood only on the toilet tissue is invariably from an anal source. However, if blood is passed into the toilet, there is no reliable way to distinguish an anal source from a colonic source and no reliable way to distinguish a distal colonic source from a proximal colonic source [20]. Certain features, such as blood dripping from the anus after bowel movements, are more often associated with an anal source but do not always separate anal from colonic sources [21].

All persons with positive fecal occult blood tests and all persons aged 50 years and older with any of the other bleeding indications should undergo initial colonoscopy. In the USA, most persons aged 40 years and older with bleeding indications undergo initial full colonoscopy but practices vary. A recent cost analysis of approaches to bleeding showed that even persons in their twenties and thirties with rectal bleeding should undergo at least initial distal colon visualization, and if no source is identified should proceed to full colon evaluation [22].

Control of active bleeding is an important therapeutic indication for colonoscopy. Hemostasis can be applied in postpolypectomy bleeding, vascular ectasias, radiation injury of the rectosigmoid, diverticular hemorrhage, and colonic varices. Control of bleeding is accomplished by any of the methods available, including monopolar or bipolar coagulation, heater probe, injection of various agents, and clipping. The method used depends largely on the personal experience of the colonoscopist but also on the nature of the lesion responsible for bleeding.

Abdominal pain and constipation

The prevalence of irritable bowel syndrome in the general population is sufficiently high that abdominal pain with or without constipation in the absence of bleeding (defined as no history of hematochezia, negative stool tests for fecal occult blood, and normal hemoglobin) is not associated with colorectal cancer [11,23]. Colonoscopy in the presence of these symptoms defines a prevalence of neoplasia similar to that defined by screening colonoscopy. When patients with these symptoms (age 50 years or older) are encountered, colonoscopy is justified based on the patient's age. Many patients younger than 50 years with these symptoms will undergo colonoscopy, sigmoidoscopy, or barium enema, as the symptoms tend to be chronic, and patients may be reassured and have an improved quality of life based on the negative examination. When abdominal pain and constipation are linked with colorectal cancer, they are often associated with late stages. In general, isolated abdominal pain with or without constipation is a poor indication for colonoscopy, except to the extent that these symptoms help to convince patients to undergo any screening that might be indicated on the basis of age or family history.

Chronic diarrhea

Colonoscopy is often performed in patients with chronic watery diarrhea to exclude collagenous or lymphocytic colitis. With this indication random biopsies should be performed, including from the proximal colon, even if the mucosa appears normal. The yield of microscopic colitis ranges from 5 to 15% and is clearly higher in older females [24]. Patients with collagenous and lymphocytic colitis generally have some abnormalities when the left colon is biopsied and therefore sigmoidoscopy and biopsy can be used as an initial diagnostic test to screen for these disorders. If chronic diarrhea is accompanied by abdominal pain, it is preferable to begin with colonoscopy and include intubation of the terminal ileum to assist in the exclusion of Crohn's disease.

Abnormal radiographs or sigmoidoscopy

Filling defects identified on barium enema or virtual colonoscopy are usually considered an indication for colonoscopy. Exceptions are patients with small polypoid defects, who are elderly or who have significant comorbidities, in which case the abnormalities can be ignored. Strictures found by radiographic imaging should be colonoscopically identified and biopsied. Routine abdominopelvic CT sometimes identifies areas of colonic thickening, believed to represent tumor or inflammation; these findings are also an indication for colonoscopy. However, the false-positive rate is high.

Colonoscopy is indicated in patients with adenomas at sigmoidoscopy [9], although in some centers colonoscopy is performed only if advanced adenomas are found during sigmoidoscopy [25].

Established ulcerative colitis

Colonoscopy can be used to evaluate the extent and severity of ulcerative colitis, which can be useful in guiding medical therapy and in the consideration of surveillance examinations. Intubation of the terminal ileum and biopsy can be useful in distinguishing ulcerative colitis from Crohn's disease, which may be critical in decisions about whether to proceed with surgery or what operation is to be performed. Colonoscopy can be used to assess disease activity when patients present with symptoms that are not clearly attributable to ulcerative colitis, although in many cases sigmoidoscopy will suffice for this purpose. In clinical trials, colonoscopy and sigmoidoscopy with biopsy are often used to assess histologic improvement as a measure of the effectiveness of a medical treatment. The use of endoscopy in clinical practice for this purpose is less well established.

Surveillance examinations in ulcerative colitis are performed in persons at risk for cancer. Interval colonoscopies and multiple biopsies are obtained in an attempt to identify premalignant neoplastic cellular changes. The initial diagnostic examination in an individual with long-standing ulcerative colitis is not considered a surveillance study. Colonoscopy is indicated 8–10 years after the onset of symptoms in patients with pancolitis (disease extending proximal to the splenic flexure) and after 15 years of left-sided disease. Surveys in the USA and the UK indicate that gastroenterologists are poorly informed about the proper intervals at which to perform ulcerative colitis surveillance and seldom use an adequate biopsy protocol [26,27]. The yield for cancer in ulcerative colitis surveillance is the lowest of any indication for colonoscopy [28] and recognized experts have argued against its use [29]. However, in the USA, surveillance colonoscopy and biopsy is standard practice. The interval of examination is usually every 2 years until 20 years after the onset of symptoms and then annually thereafter. Cost analyses suggest that the cost-effectiveness of this practice is very low [30]. Patients with primary sclerosing cholangitis appear to be at risk of colorectal cancer from the time their colitis is recognized and surveillance should begin after this diagnosis.

Established Crohn's disease

After establishing an initial diagnosis of Crohn's disease, colonoscopy has traditionally had a very limited role in clinical decision-making. The clinical response of

the patient has generally been considered of greatest value in Crohn's disease, since therapy can produce symptomatic relief without endoscopic evidence of healing. The role of colonoscopy in evaluating the response to infliximab is currently under evaluation.

The risk of developing colorectal cancer in long-standing Crohn's colitis is comparable to that of ulcerative colitis. Cancers tend to occur in areas of active disease. A surveillance protocol similar to that in ulcerative colitis should be used, although published experience is limited [31].

Postpolypectomy surveillance

Postpolypectomy surveillance accounts for 25% of colonoscopies performed in the USA [32] and up to 50% of colonoscopies in some practices. As the use of screening increases, the cost and complications associated with postpolypectomy surveillance will also increase. However, recent data suggest that initial clearing examinations have a much greater effect on colorectal cancer incidence than does subsequent postpolypectomy surveillance [33]. Therefore, recent guidelines have emphasized the limited benefits of postpolypectomy surveillance and the importance of expanding intervals between examinations. Table 10.3 summarizes three US guidelines [34–36] on postpolypectomy surveillance and the Norwegian guidelines [37]. In the USA, the American College of Gastroenterology Guideline [34] and the American Gastroenterological Association Consortium Guideline [35] are very similar, and the most important recent change has been that patients with only one or two tubular adenomas should have their first follow-up examination in 5 years rather than 3 years. The American Cancer Society Guideline [36] differs in several regards. In particular, patients with one or two negative examinations (depending on their initial adenoma findings) can be returned to general population screening (Table 10.3). The Norwegian guideline [37] reflects a perspective that places very limited value on postpolypectomy surveillance relative to the initial clearing colonoscopy (Table 10.3).

All US guidelines call for a 3-year examination in patients with three or more adenomas or with adenomas that are > 1 cm, or contain high-grade dysplasia or villous elements. Patients with numerous adenomas may require additional clearing examinations, and patients with large sessile adenomas removed piecemeal require additional follow-up at 3–6 month intervals until it is established that the polypectomy site is cleared of adenoma. In the case of distal polyps, these follow-up examinations can be performed by flexible sigmoidoscopy.

In general, patients with only hyperplastic polyps should be considered to have had normal examinations, unless they have 20 or more hyperplastic polyps [44].

Table 10.3 US and Norwegian postpolypectomy surveillance recommendations.

Finding	Next examination
<i>American Gastroenterological Association Consortium</i>	
One or two tubular adenomas < 1 cm	5 years
Normal follow-up or only hyperplastic polyps	5 years
≥ 1 cm, HGD, villous elements, or more than two adenomas	3 years
Numerous adenomas or large sessile adenoma	Clinical judgment
<i>American College of Gastroenterology</i>	
One or two tubular adenomas < 1 cm	5 years
Normal follow-up	5 years
≥ 1 cm, HGD, villous elements, or more than two adenomas, or family history of colorectal cancer	3 years
Numerous adenomas or large sessile adenoma	Additional clearing as needed
<i>American Cancer Society</i>	
One tubular adenoma < 1 cm	3–6 years; if then negative return to general screening
> 1 cm, HGD, villous elements, more than one adenoma	3 years; if negative repeat in 3 years; if still negative return to general screening
<i>Norwegian guidelines [37]</i>	
More than two adenomas, or biopsy-verified adenomas 1–4 mm left <i>in situ</i> , or adenomas plus previous gynecologic cancer and age < 75 years	5 years
HGD or villous elements and age < 75 years	10 years
One or two tubular adenomas < 1 cm or age > 75 years	No follow-up recommended

HGD, high-grade dysplasia.

Surveillance after resection of cancer

For both colon cancer and rectal cancer, the purpose of colonoscopy after resection of cancer is primarily the detection of metachronous disease. The rate of anastomotic occurrences with colon cancer is approximately 2% and most anastomotic recurrences are accompanied by intraabdominal or pelvic disease that is unresectable for cure [38]. It is clear that colonoscopy should be performed in the perioperative period to clear the colon of synchronous neoplasia. In the nonobstructed patient, this colonoscopy can be performed preoperatively. In the obstructed patient, either barium enema or virtual colonoscopy should be performed, and colonoscopy should be completed 3–6 months after segmental resection, even if the radiographic studies were negative. Guidelines differ with regard to the timing of the next colonoscopy. The American Cancer Society (Table 10.4) recommends that the next colonoscopy be performed in 1 year. This is currently the most common practice in the USA, although there is no strong evidence to support it. The rationale has traditionally been that 80% of recurrences occur within the first 2 years, but again colonoscopy has no established role in improving survival from the original cancer. This principle was verified in a recent metaanalysis of trials of intensive surveillance measures after colorectal cancer resection [39]. For reasons that are not clear, there is a higher occurrence of second primary cancers after resection

of a colorectal cancer than after excision of adenomas [7]. A recent study of patients with Stage II and III resected cancers participating in a randomized trial of 5-fluorouracil chemotherapy identified an alarming occurrence rate of second primary cancers within a short interval of the initial cancer and within short intervals of surveillance examinations, including colonoscopy [40]. Though the results of this study defy explanation, they do support the performance of colonoscopy at 1 year to identify second primaries (not anastomotic occurrences). The American Gastroenterological Association Consortium Guideline and the American Society for Gastrointestinal Endoscopy recommend that the first subsequent examination be performed in 3 years, since other than the above study [40] there is little evidence that second primary cancers develop more rapidly in patients with previous colon cancers than in patients without such cancers. After the first surveillance examination, subsequent surveillance examinations are planned, based on adenoma findings, and therefore in most cases would be performed at 3–6 years by current guidelines (see Table 10.3). However, patients with family or personal histories compatible with or suggestive of hereditary nonpolyposis colorectal cancer should continue with examinations at 1–2 year intervals.

Patients with resected rectal cancer have much higher recurrence rates than those with colon cancer, at least if traditional blunt dissection techniques are used during surgery. Conversely, patients undergoing total

Table 10.4 Indications for screening colonoscopy.

In average-risk persons: start at age 50 years, repeat every 10 years

In persons with one first-degree relative diagnosed with colorectal cancer (or adenomas) at age > 60 years: start at age 40 years, repeat every 10 years

In persons with two first-degree relatives diagnosed with colorectal cancer (or adenomas) or one first-degree relative with colorectal cancer (or adenomas) at age < 60 years: start at age 40 years or 10 years before age of diagnosis of youngest relative, repeat every 5 years

In hereditary nonpolyposis colorectal cancer: start at age 20–25 years, repeat every 1–2 years until age 40, then every 1 year

In women with endometrial or ovarian cancer diagnosed at age < 50 years: start at time of diagnosis, repeat every 5 years

In patients with FAP in whom surgery is being postponed: repeat every 6–12 months

In patients with possible or gene test proven attenuated FAP: repeat every 1 year until surgery is performed

FAP, familial adenomatous polyposis.

mesorectal excision have recurrence rates of less than 10%, which can be further lowered to recurrence rates comparable to those seen in colon cancer if patients are given neoadjuvant radiation [41] or chemoradiation in appropriate cases. Depending on anticipated recurrence rates, interval use of flexible sigmoidoscopy or endoscopic ultrasound during the first 2 years after resection is appropriate, although there are no randomized controlled trials to support either modality.

Screening

The greatest expansion in use of, and indications for, colonoscopy has come through its endorsement as a screening measure in average-risk persons. Recommendations for colonoscopy screening in the USA are summarized in Table 10.4. The position of US societies regarding colonoscopy screening in average-risk persons is summarized in Table 10.5. Current screening guidelines tend to separate screening strategies into distinct categories, giving the impression that clinicians would choose either colonoscopy every 10 years or another strategy, such as annual fecal occult blood tests plus flexible sigmoidoscopy every 5 years. However, in countries with limited resources, there is a strong rationale for mixing various options, such as sigmoidoscopy at age 50 years followed by colonoscopy at age 60 or 65 years, a strategy that may maximize impact and conserve scarce resources. Combining various options for screening can result in appropriate diagnostic pathways since the prevalence of adenomas and advanced adenomas doubles between age 50 and 60, and between age 50 and 80 the distribution of colorectal cancer shifts dramatically from the distal colon to the proximal colon

Table 10.5 Positions of US societies on average-risk screening colonoscopy.

American Gastroenterological Association Consortium and American Cancer Society

Colonoscopy every 10 years is one of five options for screening; others are annual FOBT, flexible sigmoidoscopy every 5 years, annual FOBT plus flexible sigmoidoscopy every 5 years, and DCBE every 5 years

American College of Gastroenterology

Colonoscopy is the preferred strategy whenever resources, expertise, and reimbursement are available; alternative of annual FOBT plus flexible sigmoidoscopy every 5 years is also acceptable

US Preventive Services Task Force

Colorectal cancer screening is a Grade A recommendation (should be offered to all eligible patients). There is insufficient evidence to indicate that one screening strategy is preferred; in particular, the superior effectiveness of colonoscopy may not outweigh its risks

DCBE, double-contrast barium enema; FOBT, fecal occult blood test.

[42,43]. Thus, the rationale for colonoscopy is stronger in persons aged 60 years and older than it is in younger persons.

Miscellaneous indications

Miscellaneous therapeutic indications for colonoscopy are listed in Table 10.1. In general, the use of colonoscopy for therapeutic indications has expanded and its use has particularly increased for palliation of cancer. Decompression of acute colonic pseudoobstruction is an area where the use of colonoscopy has declined, with the advent of effective medical therapy (neostigmine). Colonoscopy is now used for this indication primarily when neostigmine is contraindicated or when patients fail to respond to neostigmine.

Contraindications to colonoscopy

Contraindications to colonoscopy can be classified as absolute and relative (Table 10.6). Absolute contraindications include a competent patient who is unwilling to give consent and an uncooperative patient in whom consent has been given but in whom adequate sedation cannot be achieved. In addition, toxic megacolon, fulminant colitis, and a known free colonic perforation are usually included in this list of contraindications. Relative contraindications constitute situations in which risk is substantially increased. It may be appropriate to proceed if the expected information that can be acquired by colonoscopy or a treatment that can be given is critical to the welfare of the patient. Relative contraindications include acute diverticulitis, very large abdominal aortic aneurysms (particularly if they are symptomatic),

Table 10.6 Contraindications to colonoscopy.

<i>Absolute</i>
Competent patient who refuses to consent
Consented patient who is unable to cooperate and cannot be adequately sedated
Known perforated viscus communicating freely with the peritoneal cavity
Toxic megacolon
Fulminant colitis
<i>Relative</i>
Acute diverticulitis (diagnosis established)
Hemodynamic instability
Recent myocardial infarction or pulmonary embolism
Immediate postoperative stage
Very large and/or symptomatic abdominal aortic aneurysm
Pregnancy

patients who are immediately postoperative, and patients who have suffered recent myocardial infarction, pulmonary embolism or are currently hemodynamically unstable. Severe coagulopathies constitute a relative contraindication also, particularly for therapeutic procedures (Table 10.6). Colonoscopy can generally be performed safely during pregnancy but should be deferred in most instances if the indication does not require immediate resolution. In general, when the risks to the patient's health or life outweigh the potential benefits of colonoscopy, the procedure is contraindicated.

Summary

Colonoscopists must have a working knowledge of acceptable indications, and must know the risks and potential yield associated with each indication. The risks are then further adjusted by consideration of the patient's age and medical condition and the potential benefits are adjusted for the patient's age, gender, and family history. Colonoscopists must also consider their own skills in colonoscopy relative to the availability and expertise of local radiologists in determining the appropriateness of diagnostic colonoscopy in some patients. Finally, colonoscopists must consider the national consensus in their country regarding whether resources can be expended for indications such as screening or low-yield symptoms. When all of these factors are considered, colonoscopy will be used in a fashion that is best for patients and assists optimal allocation of all medical resources in the colonoscopist's nation.

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Chapter 11

Diagnostic Yield of Colonoscopy by Indication

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Introduction

Colonoscopy is the gold standard for the diagnosis of colon disease. In the hands of an experienced operator, colonoscopy should be complete in over 90% of cases [1,2]. Completion rates of 92–98% are reported in studies performed in expert centers [3–5]. The technical success of colonoscopy is dependent on gender, age, obesity, bowel preparation, history of pelvic surgery, complicated diverticular disease, and/or a history of peritonitis [6]. Diagnostic accuracy of colonoscopy is dependent on the quality of colon cleansing [7].

Patterns of endoscopy use in the USA were recently assessed based on a large national database: colonoscopy is most often performed for surveillance of prior neoplasia (24%) and evaluation of hematochezia (19%) and positive fecal occult blood test (FOBT) (15%) [8]. The principal focus of colonoscopy is on the diagnosis and removal of adenomatous polyps to prevent cancer development, and on the diagnosis of colorectal cancer [9]. Practice patterns of colonoscopy have also been assessed in Europe in a large multicenter study in 6004 patients [10]. In this study, the main indications for colonoscopy were surveillance after polypectomy or resection of colorectal cancer (17%), hematochezia (15%), uncomplicated abdominal pain (12%), screening for colorectal cancer (10%), chronic diarrhea (7%), and iron-deficiency anemia (IDA) (7%) [10].

Traditionally, the clinician has to rely on patient symptoms, clinical signs, laboratory data, expert knowledge of the literature, and personal experience to decide whether colonoscopy should be performed in a given clinical situation. It is possible to determine the *diagnostic yield* of colonoscopy by linking clinical indications and endoscopic findings. Clinicians are well aware that certain indications produce a higher diagnostic yield at colonoscopy than others. Colonoscopy for bleeding indications (hematochezia, iron-deficiency anemia (IDA), and melena with negative upper gastrointestinal endoscopy) has a high yield of cancers (1 per 9–13 colonoscopies) while the cancer detection rate is low in nonbleeding indications (1 per 109 colonoscopies) [9]. Depending on the study population and their referral indications, colonoscopy is “normal” or showed non-

relevant findings (e.g. small hemorrhoids, uncomplicated diverticulosis) in 46–76% of patients [10–15].

Diagnostic yield has traditionally been considered as the single most important parameter of a diagnostic procedure such as colonoscopy when judging its clinical usefulness [16,17]. Diagnostic yield is a critical parameter when assessing costs and benefits of colonoscopy in the context of an open-access healthcare system. However, diagnostic yield is often poorly defined; in most studies, it simply refers to the sum of pathologic endoscopic diagnoses found in the population under study but without any reference to clinical relevance. Diagnostic yield should certainly be defined in a more stringent manner, as the ability to detect an endoscopic finding that is potentially relevant to patient care. An endoscopic finding is of value in the context of patient management only if it *causes* the patient’s symptoms and if there is effective treatment. The diagnosis of diverticulosis, for example, may not have a clinical impact until there is a complication, such as diverticulitis or stenosis.

A normal (i.e. “negative”) endoscopy may have a positive impact on work lost through illness and use of drugs and medical consultations by excluding the presence of serious pathology and reassuring the patient. This favorable impact of reassurance on disease behavior has been reported for upper gastrointestinal endoscopy [18–22] and is likely to be observed also for colonoscopy [21]. Obviously, it is more complex to measure these outcomes than it is to measure the detection rate of colonoscopy. This chapter, dealing with the relationship between clinical symptoms, signs, and endoscopic diagnoses, does not therefore imply that only pathologic findings are “useful” in clinical practice.

The relationship between clinical presentation and endoscopic findings is imperfect and varies according to the indications and the patient population assessed (patient referral, selection bias). This relationship is far from perfect and is imprecise for nonspecific, albeit frequent, indications such as abdominal pain or constipation, while the correlation varies from acceptable to good for alarm symptoms such as hematochezia or IDA. For example, most adenomas do not produce symptoms [9]; adenoma yields at colonoscopy are, relatively speaking, independent of the indication, as

evidenced by the high yield of adenomatous polyps in screening colonoscopy studies, but are best predicted by demographic factors such as male gender and increasing age [9]. For example, the National Polyp Study initially included 9112 colonoscopies in patients without any history of polyps. Only 32.1% of these patients were endoscoped for existing symptoms; most of them had either a positive finding at barium enema or sigmoidoscopy, or a positive FOBT. Overall, 37.2% of the patients had adenomas and 6% had cancer [13].

In this chapter, the authors discuss the relationship between clinical presentation and endoscopic results in the light of patient characteristics (age, sex) and the main indications encountered in clinical practice. It is likely that the American CORI project (<http://www.cori.org>) will very soon produce relevant results in this field in a large number of patients. Unfortunately these data have not yet been published.

Patient characteristics

Age

Age is correlated to the presence of significant endoscopic lesions. Within a large European multicenter study (EPAGE) including 6004 patients, we previously reported that the diagnostic yield of colonoscopy increased gradually with age [10] and was significantly higher in patients over 55 years of age compared with patients under 55 years of age (odds ratio 1.42; 95% confidence interval (CI) 1.05–1.92). Polyps are found with higher frequency with increasing age [9]. Incidence rates of colorectal cancer increase in a regular fashion with age [23–25]. Age was found to be a significant predictor of colorectal cancer in patients referred for colonoscopy [26]. In patients over 55 years old, cancer was found in 5.7% of patients compared with 1.0% of patients aged 55 years or less ($P = 0.008$).

While polyps and cancer frequency increase with age, other diagnoses, such as inflammatory bowel disease (IBD), seem to follow an inverse relationship. Thus, in 1144 colonoscopies performed for various indications in an open-access system, the overall diagnostic yield was 20.7% in patients under 50 years old compared with 25.2% in patients aged 50 years and older ($P = \text{NS}$). In the younger patient group, 5% of the colonoscopies revealed polyps and 11% IBD, compared with 11% polyps and 2% IBD in patients aged 50 years and older [12].

Gender

In a large European multicenter study including 6004 patients undergoing colonoscopy [10], the diagnostic yield of colonoscopy was lower in women than in men (21.9% vs. 31.5%; odds ratio 0.59; 95% CI 0.52–0.68). In a

patient sample of 1144 consecutive colonoscopies performed for various indications, significant lesions were found more often in males (28.3%) than in females (19.7%) ($P < 0.001$; odds ratio 1.63; 95% CI 1.23–2.15). In particular, significant polyps and colorectal cancer were found with higher frequency in males (10.8% vs. 7.5%, $P = 0.05$) than in females (6.9% vs. 2.2%, $P < 0.001$) [12]. The National Polyp Study, including 9112 patients at initial colonoscopy, reported a higher frequency of adenomatous polyps in men (61.6%) than in women (38.4%) ($P < 0.0001$) [13].

Other factors influencing diagnostic yield

The EPAGE study showed that diagnostic yield was enhanced in high-volume centers (> 3000 colonoscopies/year; odds ratio 1.87; 95% CI 1.32–2.66).

Main clinical indications

Hematochezia

Careful distinction of the type and amount of bleeding is critical when discussing the diagnostic yield of hematochezia. A substantial number of published studies did not carefully characterize the nature of bleeding [9], which, among other factors, may contribute to the large range of differences in diagnostic yield reported in the literature.

Lower gastrointestinal bleeding may be acute, chronic, or occult. *Acute* lower gastrointestinal bleeding is defined as bleeding emanating from a source distal to the Treitz ligament that is of recent duration (arbitrarily defined as less than 3 days) and that may (severe acute lower gastrointestinal bleeding) or may not (moderate acute lower gastrointestinal bleeding) result in hemodynamic instability [27]. In most cases, acute rectal bleeding originates in the lower gastrointestinal tract, although an upper gastrointestinal origin is found in 11% of patients [28,29]. Acute lower gastrointestinal bleeding ceases spontaneously in the majority of cases [29–31]. In patients under 50 years old, an anorectal bleeding site is more commonly involved [32,33]. The most common causes vary greatly between studies. Table 11.1 and Fig. 11.1 show the six published studies [34–39], allowing clear identification of acute lower gastrointestinal bleeding, one of which [38] does not distinguish between cancers and adenomas. In these studies, the yield of colonoscopy was found to be on average 18.5% (range 3–22%) for colorectal cancer and 8.2% (range 4–9%) for polyps. Other significant findings (Table 11.1 & Fig. 11.1) were vascular ectasia, IBD, and diverticula. The source of bleeding was identified and reported in 75% of the 551 patients pooled in this table [34,38,39].

Table 11.1 Diagnostic yield of colonoscopy in patients with acute lower gastrointestinal bleeding.

Reference	Comment	Patients with hematochezia	Cancer (%)	Adenoma (%)	Vascular ectasia (%)	Inflammatory bowel disease (%)	Diverticula (%)
Caos <i>et al.</i> [34]*	Prospective; negative sigmoidoscopy	35	3	8	14	6	23
Church [35]	Prospective	27	11	4	11	4	22
Forde [36]*		25	12	8	8	4	20
Guillem <i>et al.</i> [37]		55	13	9	11	9	35
Jensen & Machicado [38]*	Prospective; negative sigmoidoscopy	100	11		30		17
Rossini <i>et al.</i> [39]*		409	22	8	4	12	15
Total		551 [†]	18.5 [†]	8.2 [†]	9.5	8.9	17.7

* Site and cause of active hemorrhage identified.

† Excluding data from Jensen & Machicado [38].

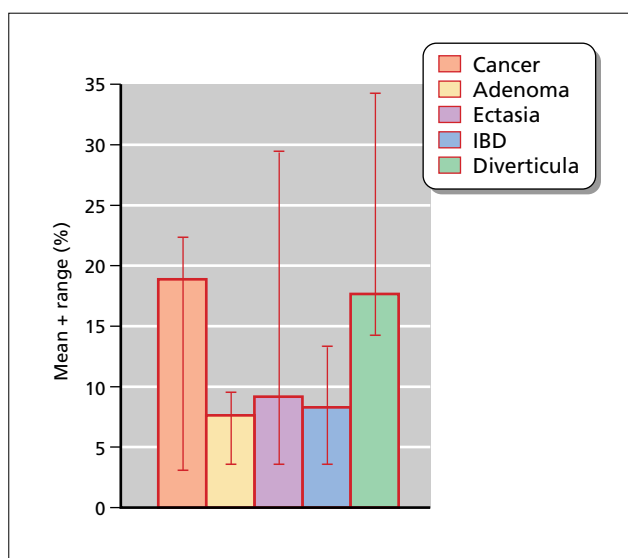


Fig. 11.1 Diagnostic yield of colonoscopy in acute lower gastrointestinal bleeding. Data from six studies (three prospective studies), 551 patients.

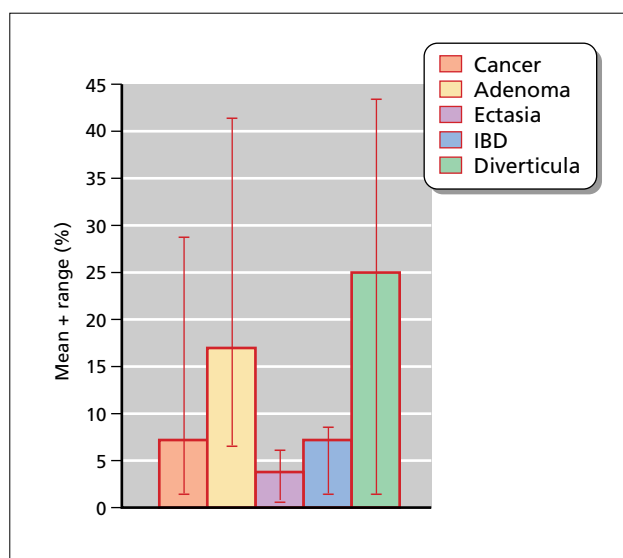


Fig. 11.2 Diagnostic yield of colonoscopy in nonemergency lower gastrointestinal bleeding. Data from 20 studies (12 prospective studies), 6952 patients.

Chronic lower gastrointestinal bleeding (nonemergency rectal bleeding) implies the passage of blood per rectum over a period of several days or more and is generally at a slow or intermittent rate (small amounts of blood on the toilet paper, blood dripping from the anus after a bowel movement). Chronic lower gastrointestinal bleeding is reported in 9–19% of the population in a given year [40–42]. Table 11.2 and Fig. 11.2 show the diagnostic yield of colonoscopy in nonemergency lower gastrointestinal bleeding. Colorectal cancer was found on average in 7.4% (range 2–29%) and adenomas in 17% (range 4–43%) of the patients [10–12,35,37,43–56] (Fig. 11.3). In some of these studies, patients had had a prior “negative” barium enema, which obviously does not preclude a high prevalence of adenomas and cancers at colonoscopy [37,46,55,56]. In patients with nonemer-

gency rectal bleeding, it was calculated, based on the available literature, that 8.9 colonoscopies were needed to detect one cancer [9].

Patients with hemorrhoids have clinically relevant lesions of the colon in 37% [57] to 62% [51]. In patients under 40 years old with chronic lower gastrointestinal bleeding, significant pathology was found at colonoscopy in 21% [43]. A recent prospective study in 468 patients showed that colonic neoplasms were found in 18% of patients with scant hematochezia (2% cancers, 16% adenomas) and that most of these tumors were located within the reach of a sigmoidoscope [47].

A recent European multicenter study in 6004 patients referred for colonoscopy confirmed that hematochezia as the main indication has a higher yield than non-bleeding indications (odds ratio 1.5; 95% CI 1.3–1.7)

Table 11.2 Diagnostic yield of colonoscopy in patients with nonemergency lower gastrointestinal bleeding.

Reference	Comment	Patients with hematochezia	Cancer (%)	Adenoma (%)	Vascular ectasia (%)	Inflammatory bowel disease (%)	Diverticula (%)
Acosta <i>et al.</i> [43]	Patients 40 years or younger; minimal passage of blood or occult blood	280	0.3	8.9	1.1	8.6	2.1
Bat <i>et al.</i> [44]	Patients 80 years or older	101	28.7	34	NS	NS	NS
Berkowitz & Kaplan [45]		123	8.9	12.2	5.7	8.1	20.3
Brand <i>et al.</i> [46]	Previous barium enema negative	221	7.2	23	4.1	5	20.8
Brenna <i>et al.</i> [11]	Prospective	194	11.8	17	NC	13	NC
Church [35]	Prospective	174	10.3	29.3	2.3	6.9	6.9
De Bosset <i>et al.</i> [12]	Prospective	256	9.8	13.3	1.2	4.3	NS
Eckardt <i>et al.</i> [47]	Prospective; patients with scant hematochezia	468	2	16	NS	7	NS
EPAGE study	Prospective; unpublished results	901	7.3	12.3	1.3	6.4	16.3
Fine <i>et al.</i> [48]	Prospective	312	10	8	4	11	13.8
Goulston <i>et al.</i> [49]	Prospective; patients > 40 years old; several diagnoses per patient	145	10	17	0.6	2.8	26
Graham <i>et al.</i> [50]	Prospective	33	9	42	3	9	27
Guillem <i>et al.</i> [37]	Colonoscopy and barium enema findings	224	15	27	2	8	16
Irvine <i>et al.</i> [51]	Prospective	71	7	37	4.2	8.4	46
Morini <i>et al.</i> [14]	Prospective; personal communication	265	10.6	17.3	0.4	5.2	NS
Mulcahy <i>et al.</i> [52]	Many patients had more than one diagnosis; polyp > 5 mm	1766	4	15	4	6.6	36
Neugut <i>et al.</i> [53]	Prospective; polyp > 1 cm or with high-grade dysplasia	861	8.6	25	NS	NS	NS
Segal <i>et al.</i> [54]	Prospective	103	3.8	30	NS	7.7	NS
Swarbrick <i>et al.</i> [55]	Had negative barium enema + sigmoidoscopy	239	10	16	1.7	10	11
Teague <i>et al.</i> [56]	Had negative barium enema	215	13	14	2	7	15
Total		6952	7.4	17	3.2	7	25

NC, not clear; NS, not stated.

(EPAGE 2002, unpublished results). In particular, colon cancer was detected more often in the case of hematochezia (odds ratio 2.6; 95% CI 1.9–3.5) compared with nonbleeding indications, in contrast to the adenoma detection rate, which was comparable between these patient groups; this is in line with previous data [9].

Church [35] reported that polyps were discovered more frequently (22%) in patients with “suspicious bleeding” (i.e. dark-red blood mixed with stool) than in outlet-type bleeding (4%) (bright-red blood during or after defecation). However, a prospective evaluation had previously shown that general practitioners and gastroenterologists were not able to reliably distinguish anal from colonic bleeding by history-taking alone [49].

Bat and colleagues [44] compared the yield of colonoscopy in patients aged 80 years and older in 101 bleeding

patients (hematochezia of at least 2 months’ duration) vs. 335 nonbleeders. Colon cancer was found in 29 of the bleeders (28.7%) and in 9.8% of the nonbleeders, while the rate of adenoma detection was similar (34% vs. 29%) in both groups. Not surprisingly, the cancer rate in this study is the highest reported for rectal bleeding due to the very elderly population under study.

Iron-deficiency anemia

IDA is encountered frequently in clinical practice. In 3027 outpatients and 3012 asymptomatic employees assessed prospectively, IDA was found in 6.8% of female patients, 2.4% of male patients, 6.0% of female employees, and 0.5% of male employees [58]. In men and postmenopausal women, IDA is principally due to gas-

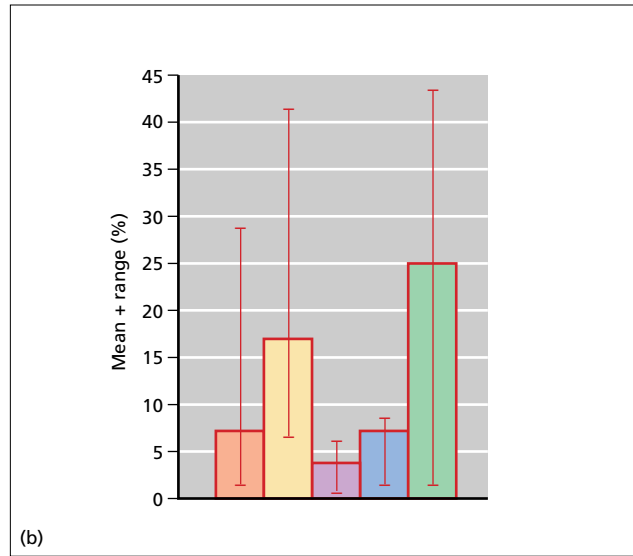
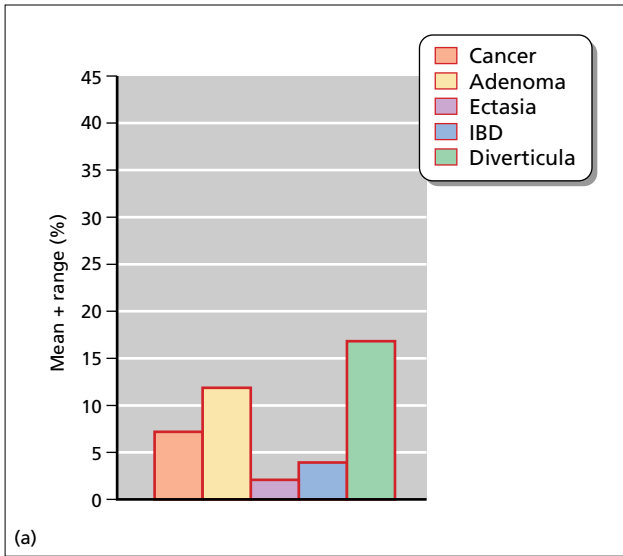


Fig. 11.3 Diagnostic yield of colonoscopy in nonemergency lower gastrointestinal bleeding: (a) EPAGE; (b) all studies.

traintestinal blood loss [59,60], generally in the form of occult bleeding [61] in patients without an obvious source of bleeding.

The diagnostic yield of endoscopy (upper gastrointestinal *and* colonoscopy overall) in IDA ranges from 12 to 86%, a relevant endoscopic lesion being found on average in 58% [61–70]. An upper gastrointestinal source was found to be the most common source of IDA (36–60% of patients), while a lower gastrointestinal source was present in 16–30% of patients [61,64,66,71,72]. No bleeding source was found in 14–41% of the patients [61,62,66,71]. Although upper gastrointestinal lesions were frequently found, the most significant concern remains the issue of colorectal cancer, particularly in patients over 50 years old. Even if an upper gastrointestinal lesion is detected, colonoscopy has a high detection rate for relevant lesions: 16% of patients with a benign upper gastrointestinal lesion were found to have colon cancer [64], while another study found 17% of patients to have both an upper and a lower gastrointestinal lesion [62], suggesting that colonoscopy should be performed even when an upper gastrointestinal lesion is found, at least in patients over 50 years old.

Most patients with IDA do not have symptoms suggesting a gastrointestinal lesion [61,64]. There is controversy as to whether site-specific symptoms are able to accurately predict the likelihood of a gastrointestinal lesion in IDA [73]. Most studies found a weak correlation or no relationship at all between patient history and the anatomic location of any lesion [61,66,71].

Colonoscopy has a substantial yield in IDA. Table 11.3 pools patients with IDA reported in the literature

[10,12,14,45,61,62,66,68,72,74–77]; 6% of these patients had colorectal cancer (range 0.4–18.1%) and 7.3% had adenomas (range 2.0–14.5%). A significant proportion of patients had vascular ectasias (4.4%) and IBD (11.7%). Three of these studies do not clearly report the rate of adenomas found at colonoscopy [66,74,77] (Fig. 11.4).

A recent large European multicenter study in 6004 patients referred for colonoscopy (EPAGE study 2002, unpublished results) assessed the yield in patients with IDA, which was present in 387 patients (Table 11.3 & Fig. 11.5). As compared to nonbleeding indications, the yield in IDA was particularly high for cancer (odds ratio 4.1; 95% CI 2.9–5.9) while adenomas were present less

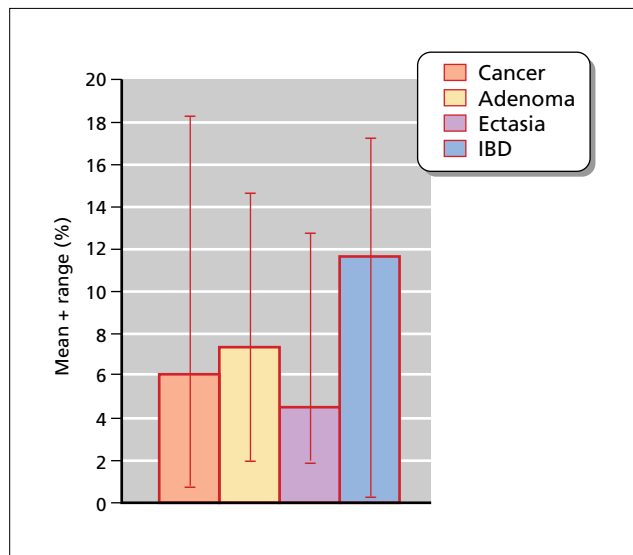


Fig. 11.4 Diagnostic yield of colonoscopy in patients with iron-deficiency anemia. Data from 13 studies (eight prospective studies), 2751 patients.

Table 11.3 Diagnostic yield of colonoscopy in patients with iron-deficiency anemia (IDA).

Reference	Comment	Patients with IDA	Cancer (%)	Adenoma (%)	Vascular ectasia (%)	Inflammatory bowel disease (%)	Diverticula (%)
Alemayehue <i>et al.</i> [74]	IDA and FOBT positive	90	9	NC	NS	NS	
	IDA and FOBT negative	38	3	NC	NS	NS	
Berkowitz & Kaplan [45]	Polyps > 1 cm or with high-grade dysplasia; 69% cecal intubation	46	2.2	8.7	NS	17.4	6.5
Bini <i>et al.</i> [68]	Premenopausal women	186	3	2	NS	1	
De Bosset <i>et al.</i> [12]	Prospective; upper gastrointestinal negative	89	6.7	7.9	5.6	1.1	
EPAGE study	Prospective; unpublished results	387	11.4	8.3	1.7	2.8	18.6
Gordon <i>et al.</i> [66]	Patients > 50 years	170	9	NS	3	4	
Joosten <i>et al.</i> [75]	Prospective; patients > 70 years	69	14.5	14.5	8.7	0	
Kepczyk & Kadakia [62]	Prospective; adenoma > 1 cm	70	5.7	10	8.6	1.4	
Morini <i>et al.</i> [14]	Prospective; personal communication	33	18.1	11	12.1	0	
Nahon <i>et al.</i> [76]	Women; polyps > 1.5 cm	241	6.2	4.1	2.1	0.4	
Nakama <i>et al.</i> [77]	Prospective						
	IDA and FOBT positive	208	13	NS	NS	NS	
Rockey & Cello [61]	IDA and FOBT negative	924	0.4	NS	NS	NS	
	Prospective	100	11	5	5	2	
Zuckerman & Benitez [72]	Prospective; FOBT positive and/or IDA	100	6	14	13	NS	
Total		2751	6	7.3	4.4	11.7	

FOBT, fecal occult blood test; NC, not clear; NS, not stated.

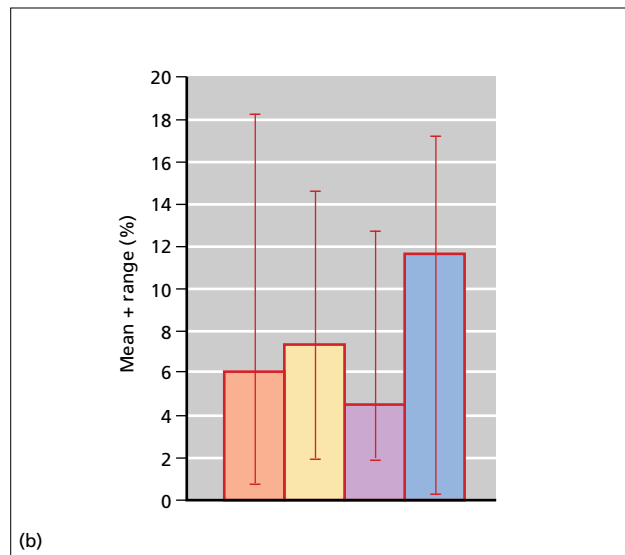
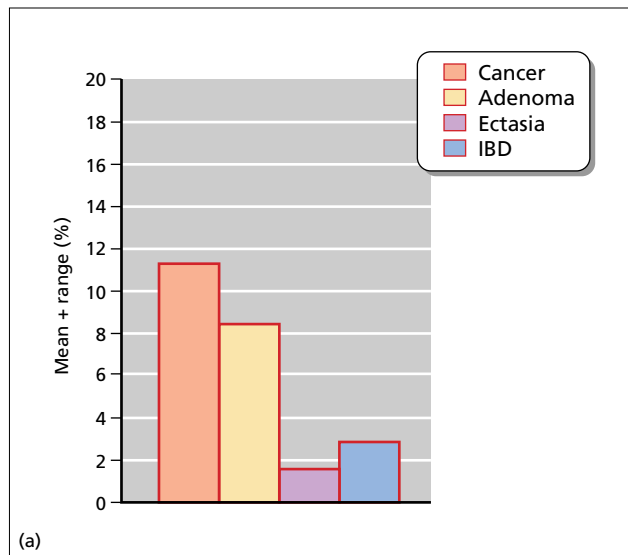


Fig. 11.5 Diagnostic yield of colonoscopy in patients with iron-deficiency anemia: (a) EPAGE; (b) all studies.

frequently (odds ratio 0.5; 95% CI 0.35–0.74) compared with nonbleeding indications.

In 241 women with IDA, a significant endoscopic lesion potentially causing IDA was found in 35.6% of patients at upper gastrointestinal endoscopy and in 13.7% at

colonoscopy [76]. Almost all significant colonic lesions were observed in patients over 50 years old. Multivariate analysis revealed abdominal symptoms, age over 50 years, and hemoglobin < 9 g/dL as predictive factors for significant endoscopic lesions [76]. The diagnostic yield for cancer is particularly high in the case of IDA and FOBT-positive results (9–13%) compared with 0.4–3% in isolated IDA [74,77].

Table 11.4 Diagnostic yield in surveillance colonoscopy after polypectomy.

Reference	Comment	Number of patients with surveillance colonoscopy	Number of examinations	Cancer* (%)	Polyps* (%)
Blumberg <i>et al.</i> [79]	Two follow-up colonoscopies	204	408	0.5	72
Brenna <i>et al.</i> [11]	Prospective	44	44	0	32
Citarda <i>et al.</i> [80]	Mean follow-up 10.5 years	1693	NS	4	NS
De Bosset <i>et al.</i> [12]	Prospective; polyps > 1 cm or with high-grade dysplasia	76	76	0	5.2
EPAGE study	Prospective; unpublished results	594	594	1.5	28.6
Jorgensen <i>et al.</i> [81]	Prospective randomized	1056	2721	0.9	27
Lund <i>et al.</i> [82]	Prospective randomized	220	NS	0.5	25
Matek <i>et al.</i> [83]		592	1281	0.3	16
McFarland <i>et al.</i> [84]	Prospective	84	252	2.3	12
Morini <i>et al.</i> [14]	Prospective; personal communication	137	137	0	29.2
Nava <i>et al.</i> [85]		44	105	0	60
Neugut <i>et al.</i> [53]	Prospective	118	165	0	30
Von Stolk <i>et al.</i> [86]	Prospective; follow-up colonoscopy at 1 and 4 years	479	958	0	35
Waye & Braunfeld [87]		133	133	0	56
Winawer <i>et al.</i> [88]	Prospective; follow-up 3 years	973	1311	0.5	29
Woolfson <i>et al.</i> [89]		109	109	0	50
Total		6556		0.5	30.4

NS, not stated.

* Percentage of patients with given lesion at one or more surveillance examinations.

Anemia has been reported to be associated with the presence of colorectal cancer. In 653 patients undergoing colonoscopy [26], colon cancer was found in 10.0% of patients with anemia but in only 3.1% of patients without anemia ($P = 0.001$). Iron deficiency is a predictor of colon cancer, as 12.7% of these patients had a cancer at colonoscopy compared with 3.5% without iron deficiency ($P = 0.001$). Approximately 13 colonoscopies are necessary to detect one cancer if the main indication for performing colonoscopy is IDA [9].

Follow-up of polyps

Surveillance after polypectomy is discussed in Chapter 39. This chapter briefly summarizes the diagnostic yield for this indication without particular emphasis on colorectal cancer screening studies and screening intervals.

No single symptom has good predictive value for the diagnosis of colon polyps. Thus most polyps are asymptomatic [78], with the occasional exception of very large polyps. The indication for performing follow-up colonoscopy after polypectomy is thus not based on clinical symptoms.

Table 11.4 and Fig. 11.6 summarize the published literature regarding the yield of surveillance colonoscopy after polypectomy [10–12,53,79–89], including the

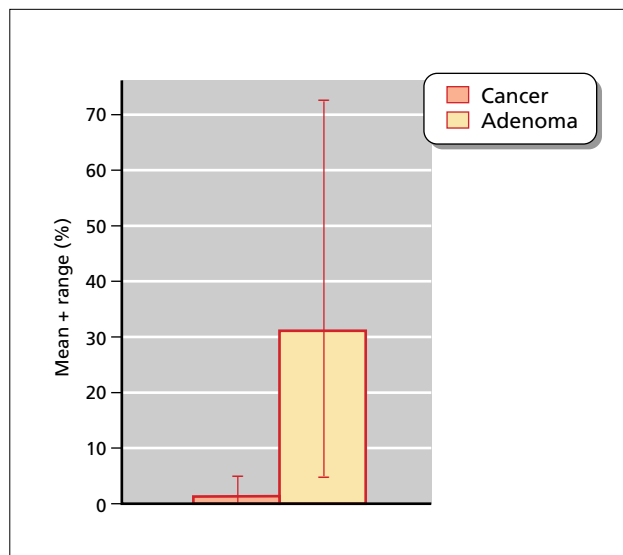


Fig. 11.6 Diagnostic yield of colonoscopy after polypectomy. Data from 16 studies (10 prospective studies), 6685 patients.

overall number of colonoscopies performed. Polyps are found on average in 30.4% (range 5–72%) and colorectal cancer in 0.5% (range 0–2.3%) of the cases. In comparison with other indications, the yield of surveillance colonoscopy after polypectomy is thus relatively low for

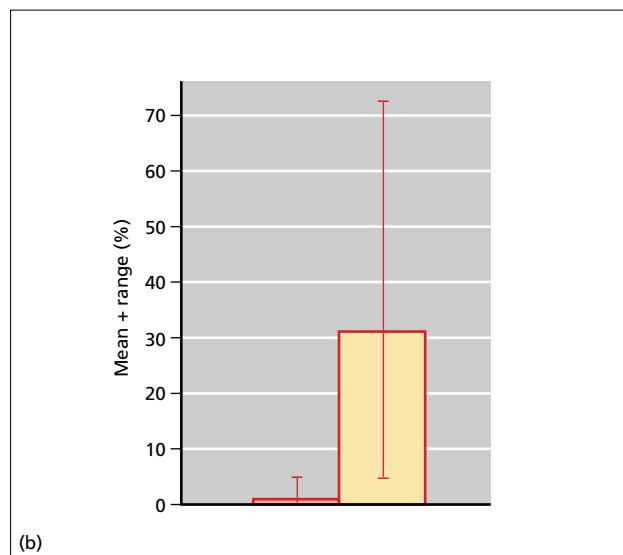
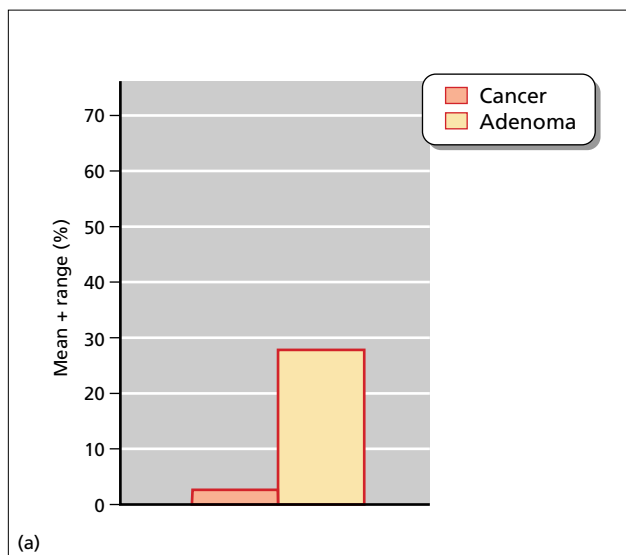


Fig. 11.7 Diagnostic yield of colonoscopy after polypectomy: (a) EPAGE; (b) all studies.

cancers and high for newly discovered adenomas [9]. Rex [9] calculated that 317 colonoscopies were necessary to detect one cancer if the main indication is surveillance after polypectomy. The cumulative proportion of recurrent polyps depends on the duration of follow-up. As an example, the cumulative proportion of recurrent polyps was close to 20, 35, and 50% after 2, 4, and 8 years of follow-up, respectively [90]. Results of the EPAGE study are shown in Fig. 11.7.

Adenomas detected at surveillance colonoscopy are generally smaller in size than those found at the initial examination [53,81,83,85,87–89]. Male gender, age, and the presence of multiple or large adenomas at initial examination resulted in a higher yield of polyps during the surveillance examination [81,88]. Multiple adenomas are predictive of advanced adenomas (> 1 cm in size, high-grade dysplasia) at follow-up colonoscopy.

Surveillance colonoscopy and polypectomy reduce the incidence of and mortality from colorectal cancer [81,88].

Follow-up after resection of colorectal cancer

It is important to distinguish between “clearing colonoscopy” and “follow-up colonoscopy” in the context of surveillance after cancer resection. The first term refers to a procedure performed before resection (or shortly after in patients with an obstruction) in order to identify and remove synchronous colonic neoplasia. The yield of clearing colonoscopy is high, showing synchronous cancer in 2.2% and synchronous adenomas in 27% of patients [91,92].

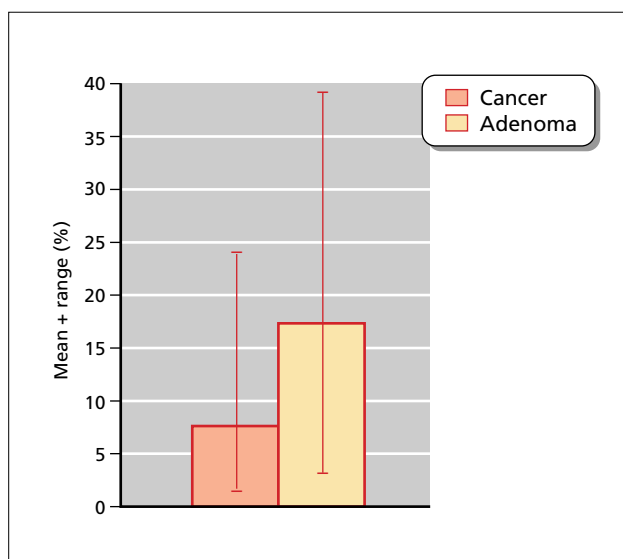


Fig. 11.8 Diagnostic yield of colonoscopy after colorectal cancer resection. Data from 20 studies (14 prospective studies), 3698 patients.

“Follow-up colonoscopy” or “surveillance colonoscopy” refers to interval colonoscopy after resection. Metachronous and anastomotic cancers occur with comparable frequency in approximately 2.7 and 3.0% of patients during surveillance [9]. However, in some studies, it remains unclear whether a clearing colonoscopy was performed before resection [11,93–96], which means that some of these tumors certainly remained unrecognized at the time of surgery.

Table 11.5 and Fig. 11.8 show the results of studies pooling 3698 patients undergoing surveillance colonoscopy after cancer resection with various time intervals and one or several colonoscopies per patient [10–12,

Table 11.5 Diagnostic yield of surveillance colonoscopy after colorectal cancer resection.

Reference	Comment	Number of patients	Number of colonoscopies	Cancer (anastomotic recurrence and metachronous)* (%)	Adenoma* (%)
Berkowitz & Kaplan [45]		52		2	17
Brady <i>et al.</i> [93]	Prospective; follow-up 2–8 years	207	445	7	NC
Brenna <i>et al.</i> [11]	Prospective	51	51	3.9	40
Carlsson <i>et al.</i> [91]	At least two postoperative colonoscopies	129	358	0.8	33
De Bosset <i>et al.</i> [12]	Prospective	66	66	3	4.5
EPAGE study	Prospective; unpublished results	284	284	3.3	19.1
Hall <i>et al.</i> [97]	Prospective	54	54	2	6
Jahn <i>et al.</i> [94]		539	1244	4	NC
Juhl <i>et al.</i> [95]	Prospective	133	316	10	38
Kjeldsen <i>et al.</i> [98]	Prospective randomized trial				
	Intensive follow-up	290		19	NS
	No follow-up	307		15	NS
	Examination at 5 and 10 years				
Kronborg <i>et al.</i> [92]	Prospective	239	710	3.8	13
Larson <i>et al.</i> [99]		68	135	7.4	35
McFarland <i>et al.</i> [84]	Prospective; mean follow-up 4.3 years	74	237	2.7	34
Morini <i>et al.</i> [14]	Prospective; personal communication	97	97	1	17.5
Nava & Pagana [96]	Follow-up 4 years	240	304	11.6	21.3
Patchett <i>et al.</i> [100]	Prospective; mean follow-up 5.5 years	132		6.1	11.4
Pietra <i>et al.</i> [101]	Prospective				
	Conventional follow-up	103		20	NS
	Intensive follow-up	104		25	NS
Shoemaker <i>et al.</i> [102]	Prospective				
	Standard follow-up	158	154	3.3 (5 of 13 diagnosed by colonoscopy)	14.5
	Intensive follow-up	167	577	1.8 (3 of 10 diagnosed by colonoscopy)	20
Unger & Wanebo [103]	Prospective	56	56	1.8	21
Weber <i>et al.</i> [104]	Prospective	75	197	4	17
Total		3625		7.6	17.2

NC, not clear; NS, not stated.

* Percentage of patients with given findings at one or more examinations.

14,45,91–104]. Most of these studies are prospective. The average yield of colon cancer was 7.6% (range 0.8–25%) in these series. The overall cancer detection rate is higher in surveillance after cancer resection compared with colonoscopy performed for surveillance after polypectomy (see Tables 11.4 & 11.5). In the setting of surveillance after cancer resection, it was calculated that 74 procedures were needed to detect one anastomotic recurrence and 82 to detect one metachronous cancer [9]. Results of the EPAGE study are shown in Fig. 11.9.

Polyps were found on average in 17.2% (range 6–40%) in surveillance after cancer resection.

Occult gastrointestinal bleeding (FOBT-positive stool)

This section briefly summarizes the diagnostic yield of isolated FOBT positivity without particular emphasis on colorectal cancer screening studies, screening intervals,

or cancer risk related to family history, and without any reference to the various FOBT methods. Screening colonoscopy is discussed in Chapter 12.

Studies assessing the yield of FOBT focus on adenomas and cancer. The yield of colonoscopy for cancer and adenomas is high in otherwise asymptomatic patients with a positive FOBT. Factors influencing this yield are patient age and whether rehydration of the test is done (resulting in reduced specificity). Most studies used FOBT without rehydration, and full colonoscopy was performed if a single or several tests were positive. In these circumstances, colonoscopy will detect colorectal cancer in 10% (range 7–22%) and adenomatous polyps in 35% (range 19–43%) of FOBT-positive subjects [9].

Table 11.6 shows the diagnostic yield in patients undergoing colonoscopy for a positive FOBT, irrespective of the study setting (mass screening, case finding) (Fig. 11.10). In these patients, colon cancer is found on average in 4.6% (range 1–22%) and polyps on average

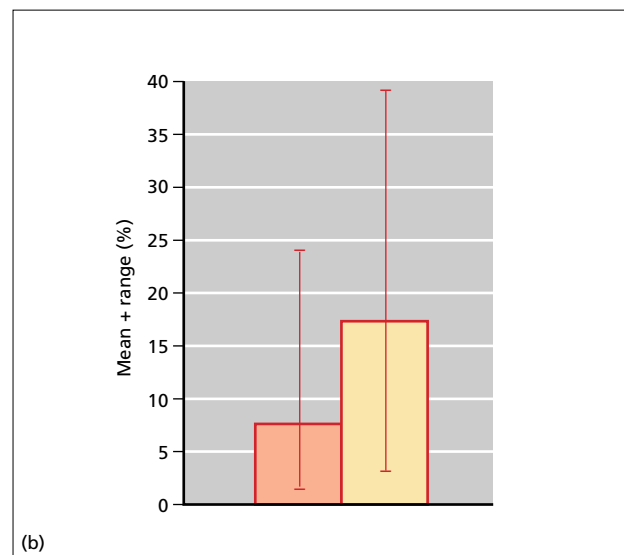
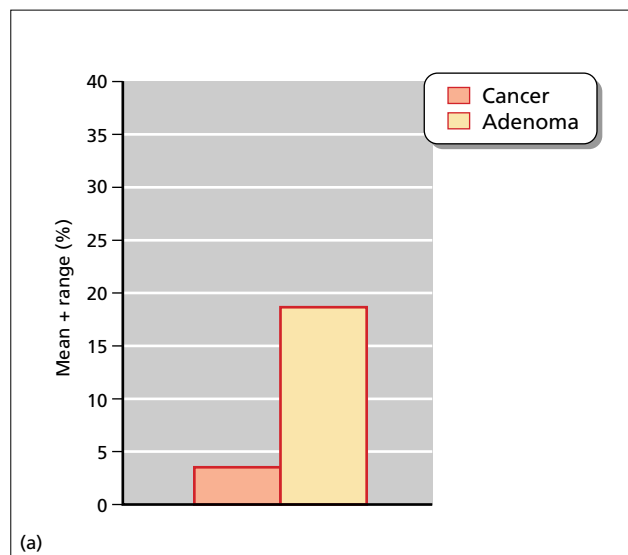


Fig. 11.9 Diagnostic yield of colonoscopy after colorectal cancer resection: (a) EPAGE; (b) all studies.

in 14.9% (range 6–43%) [10,12,35,46,68,72,77,105–116]. In a large European multicenter study, we recently confirmed that the overall yield of relevant diagnoses in FOBT-positive patients was enhanced compared with nonbleeding indications (odds ratio 1.5; 95% CI 1.03–2.2) (EPAGE study 2002, unpublished results) (Fig. 11.11). As compared to nonbleeding indications, only adenomas were detected with higher frequency in FOBT-positive patients (odds ratio 1.5; 95% 1.0–2.4), while cancer did

not occur significantly more often (odds ratio 1.02; 95% CI 0.4–2.8).

It has been calculated that 9.8 colonoscopies are necessary to detect one cancer in patients with one positive FOBT [9]. Repeating the FOBT in subjects who initially test positive, and performing colonoscopy only if a second test is positive, increases the positive predictive value of FOBT [117,118]. Thus, the yield of colonoscopy in individuals in whom two consecutive tests are positive is as high as 33% for adenomas and 38% for colorectal cancer [9]. In this situation, it was calculated that approximately 2.7 colonoscopies are necessary to detect one cancer [9].

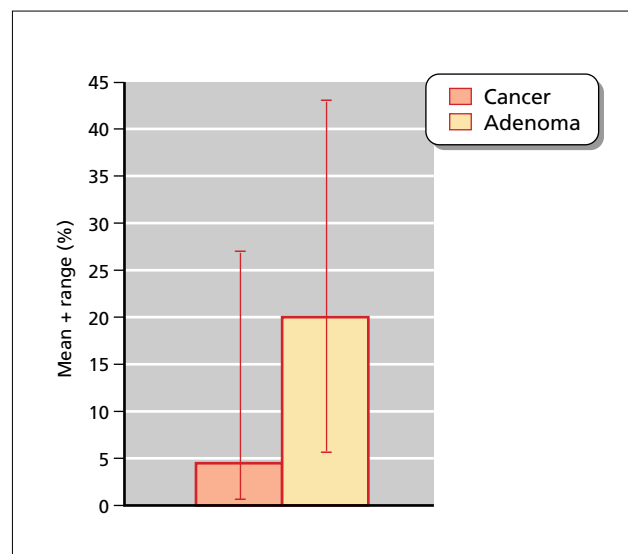


Fig. 11.10 Diagnostic yield of colonoscopy in patients with positive fecal occult blood test. Data from 22 studies (eight prospective studies), 21 395 patients.

Diarrhea

Acute diarrhea generally results from a wide variety of infectious pathogens. The use of endoscopy is generally not recommended in these patients unless they do not respond to a course of empirical therapy [119]. Chronic diarrhea means the passage of frequent or loose stools over a time period of 14 days or more. Kalra and Hamlyn [120] report an overall yield of 38% in patients with chronic diarrhea (colitis, polyps, diverticula, cancer; percentages not specified) and of 91% when diarrhea was associated with bleeding.

Table 11.7 and Fig. 11.12 summarize the diagnostic yield of colonoscopy in 1711 patients with chronic diarrhea. Colorectal cancer and adenomas were found on average in 0.4% (range 0–1.4%) and 3.2% (range 0–10.2%) respectively [10,12,14,121–123]. As compared to screening colonoscopy or colonoscopy in patients with nonspecific abdominal symptoms (pain, constipation, altered bowel habits), the diagnostic yield for polyps and colon cancer is distinctly lower in diarrhea.

Table 11.6 Diagnostic yield of colonoscopy in patients with positive fecal occult blood test (FOBT).

Reference	Comment	Number of patients	Cancer (%)	Adenoma (%)	Vascular ectasia (%)
Ahlquist <i>et al.</i> [105]	Prospective; nonrehydrated	1016	4	17	NS
Bini <i>et al.</i> [68]	Nonrehydrated				
	Adenomas > 1 cm	390	11	12	0.5
	(All adenomas)			(38)	
Brand <i>et al.</i> [46]	FOBT positive and/or IDA	59	10	25	NS
Church [35]	FOBT positive or anemia	68	19	25	NS
	+ rectal bleeding				
De Bosset <i>et al.</i> [12]	Prospective; nonrehydrated	69	8.7	18.8	NS
Eckardt <i>et al.</i> [47]	Prospective; nonrehydrated	299	4	19	NS
EPAGE study	Prospective; nonrehydrated	128	3.1	21.1	NS
	Unpublished results				
Frommer <i>et al.</i> [106]	Nonrehydrated	50	22	26	NS
	Rehydrated	91	16	23	NS
Frühmorgen & Demling [107]	Prospective; nonrehydrated	127	10	40	NS
Grazzini <i>et al.</i> [108]	Prospective	268	12.3	28	NS
Hardcastle <i>et al.</i> [109]	Prospective; first screening; nonrehydrated	837	9.9	37	NS
Hardcastle <i>et al.</i> [110]	Nonrehydrated	618	10	43	NS
Kewenter <i>et al.</i> [111]	Negative on repeat	108	1	6	NS
	Positive on repeat	67	15	22	NS
Kronborg <i>et al.</i> [112]	Prospective; nonrehydrated	209	18	41	NS
Liebermann <i>et al.</i> [113]	Rehydrated	239	4.1	40	NS
Mandel <i>et al.</i> [114]	Prospective; rehydrated; polyps > 1 cm				
	Annual follow-up	8663	1.6	6.6	NS
	Biennial follow-up	5170	2.26	8.6	NS
Nakama <i>et al.</i> [77]	Immunochemical				
	FOBT positive, IDA positive	208	13	NS	NS
	FOBT positive, IDA negative	624	8.3	NS	NS
Rasmussen & Kronborg [115]	Nonrehydrated; 15 years; eight screening rounds; adenomas > 1 cm	1536	11.8	28.6	NS
Winawer <i>et al.</i> [116]	Nonrehydrated	467	11	19	NS
Zuckerman & Benitez [72]	Nonrehydrated; FOBT positive with or without IDA	100	6	14	5
Total		21 395	4.6	14.9	

IDA, iron-deficiency anemia; NS, not stated.

Diarrhea alone thus does not appear to constitute a clear indicator of colonic neoplasia. In contrast, IBD is found on average in 10.2% of the patients (range 3.5–23%). Results of the EPAGE study are shown in Fig. 11.13.

In patients with isolated diarrhea, biopsies may establish a clinically useful diagnosis (e.g. collagenous colitis, microscopic colitis) in 5–31% of cases [121–126]. Fine and colleagues [121] report that a pathologic histology was observed in 122 (15%) of 809 patients with chronic nonbloody diarrhea, most of whom had microscopic colitis (80 patients) or Crohn's disease (23 patients). Interestingly, a correct assessment of colonic histology could have been made from biopsies of the distal colon alone in 99.7% [121]. It is unclear how many biopsies should be obtained in the work-up of chronic diarrhea in

a macroscopically normal colon [127]. The endoscopic yield of colonoscopy is particularly high in human immunodeficiency virus (HIV)-infected patients with chronic diarrhea, negative stool studies, and low CD4 counts (< 100/mm³) [128].

Abdominal pain and altered bowel habit

Abdominal pain is a significant, and often isolated, symptom in patients undergoing colonoscopy, associated or not with altered bowel habit (irritable bowel syndrome). The combination of abdominal pain and altered bowel habit is a frequent indication for colonoscopy [10]. Most textbooks emphasize that abdominal pain or change in bowel habit occurring in a patient in the colorectal cancer

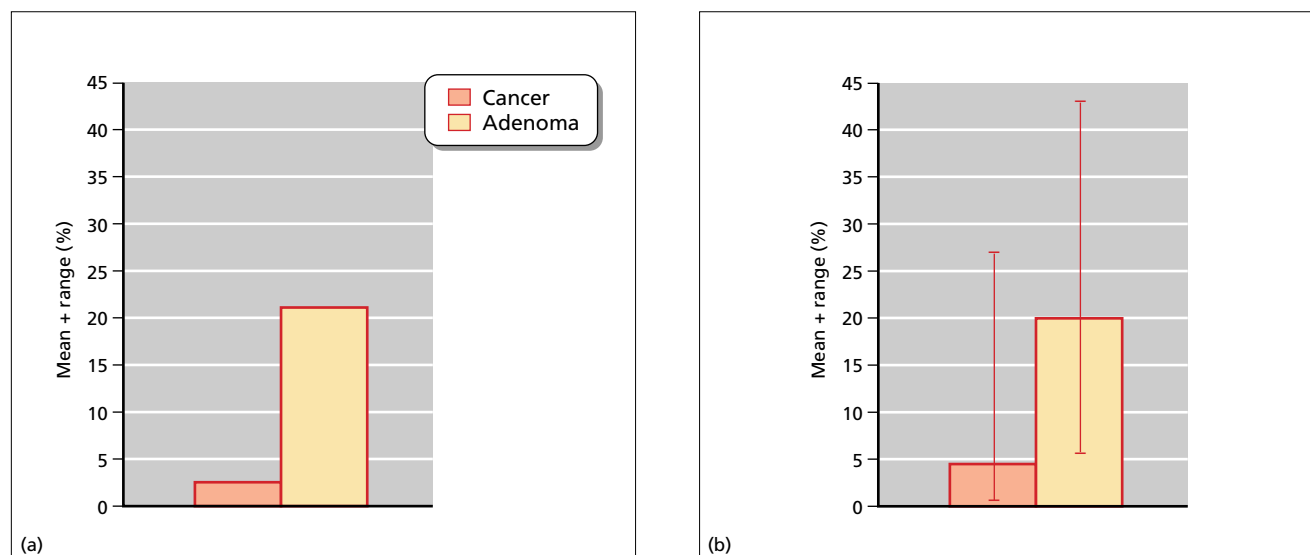


Fig. 11.11 Diagnostic yield of colonoscopy in patients with positive fecal occult blood test: (a) EPAGE; (b) all studies.

age range should prompt colonic evaluation to exclude cancer [129].

However, as shown in Table 11.8, the diagnostic yield of colonoscopy in patients with abdominal pain or altered bowel habit (particularly constipation) is low [9–12,45,53,130–136], especially in females and patients under 40 years of age [133]. Thus, colorectal cancer was found on average in 1.6% (range 0–5%) and adenomas in 12.6% (range 2.6–38%) of the patients (Fig. 11.14). Nonspecific abdominal symptoms, such as abdominal pain with or without altered bowel habit (particularly constipation), are thus not predictive of relevant lesions at colonoscopy, as they also occur with a similar frequency in an asymptomatic screening population. Although these nonspecific symptoms may not by themselves be appropriate indications for colonoscopy given

their low diagnostic yield, age-appropriate colorectal cancer case-finding may be pursued in these patients comparable to a screening population. In addition, colonoscopy confers patient reassurance that may be beneficial for the future course of symptoms. Results of the EPAGE study are shown in Fig. 11.15.

Miscellaneous indications

Screening for colorectal cancer

Since colorectal cancer screening is discussed in Chapter 12, we do not discuss the findings of endoscopic diagnoses in screening studies. We report here the results of a large European multicenter trial in 6004 consecutive patients undergoing colonoscopy for various indications; 600 patients were asymptomatic and had the procedure for screening purposes. The overall yield was 44.2%, including cancer in 1%, adenomas in 14%,

Table 11.7 Diagnostic yield of colonoscopy in HIV-negative patients with diarrhea.

Reference	Comment	Number of patients	Cancer (%)	Adenoma (%)	Inflammatory bowel disease (%)	Collagenous or lymphocytic colitis (%)
De Bosset <i>et al.</i> [12]	Prospective	90	1.1	6.6	13.3	10
EPAGE study	Prospective; unpublished results	412	1.4	10.2	9.5	7.2
Fine <i>et al.</i> [121]		809	0	0	3.5	10
Morini <i>et al.</i> [14]	Prospective; personal communication	27	0	7.4	7.4	
Patel <i>et al.</i> [122]	Sigmoidoscopy ($n = 77$) or colonoscopy ($n = 128$) Adenomas > 5 cm	205	0	1.5	3.5	2.4
Shah <i>et al.</i> [123]	Polyps < 3 cm not considered	168	0	0.6	16	7.8
Total		1711	0.4	3.2	6.2	8

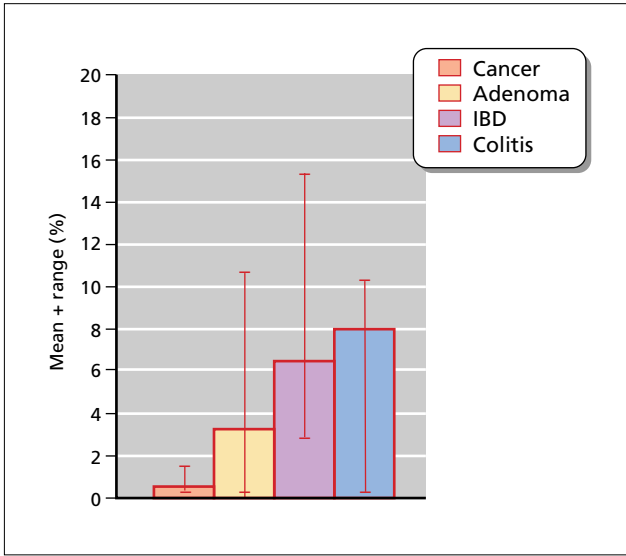


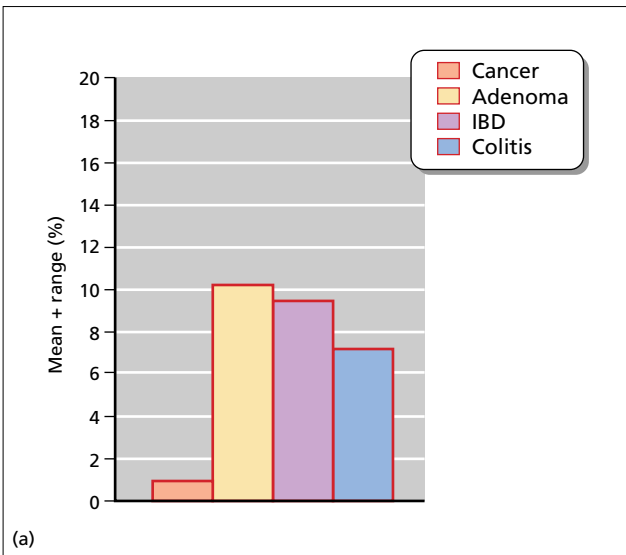
Fig. 11.12 Diagnostic yield of colonoscopy in HIV-negative patients with diarrhea. Data from six studies (four prospective studies), 1024 patients.

diverticulosis in 11.8%, and IBD in 0.5% (EPAGE study 2002, unpublished results).

Unexplained melena

In patients with melena not explained by upper gastrointestinal endoscopy, colonoscopy yields a diagnosis of polyps and cancer in 23% and 11% [46] and 8% and 9% [137], respectively. The 53 patients in the latter study [137] had a negative barium enema before under-

Fig. 11.13 Diagnostic yield of colonoscopy in HIV-negative patients with diarrhea: (a) EPAGE; (b) all studies.



going colonoscopy. Angiectasia was found in 4% of patients [46]. The number of colonoscopies needed to detect one cancer in patients with melena after a negative upper gastrointestinal endoscopy was calculated to be 9.9 [9].

Unexplained weight loss

Weight loss may be associated with a wide variety of diseases, including gastrointestinal cancer and IBD. Weight loss, along with age and IDA, has been reported to be predictive of colorectal cancer [26]. Weight loss was reported in 10.8% of patients with colon cancer compared with 3.9% of patients without colon cancer ($P < 0.05$). In a recent study, a small subset of 25 of 1144 patients undergoing colonoscopy for various indications presented with isolated weight loss as their main symptom. Colorectal cancer was found in 16%, IBD in 4%, and infectious or microscopic colitis in 8% [12]. In a larger European multicenter study (6004 patients), colonoscopy was performed for otherwise unexplained weight loss in 119 patients. In these patients, cancer was found in 5.9%, adenomas in 15.1%, IBD in 5.0%, and diverticulosis in 18.5%.

Known IBD

Colonoscopy in patients with known IBD is generally performed to reassess the extent of disease, to exclude complications, and for surveillance with respect to colorectal cancer. Screening colonoscopy in general is discussed in Chapter 12 and colonoscopy in IBD, including screening in ulcerative colitis and Crohn’s disease, in Chapter 48.

In known IBD, subsequent colonoscopies will obviously yield pathologic findings related to the preexistent

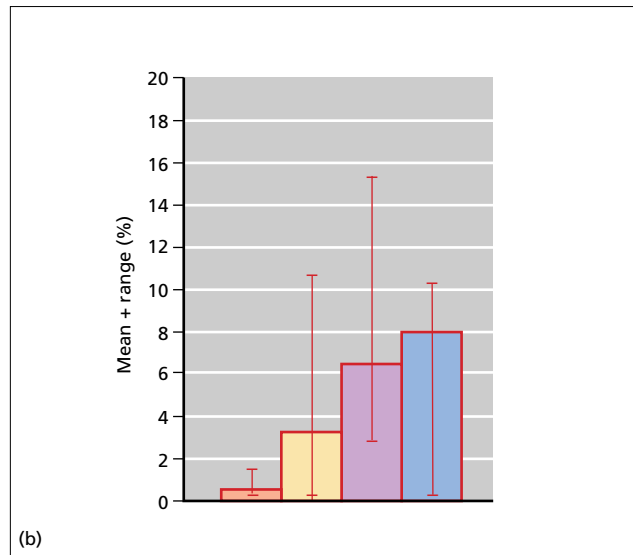


Table 11.8 Diagnostic yield of colonoscopy in patients with abdominal pain or altered bowel habit.

Reference	Comment	Number of patients	Cancer (%)	Adenoma (%)	Inflammatory bowel disease (%)	Diverticula (%)	Stricture (%)
Berkowitz & Kaplan [45]	Abdominal pain	55	1.8	11	9.1	16.4	
	Abnormal bowel habit	79	1.3	10	11.4	21.5	1.3
De Bosset <i>et al.</i> [12]	Prospective						
	Abdominal pain	254	0.8	7	0.8	NS	2
Brenna <i>et al.</i> [11]	Constipation	73	1.4	6.8	0	NS	
	Prospective; gastrointestinal symptoms	117	0.8	6	2	NS	3
EPAGE study	Prospective; unpublished results; change in bowel habit	359	3.5	13	2.9	22.6	NS
Lasson <i>et al.</i> [131]	Prospective; abdominal pain	281	0.7	6.8	8.9	8.5	NS
Liebermann <i>et al.</i> [132]	Nonspecific abdominal symptoms; polyp or mass > 1 cm	1899	7.3		NS	NS	NS
Mulcahy <i>et al.</i> [133]	Abdominal pain	389	0.5	2.6	1	NS	NS
Neugut <i>et al.</i> [53]	Prospective; abdominal pain and/or change in bowel habit	311	5	19	NS	NS	NS
Pepin & Ladabaum [134]	Constipation	358	2	38	NS	NS	NS
Rex [9]	All patients with one or more negative FOBT	75	0	31	NS	NS	NS
Sardinha <i>et al.</i> [135]	Patients > 80 years; abdominal pain; change in bowel habit	107	2	NS	NS	NS	NS
Schmitt <i>et al.</i> [136]	Prospective; abdominal pain	794	0.6	7.7	2.6	NS	NS
Total		3252*	1.6*	12.6*	3.2		

FOBT, fecal occult blood test; NS, not stated.

* Excluding data from Liebermann *et al.* [132].

IBD in most patients. We recently studied the yield of colonoscopy in 1144 patients, among whom was a subset of 40 patients with known IBD. IBD was present in 65%, another form of colitis (infectious) in 2.5%, and stenosis

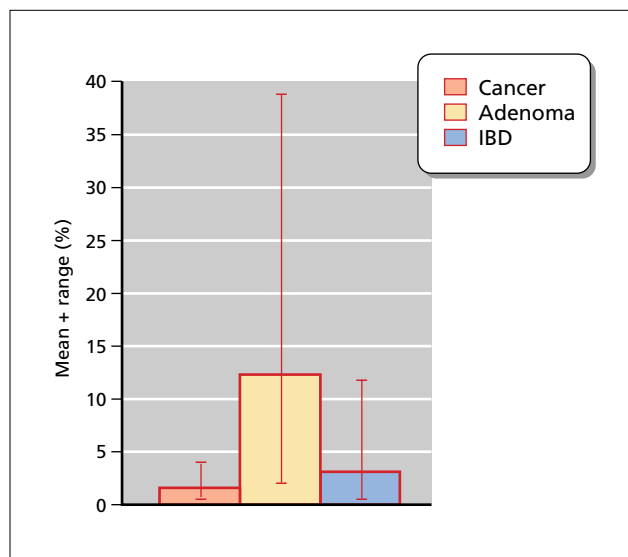


Fig. 11.14 Diagnostic yield of colonoscopy in patients with abdominal pain or altered bowel habit. Data from 12 studies (six prospective studies), 3252 patients.

in 10%; 22.5% of the procedures showed a normal colon [12]. One study reported an overall yield of 74% in 43 patients with IBD, including one nonneoplastic stenosis, but no cancer and no polyps (S. Morini, personal communication). Within the context of the EPAGE study, we assessed, in 6004 patients undergoing colonoscopy, the diagnostic yield of findings other than IBD in patients with known ulcerative colitis and known Crohn's disease (EPAGE study 2002, unpublished results). In 201 patients with known ulcerative colitis, we found cancer in 1%, adenomas in 3.5%, nonadenomatous polyps in 2.0%, and diverticulosis in 0.5%. In the 158 patients with known Crohn's disease, cancer was found in 0.6%, adenomas in 1.3%, nonadenomatous polyps in 1.3%, and diverticulosis in 0.6%.

Diagnostic yield of routine ileoscopy

Intubation of the ileum is not routinely performed during colonoscopy. Ileal intubation is one way to indicate completeness of the procedure. A skilled endoscopist can inspect the terminal ileum in about 90% of cases in which such examination is needed [1]. In practice, ileoscopy is not routinely performed. A recent European multicenter trial in 6004 patients undergoing colonoscopy found that ileoscopy was performed in 29.6% of colonoscopies reaching the cecum [138].

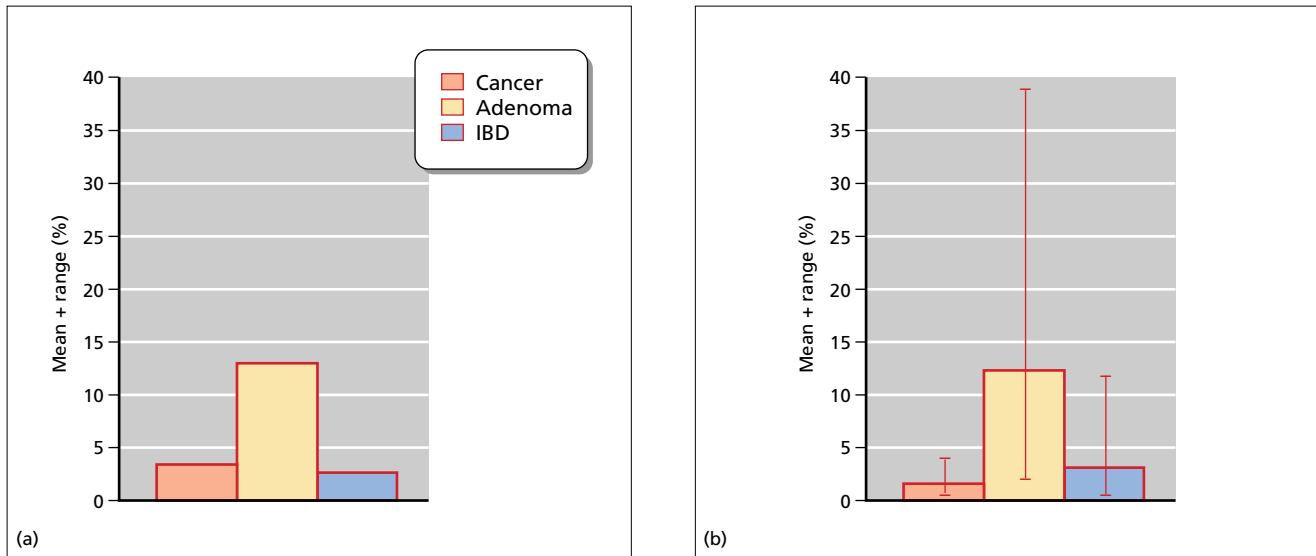


Fig. 11.15 Diagnostic yield of colonoscopy in patients with abdominal pain or altered bowel habit: (a) EPAGE; (b) all studies.

In one study in 138 consecutive colonoscopies, ileoscopy revealed a diagnosis in eight patients (6%). In half of these patients, the diagnosis was made based on ileoscopy alone. The yield of ileoscopy was 2.7% in asymptomatic patients undergoing screening colonoscopy and 29% in patients complaining of diarrhea [139]. Another prospective study in 295 consecutive patients [140] reported macroscopic abnormalities of the ileum in 4 of 213 patients (1.8%) in whom ileoscopy was possible, one-quarter of whom also had abnormal histology of the ileal mucosa (0.5%). However, this study did not indicate patient symptoms. Ileoscopy is obviously particularly useful in patients with symptoms suggesting IBD in order to exclude isolated ileal disease or to facilitate the differential diagnosis between Crohn's disease and ulcerative colitis [141]. Furthermore, ileoscopy seems to be indicated in patients with chronic diarrhea, especially in HIV-positive patients [142].

Diagnostic reliability of colonoscopy

Colonoscopy is more sensitive than barium enema and allows biopsies and endoscopic therapy. The sensitivity of barium enema and colonoscopy for diagnosing colorectal cancer was 84% and 95% in a recent retrospective study [143]. A controlled and blinded comparison of both procedures was made in the National Polyp Study where 580 patients underwent 862 paired examinations [144]. Barium enema detected a polyp in only 39% of cases in which a polyp was subsequently found during colonoscopy, and in only 48% in patients with advanced

adenomas greater than 1 cm in diameter. Furthermore, barium enema was falsely positive in 14%. In a large nonrandomized controlled trial [88] in 21 000 patients aged over 40 years, barium enema missed 25% of the lesions found at colonoscopy.

Insufficient procedural competence and experience on the part of the endoscopist may decrease the value of colonoscopy [145]. Even in expert hands, there is a significant miss rate of polyps. Rex and colleagues [146] performed two colonoscopies on the same day (back-to-back colonoscopy) in 183 patients randomly assigned to the same or another endoscopist. The overall miss rate of adenomas was 24%; it was 27% for adenomas ≤ 5 mm, 13% for adenomas 6–9 mm, and 6% for adenomas ≥ 1 cm. Although considered as the gold standard in the diagnostic armamentarium of colonic disease, the performance characteristics of colonoscopy are not optimal, even in the hands of an expert operator and under ideal conditions.

The quality and diagnostic reliability of the procedure are further dependent on several other factors. Much emphasis has been placed on the duration of colonoscopy and in particular on the time needed to reach the cecum. Overall duration may be significant with respect to procedural efficiency in a context of cost constraints, waiting lists at endoscopy units, and the need for endoscopists and endoscopes. However, it is not acceptable that an overly rapid endoscopic technique should render the procedure less tolerable or reduce its diagnostic reliability. Withdrawal time seems to be more critical for diagnostic yield, particularly colonic distension, adequate suctioning and cleaning, and adequate time spent examining the colon. The quality of withdrawal is critical for the detection rate of adenomas [147]. In fact, it has been shown very recently that individual endoscopists'

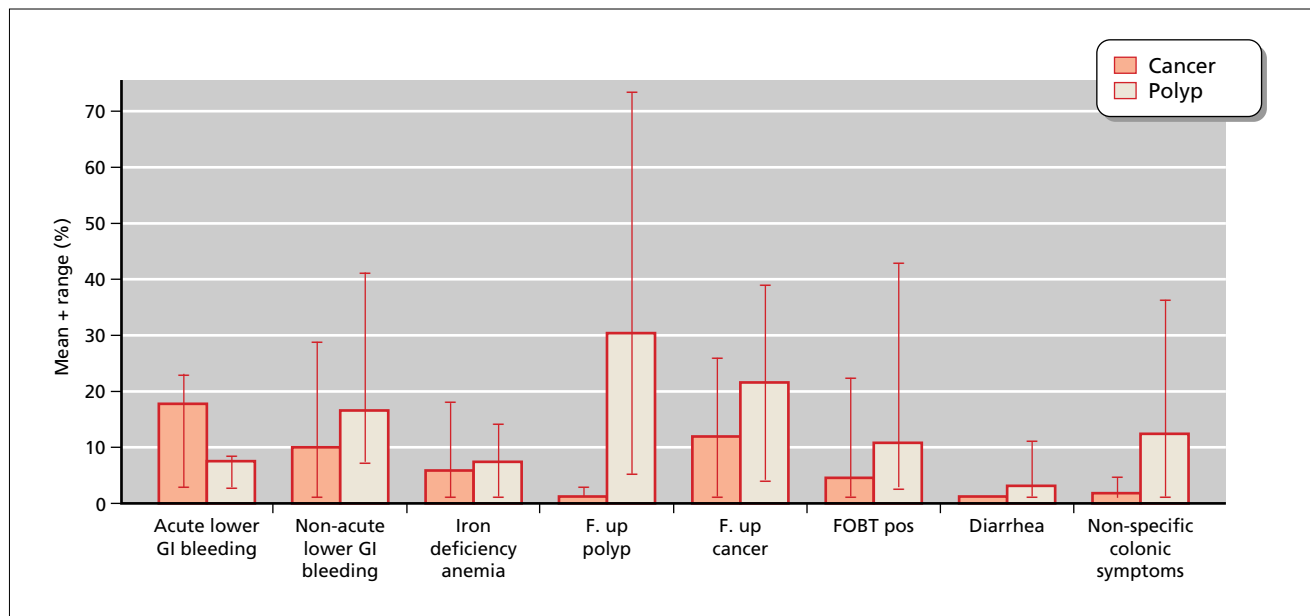


Fig. 11.16 Diagnostic yield of colonoscopy by indication.

procedure times correlate with the rate at which they identify multiple or clinically significant polyps [148]. We recently assessed technical aspects of performance of colonoscopy in 6004 European patients referred for colonoscopy [138]. The mean overall duration of colonoscopy was 22.8 min, including a mean withdrawal time of 10.1 min. In the same study, we found that colon cleansing quality was highly associated with the total duration of the procedure ($P < 0.001$), the difficulty of colonoscopy ($P < 0.001$), and the overall yield of relevant endoscopic diagnoses ($P = 0.002$), particularly of adenomas ($P < 0.001$) (EPAGE study 2002) [149].

Summary

For the clinician, the yield of relevant diagnoses is one of the most important outcomes of a diagnostic procedure such as colonoscopy. While appropriateness of indications refers to the quality of the indication, the diagnostic yield refers to endoscopic lesions that are potentially relevant to the patient's care, in conjunction with clinical symptoms and signs. Unfortunately, the relationship between endoscopic findings and clinical presentation is imperfect, particularly in light of the fact that endoscopic lesions (e.g. polyps) may be asymptomatic [150]. Patient age and gender have a major impact on the diagnostic yield of colonoscopy, increasing age being associated with a higher rate of lesions.

A main focus of the use of colonoscopy is the diagnosis and removal of adenomas and the diagnosis of colorectal cancer. In cancer detection, hematochezia, IDA, follow-

up after cancer resection, and positive FOBT have a high diagnostic yield (Fig. 11.16). In contrast, nonbleeding colonic symptoms (diarrhea, abdominal pain, altered bowel habit) and surveillance after polypectomy have a lower yield of cancer (Fig. 11.16). Incidence rates of colorectal cancer increase consistently with age. Patient age is thus an important predictor of colorectal cancer in patients referred for colonoscopy.

The yield in the detection of adenomas is less dependent on the indications than the detection of cancer, due to the high prevalence of polyps found in screening colonoscopies or in patients with nonspecific symptoms. The adenoma detection rate is highest in the follow-up of polyps, follow-up of cancer, in patients with positive FOBT (Fig. 11.16), and in nonemergency lower gastrointestinal bleeding (see Fig. 11.2). IBD is a relatively common finding in hematochezia and diarrhea.

Although diagnostic yield is important, it must be kept in mind that colonoscopy may also be beneficial to patients if it excludes a clinically relevant lesion by conferring reassurance.

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Chapter 12

Screening Colonoscopy: Rationale and Performance

David Lieberman

Introduction

Colorectal cancer (CRC) is the second leading cause of cancer death in North America and western Europe [1]. As populations live longer due to advances in medicine and public health, rates of CRC are likely to increase. The biology of CRC offers an opportunity for both early detection and prevention. Most cancers evolve from pre-malignant adenomas over a period of many years; spread of malignancy from the colon to sites outside the colon likewise occurs over years. Screening of asymptomatic populations has demonstrated that cancers can be detected at early, more curable stages compared with unscreened controls. Furthermore, studies have demonstrated that detection and removal of premalignant adenomas can prevent incident cancers [2,3]. Therefore, if screening tests could identify patients with high-risk adenomas, many cancers could be prevented, mortality reduced, and the burden of caring for patients with cancer diminished. If the target of screening is the advanced adenoma, we should ask: how effectively do screening tests identify patients with advanced adenomas?

There is consensus that colonoscopy should be the preferred screening test for individuals known to have higher than average risk [4]. Higher-risk categories include individuals with familial hereditary syndromes (familial polyposis, hereditary nonpolyposis CRC), chronic colitis due to ulcerative colitis or Crohn's disease, and a family history of CRC in a first-degree relative. Patients with a personal history of adenoma or cancer should receive colonoscopic surveillance, and are not considered part of a screening cohort.

Recent studies [5,6] have raised questions about whether colonoscopy should also be a preferred screening test in average-risk individuals. The performance characteristics of several screening modalities in average-risk populations have been scrutinized by the United States Preventive Services Task Force (USPSTF) and by expert multidisciplinary panels [4,7–10]. All the expert panels strongly recommend that population screening should begin for average-risk individuals at age 50 years. They have noted that colonoscopy is more effective than other screening tests for polyp detection. Although some experts have argued that colonoscopy

itself should be the preferred screening test [8], others have argued that it should be one of several screening options [4,7,9].

This chapter reviews the rationale for considering colonoscopy as a primary screening test in average-risk populations and discusses implementation issues including compliance, resources, and cost.

Rationale for screening

Screening with colonoscopy should be considered in the context of other screening tests. For each test we should ask the following questions.

- 1 What is the likelihood that the test will detect the target lesion (advanced adenoma or early cancer)?
- 2 Are there programmatic issues, such as need for repeat testing, which impact effectiveness?
- 3 What are the potential harms?

Fecal occult blood test

Three randomized controlled trials have compared population screening using the fecal occult blood test (FOBT) with no screening [11–13]. Although there were differences in study methods, the findings are consistent across all the studies. Cancers are detected at earlier stages in screened compared with unscreened subjects, and this translates into significant mortality reduction of 15–33% over time [11–13]. Rehydration of FOBT slides increases sensitivity but reduces specificity, so that many more patients will receive colonoscopy for false-positive results over time. In the Minnesota study [11], 38% of subjects in the FOBT arm received colonoscopy during the first 13 years of the study. One analysis has suggested that some of the benefit of the FOBT could be explained by random assignment to screening colonoscopy [14].

In the Veterans Affairs (VA) Cooperative Study [15], average risk subjects ($n = 2885$) had both one-time rehydrated FOBT and screening colonoscopy. FOBT was positive in 50% of patients with cancer, consistent with other studies [16,17]. However, among patients with advanced neoplasia without invasive cancer (defined as adenoma with high-grade dysplasia or villous histology,

or tubular adenoma ≥ 1 cm), FOBT was positive in only 21.6%. Moreover, it is likely that if rehydration had not been used, the positive rate would have been lower. These results suggest that *one-time* FOBT has serious limitations for detection of high-risk adenomas. If FOBT is to be used for screening, a program of repeat screening must be developed. Compliance with repeat screening is poor. There is some concern that patients may be falsely reassured after a negative test, and not return for repeat testing [7]. If the FOBT is positive, there is consensus that patients should undergo complete colonoscopy. This represents a second step during which compliance can break down.

These studies support the hypothesis that population screening of average-risk subjects could reduce CRC mortality. FOBT is a poor test for detection of advanced adenomas. Although there is some evidence that screening with FOBT can lead to reduction in cancer incidence (due to polyp detection and removal) [3], this reduction is modest. The need for frequent repeat testing and appropriate follow-up of positive tests with colonoscopy represent important program limitations.

Flexible sigmoidoscopy

There is evidence from two case-control studies [18,19] that exposure to sigmoidoscopy is associated with a reduction in colon cancer mortality, in that portion of the colon examined. In these studies, patients with death due to CRC were ascertained and an age-matched control group without CRC was used for comparison. Selby and colleagues [18] compared 261 patients with fatal rectosigmoid cancers (within reach of the sigmoidoscope) to 868 age- and sex-matched controls; 8.8% of cases had sigmoidoscopy compared with 24.2% of controls, suggesting that endoscopic sigmoid screening could reduce the risk of fatal cancers within the range of the sigmoidoscope (odds ratio 0.41). Moreover, the benefit remained strong even when the most recent examination was 9–10 years earlier. Newcomb and colleagues [19] found similar results. Both studies did not find that sigmoidoscopy reduced the likelihood of fatal cancers of the right colon, perhaps because such tumors would not be readily detected with sigmoidoscopy. Muller and Sonnenberg [20] reported another case-control study in a VA population to determine the impact of either sigmoidoscopy or colonoscopy on CRC risk. Compared with controls, patients with CRC were less likely to have had prior endoscopic examinations of the colon (odds ratio 0.51 for colon cancer; 0.55 for rectal cancer). Two ongoing randomized trials using flexible sigmoidoscopy will report findings in the next few years [21,22].

These case-control data provide compelling evidence that screening sigmoidoscopy could substantially

reduce CRC mortality, particularly from tumors in the distal colon. An important limitation is that a large portion of the colon is not examined at sigmoidoscopy. If most patients with advanced neoplasia in the proximal colon had index adenomas in the distal colon, which would lead to complete colonoscopy, then sigmoidoscopy would be a sensitive screening test.

Two screening colonoscopy studies reported the findings of complete colonoscopy, and estimated the potential findings of screening sigmoidoscopy in average-risk subjects [5,6]. Advanced neoplasia was more likely to be found in the distal colon (55% in the Indiana study; 53% in the VA study). Both studies found that more than 50% of patients with advanced proximal neoplasia (beyond the reach of the sigmoidoscope) would not have been identified with sigmoidoscopy, even assuming that any index adenoma would lead to colonoscopy. In addition, both studies found that as average-risk subjects age, they are more likely to harbor advanced proximal neoplasia and that these are less likely to be identified with sigmoidoscopy alone.

Sigmoidoscopy is able to detect advanced adenomas and early cancers in the area examined. The key limitation of sigmoidoscopy is that a large portion of the colon is not examined; some patients with advanced proximal neoplasia would go undetected. There is also concern that with increasing age, sigmoidoscopy may be less effective.

Combined flexible sigmoidoscopy and FOBT

The American Cancer Society has long recommended screening with both FOBT and flexible sigmoidoscopy beginning at age 50 years [9], among other options. Intuitively, this combined approach should have a greater impact on CRC mortality than either test alone. In one study [23], patients were offered sigmoidoscopy with or without FOBT. Although the patients were not randomly assigned to groups, the groups were comparable. Follow-up was irregular and compliance with follow-up testing poor. During the 9-year follow-up, 144 cases of CRC were found but only 28 were actually detected through screening. The major finding was that patients screened with both FOBT and sigmoidoscopy had better long-term survival after detection of cancer compared with controls, suggesting a benefit from evaluation of positive screening tests. The overall mortality rate of the two groups was similar.

In the VA Cooperative Study [15], combined screening with one-time FOBT and sigmoidoscopy would have identified 76% of patients with advanced neoplasia, only slightly better than sigmoidoscopy alone (70%). With increasing age, there was a trend for decreasing efficacy of the combined screening approach. Modeling [24–26] has suggested that the combined approach could be

more effective and less costly than other screening approaches if tests are performed programmatically and on a regular basis, as is recommended (annual FOBT and sigmoidoscopy every 5 years). However, the models require assumptions about compliance with initial testing and follow-up colonoscopy after positive tests, which may not be realistic in clinical practice.

Radiographic colon imaging with barium, computed tomography and magnetic resonance imaging

No large studies have evaluated colon imaging with barium in an average-risk population. The USPSTF rates barium as “unknown” with regard to effectiveness in reducing incidence and mortality from CRC, and only “fair” with regard to ability to detect cancer and advanced neoplasia. The National Polyp Study found that the sensitivity of barium studies for detection of polyps larger than 1 cm was 48% [27].

The data on computed tomography or magnetic resonance imaging of the colon are preliminary and the technology is still evolving. The range of sensitivity for large polyps is 40–96%, suggesting wide variation in either skill or technique. Currently, no review panel has recommended screening with these modalities, although they have captured the attention of the public.

Possible future tests

There are other screening modalities that show promise. When specific gene mutations were identified in patients with familial polyposis (adenomatous polyposis coli gene on chromosome 5) and hereditary nonpolyposis CRC (mismatch repair gene mutations), there was great hope that molecular genetics would provide a simple blood test to risk-stratify otherwise average-risk subjects. Such screening was touted to the public in the *New York Times* in the 1990s. The reality of genetic testing to date has been sobering, but there has been recent progress. Several groups have identified genetic mutations in stool samples. If tumors slough cells with genetic mutations into the bowel lumen and if these mutations can be identified, it may be possible to select individuals for colonoscopy based on the stool profile. This “needle in a haystack” approach is complicated by the fact that there is no single mutation which identifies all high-risk patients. New tests that search for several of the most common genetic alterations associated with CRC are under study [28]. With the development of the Human Genome Project has come the science of proteomics: understanding of the relationship of a gene mutation to specific protein product. If altered protein products are circulating in the blood, it may be possible to screen patients with blood tests.

The case for screening with colonoscopy

Rationale

Colonoscopy can examine the entire colon in more than 90–95% of procedures, if performed by a fully trained endoscopist. Polypectomy can be performed at the same time. Given these obvious advantages, we should ask: why not perform screening colonoscopy?

Arguments against screening with colonoscopy

General criteria for screening tests applied to the population are summarized in Table 12.1. Colonoscopy is an invasive and expensive test. The risk of perforation, serious bleeding, and cardiopulmonary events is low when performed by experienced endoscopists (0.3–0.5%), but if applied to the general population could account for considerable morbidity [29]. If only 5–6% of the adult population will develop CRC during life, most patients will not benefit from colonoscopy. Ideal screening would target colonoscopy at the patients most likely to have advanced neoplasia or cancer, and would not employ an expensive invasive test to populations with a relatively low pretest probability of disease. However, the ideal simple test has been elusive. Lacking the perfectly sensitive and adequately specific noninvasive screening test, screening with colonoscopy is now recommended as a screening option by all expert panels in the USA, though not in Canada, Europe, or Australia.

Arguments for screening with colonoscopy

Relative to other screening tests, there is substantial evidence that colonoscopy is very accurate for detection of significant neoplasia. In two tandem colonoscopy studies, in which patients had two colonoscopies performed during the same session, the miss rate for polyps greater than 1 cm was less than 10% [30,31]. Since these studies were performed by experts, it is possible that in clinical practice more lesions are missed by less expert endoscopists. Specificity for detection of neoplasia approaches 100%, because biopsies are usually obtained that confirm the histologic presence of neoplasia.

The ability to prevent incident cancers or reduce mortality with primary screening colonoscopy has never been tested in a clinical trial. However, there are several lines of indirect evidence which endorse the potential effectiveness of colonoscopy. First, the FOBT trials all recommended colonoscopy as the follow-up test after a positive FOBT. It was colonoscopy which identified the early cancers that led to a survival advantage in screened populations. Lang and Ransohoff [14] performed a posthoc analysis of the Minnesota FOBT study, in which 38% of subjects in the screened group received

Table 12.1 Criteria for population-based screening test.

General criteria	Colorectal cancer
Relatively common disease	150 000 new cases/year 5–6% risk in adults
Serious consequences	55 000 deaths/year Second most common cause of cancer death
Recognized as problem	Increasing public and provider recognition
Asymptomatic phase during which screening could detect disease	Yes
Screening test is noninvasive, low risk	Yes for FOBT Imaging requires preparation, but is low risk Colonoscopy invasive, with higher risk
Screening test is inexpensive	Costs are similar for all screening programs
Tests are sensitive enough to detect disease at curable phase	Yes for all tests Colonoscopy more sensitive than other tests
Tests are specific (high false-positive rates increase cost if patients have expensive evaluations)	Nearly 100% for endoscopic tests FOBT: rehydration increases false-positive rate Poor specificity for imaging studies
Available health services for diagnostic follow-up of positive tests	Uncertain if there are enough fully trained endoscopists
Therapy during asymptomatic phase will favorably alter natural history	Yes
Effective therapy if cancer found	Yes, if early stage

FOBT, fecal occult blood test.

colonoscopy over 13 years of study. They attributed much of the mortality reduction to high rates of colonoscopy, with only a portion of benefit derived from performance of FOBT. In the follow-up of the Minnesota study, the subsequent incidence of CRC was reduced in patients who had been screened, a benefit attributed by the authors to colonoscopy with polypectomy [3]. The second line of evidence is extrapolated from the case-control studies of sigmoidoscopy. These studies found a significant reduction in fatal colon cancers in that portion of the colon examined. There was no reduction in mortality from proximal colon cancers [18]. It is logical to assume that if more colon is examined, the benefit could be extended to as much of the colon as can be examined. The third line of evidence comes from the National Polyp Study [2], in which patients underwent complete colonoscopy with polypectomy and were followed over the next 5 years. When compared with reference populations, the incident rates of CRC were reduced by 76–90% in the study subjects. Although the comparison groups differed from the study subjects, the marked reduction in expected incidence is compelling. Finally, a case-control study in the VA population found that patients diagnosed with CRC were less likely to have had prior colonoscopy compared with patients without CRC [20]. The risk reduction of 53% for colon cancer and 39% for rectal cancer was significant. These studies provide compelling indirect evidence that screening colonoscopy could be effective, i.e. reduce colon cancer mortality and incidence.

Several investigators have modeled colon cancer screening and evaluated a broad range of assumptions

regarding accuracy, compliance, and harms. The conclusion of the most recent analyses is that colon cancer incidence could be reduced by 58–86% and that CRC mortality could be reduced by 64–90% [32].

Patient acceptance

Patient acceptance of colonoscopy as a screening test is unknown. Colonoscopy is well accepted when recommended for evaluation of other positive screening tests and other gastrointestinal symptoms. In the VA Cooperative Study, nearly two-thirds of eligible subjects who were offered colonoscopy completed the examination. The VA population may not be generalizable, but this study does demonstrate that good compliance can be obtained when procedures are fully explained. Acceptance of sigmoidoscopy is estimated to be 25–50% [33]. Although acceptance of one-time FOBT may exceed 75%, compliance with repeat FOBT is poor. A colonoscopy screening program may require only one or two examinations in a lifetime, a factor that may enhance program performance compared with other programs requiring frequent repeat testing and colonoscopic follow-up of positive screening tests.

Benefits/harms

The largest study to report complications of colonoscopy is VA Cooperative Study 380 [29]. Serious complications, definitely attributed to colonoscopy, occurred in 0.3% of patients receiving screening colonoscopy. The most common serious complications were serious bleeding

and myocardial infarction or serious arrhythmia. Most of the serious complications occurred in association with polypectomy. The serious complication rate of a diagnostic colonoscopy was 0.1%. Less serious complications were common, including vasovagal events (5.4%), transient oxygen desaturation (4.4%), abdominal pain requiring termination of the procedure (0.9%), and minor gastrointestinal bleeding that did not require hospitalization or intervention (0.2%). Since these procedures were performed by experts, it is not known if complications would be more common in community practice. Studies are currently underway to measure 30-day complication rates in diverse clinical practice settings.

Resources

The algorithm of every CRC screening program eventually leads to colonoscopy to evaluate positive tests. Public and provider awareness of the benefits of colon screening has increased over the past few years. A Gallup poll in 1998 indicated that nearly 90% of the public was aware of the potential benefits of colon screening. In March 2000, a prominent television personality had a screening colonoscopy performed on her program, with the goal of diminishing public fear of the test. An aggressive public education campaign followed the program. Despite this increased public awareness, compliance with screening has been poor: only 30–40% of the age-eligible population have had the recommended screening. However, there are indications that this may improve over the next few years. In 1998, the Department of Health and Human Services added colon screening with FOBT or sigmoidoscopy as a Medicare benefit for average-risk individuals, and colonoscopy for individuals with a positive family history. In July 2001, the federal government extended the benefit to include colonoscopy screening for all. Healthcare systems such as the Department of Veterans Affairs have initiated annual reminders to primary providers to encourage FOBT. Health maintenance organizations like Kaiser have enrolled all age-eligible patients into flexible sigmoidoscopy screening programs. The National Cancer Institute and the Centers for Disease Control are dedicating resources to study strategies which will improve compliance.

By 2000, most gastrointestinal practices in the USA were confronted with increased demand for colonoscopy services. During this same time period of the late 1990s, there was a decline in the number of gastrointestinal fellowship positions in the USA. The shifting demand for colonoscopy and the decline in newly trained endoscopists has raised concerns about whether there are sufficient resources to provide colonoscopy screening to the general population.

Rex and Lieberman [34] examined some of the assumptions that underlie the demand for services.

They assumed that some patients would have comorbid conditions which would preclude screening, some would have examinations to evaluate symptoms, and a large number would be noncompliant. In a “best-case” scenario, 60% of the population would be compliant with screening. Therefore, rather than a stampede to screening colonoscopy, the demand may more closely resemble a traffic jam. If traffic patterns are understood, most traffic jams have engineering solutions. To offer colonoscopy services with existing resources, Rex and Lieberman made several recommendations.

1 Improve the efficiency of delivering colonoscopy. Most endoscopy units are not efficient with regard to room scheduling and turnover. Endoscopists could develop open-access systems for screening of otherwise healthy individuals, and use physician extenders to obtain consent and perform initial history and physical examinations. Support personnel could handle much of the postprocedure follow-up with patients who do not have complex pathology.

2 Shift current colonoscopy resources. In the USA, 20–25% of colonoscopy procedures are performed for surveillance of prior adenomas (D. Lieberman, unpublished data from the Clinical Outcomes Research Initiative [CORI] database). Based on the VA Cooperative Study [5], more than 70% of patients found to have adenomas at screening will have only small (<1 cm) tubular adenomas. The Indiana colonoscopy study found that 65% of patients with neoplasia had only small tubular adenomas [6]. Data from the National Polyp Study [35] suggest that these patients may have a low risk of serious pathology at surveillance examinations. Extending the interval for surveillance of patients with low-risk lesions could shift considerable resources towards screening. Rex [36] estimated that screening will have a greater yield than surveillance (64 colonoscopies to detect one cancer for screening average-risk male vs. 317 colonoscopies to detect one cancer in postpolypectomy surveillance). If specialists in gastroenterology spend more time performing colonoscopy and less with flexible sigmoidoscopy, this will allow some resource shifting. This trend is currently observed in the CORI database, which shows a significant decline in sigmoidoscopy as a fraction of endoscopic practice by gastrointestinal specialists (D. Lieberman, unpublished data).

In summary, existing resources can be provided more efficiently and selectively to increase the capacity for screening colonoscopy (or colonoscopy to evaluate other positive screening tests).

Cost

Several recent analyses of colon screening costs have reached similar conclusions: screening with any of the recommended tests is cost-effective relative to other

medical interventions, and could even be cost-saving if large numbers of cancers can be prevented [24–26, 37–41]. The analyses show that various screening tests are quite similar in programmatic costs over life, roughly \$20 000 per life-year saved. The analysis of these studies by the USPSTF stated that the current evidence is insufficient to determine the most effective or cost-effective strategy for screening [32].

Important assumptions in these analyses include the rate of cancer prevention and the cost of cancer care. In the USA, the cost of care for patients with CRC probably exceeds \$50 000 [42]. This cost includes diagnostic studies, cancer surgery, chemotherapy or radiation therapy, postcancer surveillance, and end-of-life care if detection is late. As the cost of cancer care increases, averting this cost by detection and removal of advanced adenomas will probably result in cost-saving. In each model, colonoscopy results in the greatest potential for cancer prevention because of the highly accurate detection and removal of adenomas.

If cost differences between the screening tests are small, why are many insurers reluctant to include colonoscopy screening as a benefit to their clients? From the standpoint of the insurer, screening is a large investment with potential downstream benefit. If cancers are averted, then the cost of cancer care can be reduced, although this benefit may not be realized for many years. If individuals change insurance coverage frequently, the insurer may not wish to make a large “up-front” investment for a downstream benefit that may occur after the individual is no longer covered by the insurer. Among the screening test options, colonoscopy would represent the largest up-front investment. If we approach the screening from a societal point of view (a lifetime, single-payer system), an effective cancer prevention program would be a worthwhile investment.

Screening colonoscopy: areas of uncertainty

Colonoscopy screening has not been studied in a clinical trial. Therefore, the balance of benefits and harms remains uncertain. Although there is little doubt that colonoscopy is beneficial in the evaluation of other positive screening tests (FOBT, sigmoidoscopy, imaging), it is uncertain if whole-population colonoscopy screening would necessarily confer the degree of benefit that would justify the risk and resource utilization. For colonoscopy to be effective, the examinations will need to be accurate and complete, and performed with minimal risk. The overall success rate and risk of colonoscopy in community practice is unknown and requires study. Future advances in colonoscopy technology may improve success rates and reduce risk.

The “holy grail” of screening is mortality reduction. Some may argue that if all-cause mortality is not reduced

by colon cancer screening, then the benefit may not offset harm. For example, let us assume that a hypothetical individual would have died from CRC at age 80 years. If his colon cancer is prevented by screening but he has a myocardial infarction and dies at age 80, is there a benefit? Although society is spared the cost of caring for a patient with cancer, would the resources spent for screening have been better spent on some other form of healthcare? These are difficult questions to answer in clinical trials. The modeling analyses are helpful because they account for all causes of death, and consistently show that there is a benefit from screening. A clinical trial to resolve this issue would require 10–20 years, large numbers of patients, and an enormous budget. As in other areas of medicine, we may lack precise information for medical decision-making. As new data become available from the VA Study follow-up and the CONCeRN trial [43] in women, they can be incorporated into the models and reduce areas of uncertainty.

The appropriate timing for screening colonoscopy is uncertain and has implications for cost, resource utilization, and benefit. Imperiale and colleagues [44] found that detection of serious pathology is uncommon in asymptomatic persons aged 40–49 years who had screening colonoscopy. Ness and colleagues [39] found that screening colonoscopy at age 50–54 years would be cost-effective compared with no screening. The VA Cooperative Study data showed that the prevalence of any advanced pathology in men aged 50–59 years was 5.7%, and few had cancer. Only 2% had advanced proximal neoplasia and most of these patients would have been detected with sigmoidoscopy [5]. In contrast, 4.9% of patients aged 60–69 years and 5.9% of patients aged 70–74 years had advanced proximal neoplasia. Less than half of these patients would have been detected with sigmoidoscopy. Therefore, a strategy of screening sigmoidoscopy during the sixth decade followed by complete colonoscopy at age 60 years might be a cost-effective screening strategy in men.

Expert groups have recommended that colonoscopy screening be performed at 10-year intervals, based largely on the expected natural history of progression of colonic neoplasia. There has not been a study evaluating a 10-year interval. Rex and colleagues [45] performed follow-up colonoscopy at 5.5 years in 154 average-risk persons who had a negative baseline colonoscopy; only one patient had an adenoma greater than 1 cm. These data suggest that a 6-year interval is quite safe. Would a negative screening colonoscopy at age 60 years identify a low-risk person who does not need further screening? These data are crucial to decision-making about when to stop screening. The VA Cooperative Study will follow its population for 10 years, and will provide some prognostic information in men who have had a baseline screening colonoscopy. For now, there is some uncertainty about the appropriate screening interval.

Will screening colonoscopy likely be replaced by new methods of screening? This is an important question because of resource utilization. If society determines that screening colonoscopy should be offered to everyone, significant resources will need to be dedicated to provide endoscopy services and train endoscopists. If colonoscopy is subsequently replaced, then there will be issues of excess capacity and wasted resources. The ideal screening test of the future will target colonoscopy precisely at those patients most likely to develop cancer. If a genetic or biologic marker could successfully risk-stratify patients, colonoscopy may only need to be offered to the 10–20% of the population who develop high-risk lesions. For patients with sporadic CRC, this ideal test remains in the distant future. In the best-case scenario, once a marker was identified, years of testing would likely precede widespread acceptance. Imaging studies are not likely to provide precise targeting because they will identify patients with advanced and non-advanced lesions. Unless clinicians are willing to ignore small polyps found on imaging studies, these tests are not likely to reduce the need for colonoscopy services. Therefore, for the next generation, colonoscopy will be the most accurate test for assessing risk and enhancing prevention.

Summary

CRC screening with colonoscopy in average-risk populations could have a significant impact on CRC incidence and mortality [32]. Advantages over other forms of screening include the ability to examine the entire colon and remove pathology during the examination. Uncertainties exist about the application of the procedure in practice. Would completion rates and complication rates be similar to those reported from clinical trials? Further study is needed in community practice. Would one or two examinations during a lifetime be sufficient if they are negative? Are there sufficient resources to provide colonoscopy to large populations? Despite these questions, there is little doubt that colonoscopy screening would have a large impact on CRC incidence and mortality. Until selective screening can be targeted at those individuals most likely to develop CRC, colonoscopy screening may offer the most effective means for reducing mortality.

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Chapter 13

Cost-effectiveness of Colonoscopy Screening

Amnon Sonnenberg

Introduction

Colonoscopy has a wide range of clinical applications, from its use as the primary diagnostic tool for all colonic diseases to a treatment modality in an ever-increasing variety of clinical indications. In each instance, the use of colonoscopy is governed by the interplay between its medical effectiveness and costs, as well as the availability of other competing medical options. A large portion of the clinical use of colonoscopy is still focused on the diagnosis and prevention of colorectal cancer and this chapter deals with the cost-effectiveness of colonoscopy in the prevention of colorectal cancer.

The primary goal of any medical intervention relates to medical success rather than inexpensive management. Cost is only of secondary relevance compared with the primary concerns about the most efficacious prevention, diagnosis, or therapy. Costs become relevant if assessed in conjunction with medical effectiveness. In comparing two competing management options, four potential scenarios can arise. If the first option is cheaper and better than the second option, the decision in its favor is easy. The decision against the first option is similarly easy if the first option is more expensive and worse than its alternative option. It is the mixture of medically better but more expensive or medically worse but less expensive outcomes that are difficult to decide unequivocally. Ideally, comparison of cost-effectiveness ratios would provide a means for comparison of such options [1,2].

General principles of cost-effectiveness analyses

In cost-effectiveness analyses (CEA), one calculates the ratio of costs per effectiveness of the medical intervention [1,2]. The effectiveness is measured in terms of quality adjusted life-years (QALY) gained through the intervention. Health-related quality of life (HRQL) is measured on a scale between 0 (death) and 1 (perfect health) and is used as a multiplier for life-years to adjust for the different values of lifetime spent in various disease states. A low cost-effectiveness ratio indicates a highly cost-effective medical intervention with low investment costs per yield. The general use of CEA and

QALY is encouraged, because it potentially allows one to compare the cost-effectiveness of a large variety of health measures, e.g. appendectomy, vaccination, or tooth filling, and design policies that distribute scarce healthcare resources according to an objectively measured need.

Effectiveness of screening is measured in terms of life-years saved through prevention of colorectal cancer and improved survival by detecting cancer at earlier cancer stages. The cost-effectiveness of colonoscopy or other alternatives for screening is calculated as the average costs per life-years saved (average cost-effectiveness ratio, ACER). Rather than calculate an absolute value, cost-effectiveness is frequently calculated in comparison with other strategies. The marginal or incremental cost-effectiveness ratio (ICER) corresponds to the additional costs needed to spend in order to save one additional life-year in comparison with another strategy. In mathematical terms:

$$\text{ICER} = \frac{\text{costs}_1 - \text{costs}_2}{\text{QALY}_1 - \text{QALY}_2} \quad [13.1]$$

where the indices 1 and 2 refer to the first and second medical strategy, respectively, compared with each other. Frequently, the cost-effectiveness of prevention is compared with a strategy of no cancer prevention or no screening.

It has been argued that in making a decision, a policy-maker could rely directly on the various cost-effectiveness ratios published in the medical literature [2]. The outcome of CEA is heavily dependent on the types of variables considered by the analysis and the assumptions built into the decision model. Despite multiple efforts at standardization, no two diseases are alike and submit to similar types of cost analyses. If one truly tries to include all factors that contribute to the management of a disease and tally even its most remote implications, the actual medical question becomes diluted by a large variety of nonmedical issues, such as cab fare to the hospital or patient placement in a nursing home. QALY is an effectiveness parameter that does not apply to all diseases and that does not provide a reliable measure for all medical achievements, e.g. in treating dental cavities, managing irritable bowel syndrome, or just ruling

out the presence of a serious disease with a negative test. Although costs were initially introduced only as an accounting trick to make the heterogeneous variety of social and medical items commensurable, their introduction into the analysis has brought economists into the fray who harbor a completely different set of interests from physicians.

Economists are primarily concerned with scarcity of resources and the maximization of resource utilization. Although in many CEA the focus has shifted from a medical to an economic perspective, physicians may still misread them to provide guidance on the best medical management. From the perspective of a physician, medical arguments should prevail over economic arguments. Costs are only relevant to a physician as a general way of accounting for the large variety of otherwise incommensurable quantities that may bear on a medical decision. CEA are helpful and most reliable when striving to compare different medical management strategies, such as fecal occult blood testing vs. colonoscopy or repeat vs. single colonoscopy. If done properly, comparative CEA subject all management options to a similar set of constraints, assumptions, and costs. CEA are less suited to providing absolute measures of cost-effectiveness or general guidance about the actual implementation of a particular medical strategy.

Small costs in a great many as opposed to great effects in a small few

At least in principle, the decision for or against screening is governed by a rather simple balance: the end result must justify the initial investment in screening. The risks and costs of screening affect the entire population, whereas the preventive measures benefit only a small fraction of the population (Fig. 13.1). This interplay between the entire population and a subfraction prone to develop cancer adds the perspective of probability to the analysis. The costs of the screening procedure are usu-

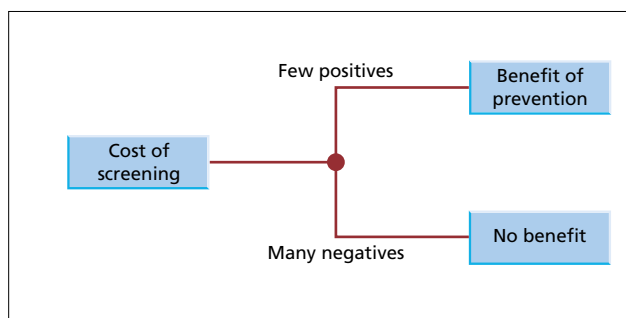


Fig. 13.1 Decision tree demonstrating the general principles of screening. The costs of screening are accrued in the entire population, whereas its benefits affect only a minority of patients.

ally small when compared with their potential benefit. For instance, a single colonoscopy costing \$1000 can save a life worth, say, \$1 000 000. However, the relatively inexpensive test must be applied multiple times to a large population of subjects in order to gain a benefit in one or few patients. In other words, colonoscopies may need to be performed 1000 times before one single cancer case is detected in a timely fashion to save a single life. On one hand, this balance may shift in disfavor of screening if the screening procedure itself results in life-threatening and costly complications. On the other hand, if screening is associated not only with life-saving measures in one patient but also with extended life in another case and prevention of cancer altogether in yet another set of patients, the balance may shift yet again, this time in favor of screening.

To avoid the contentious issue of assigning a monetary value to human life, health economists have largely abandoned cost-benefit analyses and resorted to CEA. Instead of translating medical benefits into costs, the end result is usually measured in terms of QALY, life-years saved, or some other outcome parameter indicating the effectiveness of screening. The investment in screening and its potential risks and adverse effects are still measured as monetary cost. Cost lends itself to be used as the common denominator for the multitude of heterogeneous entities touched upon by the analysis. It is a widely used means of measurement and people are intimately familiar with its meaning and ubiquitous applicability. These items include, among others, cost of the screening procedure and its potential complications, costs of cancer care, and absenteeism from work.

The tree in Fig. 13.1 represents only a crude presentation of the issues involved in screening. In Fig. 13.2, the initial tree is expanded to depict in more detail other potential events and outcomes associated with screening. Besides screening, the option of nonscreening is added as a lower branch to the tree. The results of screening are broken down into true and false. Lastly the more detailed outcomes differentiate between patients who do and do not fully benefit from prevention. It is obvious that even this tree is far from complete and that it could be expanded much further, e.g. by considering the influence of repeat screening procedures, the concomitant or subsequent use of different screening tests, or patient noncompliance with the screening procedure.

Cost-effectiveness of decennial colonoscopy

The decision tree shown in Fig. 13.2 becomes an unhelpful instrument when tackling decision problems that involve many screening options, test outcomes, and therapies. The tree is difficult to appreciate and the reader is overwhelmed by the amount of detail. It is also

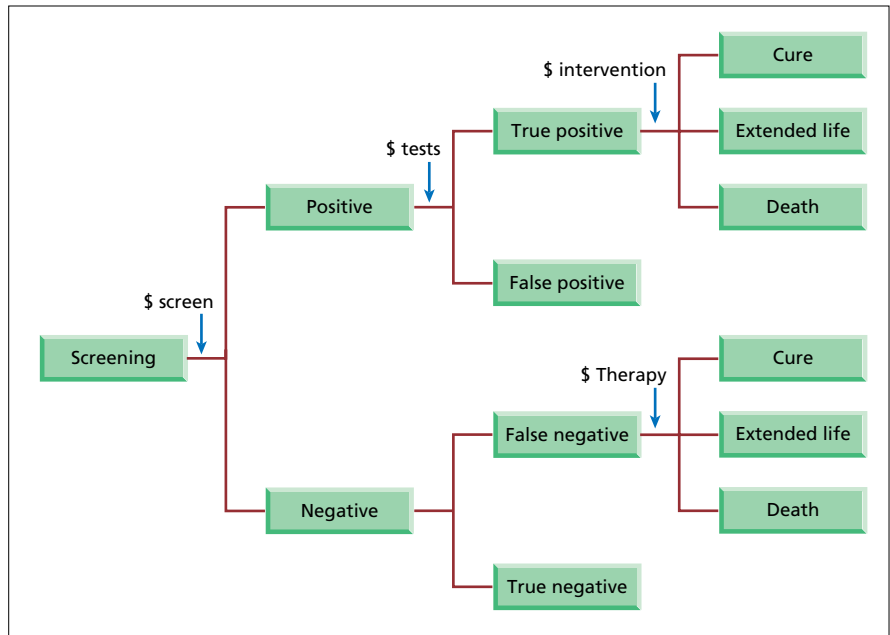


Fig. 13.2 Expanded decision tree of screening. The arrows symbolize transitions that are associated with costs.

less well suited for handling the impact of decisions and events that occur repetitively and change over time, such as surveillance colonoscopy after polypectomy, time-dependent decline in compliance, or age-related rise in cancer incidence. The transition from polyp to cancer and the time-dependent evolution of cancer are better modeled by a Markov process [3]. In a Markov process, medical events are modeled as transitions of patients among a set of predefined health states, the occurrence of each transition being governed by a probability value (Fig. 13.3). The circles in Fig. 13.3 symbolize the various health states, while the arrows symbolize transition probabilities among them. The time frame of the analysis is divided into equal increments of 1 year, during which patients may cycle from one state to another. The initial population comprises 100 000 subjects aged 50 years who at the start are offered screening colonoscopy. Depending on the initial compliance rate, subjects undergo a colonoscopy or enter the pool of noncompliant persons. After a normal colonoscopy (without adenomatous polyp), subjects enter a new state labeled “status post colonoscopy.” In subjects compliant with a repeat screening, a colonoscopy is scheduled every 10 years. In the case of an adenomatous polyp, surveillance colonoscopy is repeated every 3 years until adenomatous polyps are no longer found. Subjects in any Markov state can develop colorectal cancer, the probability being given by the age-specific incidence rate. The likelihood of developing cancer is reduced in subjects after a normal colonoscopy or after polypectomy, depending on the rate of preventive efficacy assigned to the procedure. The length of time for which colonoscopy plus polypectomy provide protection against colorectal can-

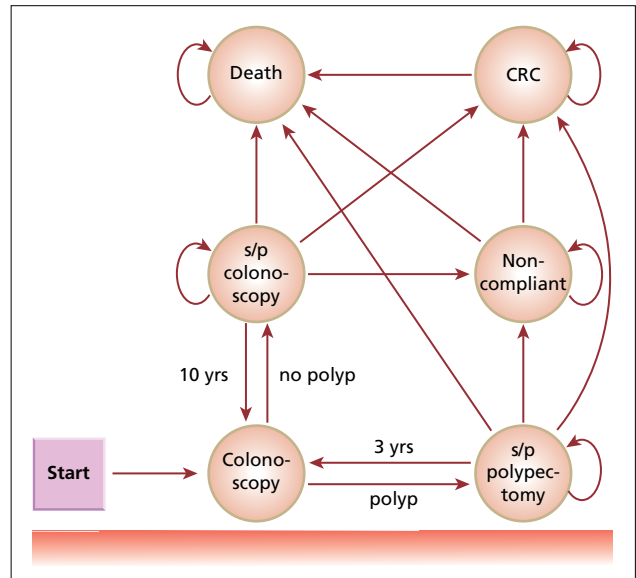


Fig. 13.3 Markov state diagram of screening for colorectal cancer (CRC) by repeat colonoscopy. The arrows symbolize transitions between the various states. Noncompliant, subjects noncompliant with repeat colonoscopy. s/p, status post.

cer is equal to the screening interval. The population in each state is also subject to the annual age-specific death rate of the US population.

The transition probabilities built into the model are taken from the literature, including a 40% mortality from colorectal cancer, a 75% efficacy of colonoscopy in preventing colorectal cancer, and a 1% annual incidence rate of colorectal adenomas. In a set of sensitivity analyses

these values are varied over a wide range. The costs for medical, surgical, and diagnostic services represent the average payments allowed for each service by the U.S. Health Care Finance Administration. The costs also include the possibility of hospitalization for bleeding or perforation after colonoscopy with or without polypectomy and cost estimates for the medical care of subjects with colorectal cancer. The costs accrue every time subjects pass through transitions that are associated with healthcare utilization. Effectiveness is measured in terms of life-years that accumulate in subjects who stay alive after each cycle. The number of life-years saved through screening corresponds to the difference in life-years lost from cancer-related deaths between two Markov models with and without screening. All future costs arising from screening or care of colorectal cancer and all future life-years saved through screening are discounted at an annual rate of 3% [4].

The ACER of colonoscopy every 10 years is \$28 000 per life-year saved. The ICER of colonoscopy compared with no screening amounts to \$11 000 per life-year saved. In comparison with other medical interventions, such ACER and ICER values are considered quite cost-effective and colonoscopy appears a strategy worthwhile pursuing [5]. More frequent colonoscopies, e.g. every 5 instead of 10 years, increase the ACER and ICER of cancer prevention by making the screening procedure more costly. Changes in the surveillance interval after polypectomy exert only a small influence without affecting the relative differences among competing screening programs. Any decrease in the efficacy of colonoscopy plus polypectomy in preventing colorectal cancer also increases the ACER and ICER of colonoscopy.

Cost-effectiveness of alternative screening procedures

Single colonoscopy

Although repeat colonoscopies every 5–10 years represent the most effective screening strategy for colorectal cancer, it has not been widely used because of its associated high costs and relatively low patient compliance. To escape these shortcomings, some authors have suggested a one-time only screening colonoscopy after age 50 [6–9]. In a previous study it was shown that the best period to schedule a single colonoscopy lies between 65 and 70 years of age [9]. At this age a balance is achieved between a declining life expectancy (leading to a reduced impact of any life-saving measures) and a rising incidence of colorectal cancer. Screening by a single colonoscopy at age 65 is modeled similarly to screening by multiple colonoscopies, as shown by Fig. 13.3 [10]. However, no repeat colonoscopy is scheduled after the initial colonoscopy or after a successful polypectomy.

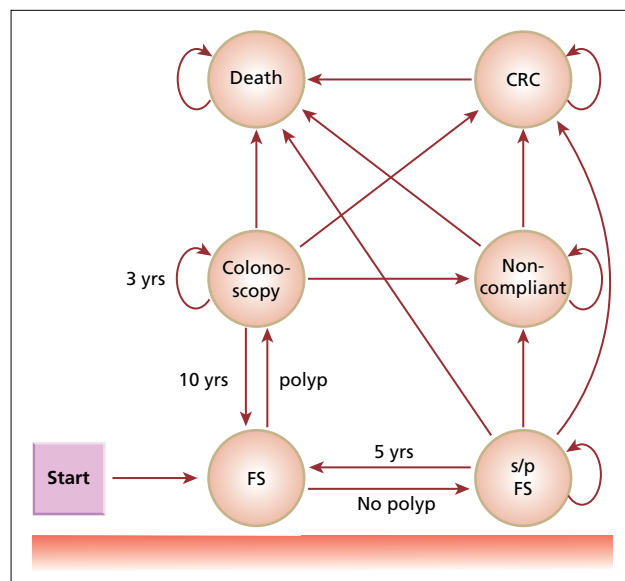


Fig. 13.4 Markov state diagram of screening for colorectal cancer (CRC) by flexible sigmoidoscopy (FS). s/p, status post.

From the age of 50–64 years and after the age of 75 years, subjects are exposed to the age-specific incidence rate of colorectal cancer without any potential protection from colonoscopy and polypectomy. The smaller fraction of cancers prevented by a single screening colonoscopy is associated with fewer life-years saved. The ACER of a single colonoscopy is \$55 400. Compared with no screening, a single colonoscopy represents an extremely cost-effective screening strategy of less than \$3000 per life-year saved.

Flexible sigmoidoscopy

The cost-effectiveness of screening by flexible sigmoidoscopy is modeled similarly to screening by decennial colonoscopy (Fig. 13.4) [3]. Instead of colonoscopy, the simulation is started with 100 000 subjects being offered screening through flexible sigmoidoscopy. The transitions out of this initial state depend on whether a polyp is found during sigmoidoscopy. After a normal (negative) flexible sigmoidoscopy without adenomatous polyps, subjects stay in the pool waiting for the next screening sigmoidoscopy in 5 years. The remainder of the model is similar to that of colonoscopy. Besides the states shown in Fig. 13.4, the actual model was simulated with an additional status to account for noncompliant patients regarding repeat flexible sigmoidoscopies or follow-up colonoscopies after a positive flexible sigmoidoscopy. About 45% of all polyps are within the reach of flexible sigmoidoscopy [11–13]. According to the model, screening by flexible sigmoidoscopy prevents 34% of all colorectal cancers. Although the investments in screening with flexible sigmoidoscopy reduce the number of

colonoscopies used for screening, an ACER of \$74 000 and an ICER of \$36 500 compared with no screening make this strategy far more expensive than any strategy using colonoscopy. Screening by flexible sigmoidoscopy is most sensitive to the costs of the procedure itself. The only way to salvage sigmoidoscopy as a screening procedure would be to offer it at very low cost. Currently, flexible sigmoidoscopy costs \$400, compared with \$695 for a simple colonoscopy and \$1004 colonoscopy plus polypectomy. If the cost of flexible sigmoidoscopy drops below a threshold of \$170, its ICER (compared with no screening or with screening using fecal occult blood test) makes it a cost-effective alternative to colonoscopy as a secondary screening procedure. Moreover, if polyps can be removed during flexible sigmoidoscopy without need for a follow-up colonoscopy, this strategy also becomes a cost-effective screening alternative.

Fecal occult blood test

In prospective trials the fecal occult blood test (FOBT) was shown to reduce colorectal cancer-related mortality, on average by 18% [14]. Since it also appears to be a cheap test, it has been suggested that it would represent a cost-effective alternative for screening colorectal cancer [6,15–18]. In our own analysis, its cost-effectiveness was assessed using a Markov process very similar to the one shown in Fig. 13.4 for flexible sigmoidoscopy [3]. In the case of FOBT, the lower two states of Fig. 13.4 represent “FOBT” and “status post FOBT.” The simulation is started with 100 000 subjects being offered screening through FOBT. The transitions out of the initial FOBT state depend on whether the test is negative or positive. After a negative FOBT, subjects stay in the pool waiting for the test repetition in a year’s time. In case of a positive FOBT, subjects undergo a colonoscopy. After a negative colonoscopy, FOBT is abandoned for a period of 10 years. In addition to many similar transition probabilities from the previous models, the present Markov process assumes a 40% sensitivity and 97.5% specificity of FOBT for colorectal cancer.

Compared with no intervention, screening by FOBT prevents 16% of all colorectal cancers. In detecting earlier cancer stages, FOBT leads to an additional 2% reduction in mortality beyond cancer prevention alone. Compared with no screening, only \$9700 (ICER) are spent to save one additional life-year. FOBT represents a relatively cost-effective option when compared with no screening.

The outcome of the simulation is mostly influenced by the costs of the FOBT itself and the test characteristics. The baseline cost of \$3.50 for the FOBT may be overly optimistic because it does not include any cost for physician visit and test management. The ICER of FOBT is linearly dependent on the costs of delivering the test. A

rise in costs (from baseline \$3.50) to \$7 or \$14 raises the ICER of FOBT in comparison with no screening to \$12 600 or \$18 400, respectively. An increase in both test sensitivity and specificity reduces the ICER. Within the broad ranges tested in the sensitivity analysis, their overall influence on the ICER does not exceed \$2000. Because screening based on flexible sigmoidoscopy or FOBT both depend on colonoscopy as their final arbiter, shortening of the interval between repeat colonoscopies also renders these two screening strategies more expensive and less cost-effective. Similarly, any decrease in the efficacy of colonoscopy plus polypectomy in preventing colorectal cancer increases the ACER and ICER of other screening methods as well.

Under base case conditions, patient compliance with the screening program is assumed to be perfect. Since the initial compliance determines how many persons enter the screening program, it influences the overall number of cancers prevented and the total costs in a linear fashion. However, the initial compliance rate does not affect the cost-effectiveness ratio of any individual program. A decrease in compliance associated with test repetition results in higher costs per life-year saved. FOBT is particularly sensitive to changes in compliance with repeat testing because it is done more frequently than colonoscopy. Only a slight decrease in compliance with repeat FOBT increases its ICER (compared with no screening) far above the ICER of colonoscopy. A low compliance with colonoscopy following a positive FOBT also renders the initial FOBT less efficacious and increases its associated costs per saved life-year. Because it depends on several types of patient compliance, screening by FOBT is generally far more sensitive to changes in compliance than a colonoscopy screening program.

CEA comparison of competing screening strategies

Table 13.1 illustrates a comparison of various analyses that use variations of a similar Markov process to estimate the cost-effectiveness of competing strategies to prevent colorectal cancer in the general population. All analyses assume perfect compliance and do not include costs or quality adjustment of the life years saved. As highlighted in the previous sections, all values shown in Table 13.1 can easily be shifted upward or downward by assuming a set of more or less favorable costs and prevention outcomes. Based on the limited evidence provided by the analyses, the ACERs of all six medical interventions fall between \$28 000 and \$82 000. When compared with no prevention, single colonoscopy, FOBT, and decennial colonoscopy are associated with the smallest ICER and appear the most cost-effective strategies.

Compared with no screening, a single colonoscopy represents a very cost-effective screening strategy of less

Table 13.1 Outcomes of competing programs to prevent colorectal cancer.

	No prevention	FOBT	Sigmoidoscopy	Single colonoscopy	Decennial colonoscopy
<i>Effectiveness</i>					
Expected number of CRC without screening	5904	5904	5904	5904	5904
Number of prevented CRC	0	926	2027	1352	4428
Life-years saved	0	1896	3636	2604	7952
Reduction in mortality (%)	0	18	34	23	75
<i>Resource utilization</i>					
Number of FOBT	0	2 464 606	0	0	0
Number of sigmoidoscopies	0	0	623 597	0	0
Number of colonoscopies	0	69 794	27 319	86 184	365 456
<i>Costs</i>					
Costs of FOBT (\$)	0	5 497 809	0	0	0
Costs of sigmoidoscopy (\$)	0	0	163 313 218	0	0
Costs of colonoscopy (\$)	0	33 640 016	16 281 508	41 091 209	189 667 598
Cost of care for CRC (\$)	136 452 922	115 715 753	89 619 575	103 124 901	34 113 230
Total costs (\$)	136 452 922	154 853 577	269 214 301	144 216 110	223 780 829
<i>Cost-effectiveness</i>					
ACER costs/saved life-years (\$)	∞	81 678	74 032	55 386	28 143
ICER compared with no prevention (\$)		9705	36 509	2981	10 983

Numbers in the table relate to a cohort of 100 000 persons aged 50 and followed on average for 28.5 years until the time of death. Future life-years saved and future costs were discounted using an annual rate of 3%. ACER, average cost-effectiveness ratio; CRC, colorectal cancer; FOBT, fecal occult blood test; ICER, incremental cost-effectiveness ratio.

than \$3000 per life-year saved. Repeat decennial colonoscopies could save two to three times more lives than a screening program based on a single colonoscopy. If third-party payers are able to provide the financial resources and subjects are willing to participate, a screening program comprising repeat colonoscopies represents the better yet more expensive alternative. Under tighter economic conditions with only limited funds available for cancer screening, a single colonoscopy between the age of 65 and 70 years offers a relatively cheap and highly cost-effective means of screening for colorectal cancer. The ICER of colonoscopy compared with no screening amounts to \$11 000 per life-year saved, which is only slightly higher than the ICER of FOBT. Colonoscopy is also associated with a relatively modest ICER when compared as an add-on to FOBT alone, i.e. \$11 400 per life-year saved. In screening using flexible sigmoidoscopy, the costs saved on colonoscopies are partly offset by the additional expenses for two procedures in all patients with distal polyps and the higher expenses for cancer care among patients with missed proximal cancers.

Costs of inconclusive tests and colonoscopy as the final arbiter

Computer-assisted colonography is a new technique that uses data generated from computed tomography

(CT) or magnetic resonance imaging (MRI) to create two- and three-dimensional scans of the colon. Advanced imaging software creates axial and reformatted two-dimensional images of the colon, as well as simulated endoluminal images. When computer-generated endoluminal images are displayed at a fast rate of 15–30/s, virtual colonoscopy provides the illusion of traveling through the colon. For both techniques the bowel needs to be cleansed in the same way as for a barium enema or colonoscopy. The colon is then inflated with a single contrast of gas or a water-based enema. Both techniques have been reported to yield a sensitivity over 75% and a specificity over 90% in detecting colorectal cancer and polyps of 10 mm or more in size [19–21]. Using CT or MRI colonography for screening of colorectal cancer would reduce the number of colonoscopies. This cost saving is gained at the expense of exposing all subjects with suspected polyps or cancers to two procedures, i.e. colonography plus colonoscopy. In principle, screening CT or MRI colonography is associated with a similar situation as all other screening procedures whose findings need to be followed by a subsequent colonoscopy. After a positive FOBT, for instance, a colonoscopy is needed to assess the colon for the presence of neoplasm. In the USA, polyps found during flexible sigmoidoscopy result inevitably in a colonoscopy administered for polypectomy and to evaluate the remainder of the colon.

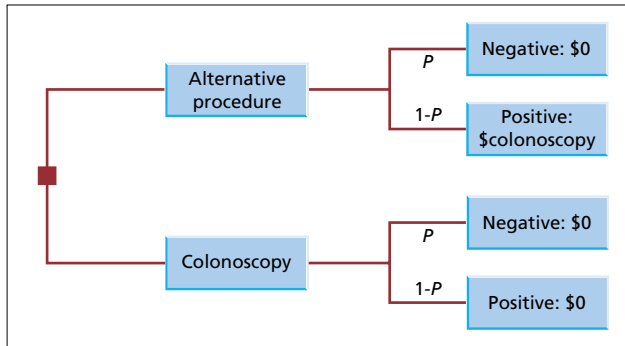


Fig. 13.5 Decision tree for calculating the threshold probability when a test becomes a viable alternative to colonoscopy. Both procedures (colonoscopy or its alternative) are associated with the same two potential outcomes, i.e. negative vs. positive finding. A positive finding of the alternative procedure needs to be followed by an additional colonoscopy.

Newer tests designed to screen stool specimens for a variety of cancer-related genes face a similar need for colonoscopy as final arbiter in the case of a positive finding [22].

In Fig. 13.5, this medical scenario is modeled as a simple decision tree. A threshold analysis is used to determine the probability of a normal finding, i.e. no colorectal polyps or cancers that would render screening with colonography the less expensive approach [23]. The decision between colonoscopy or another screening alternative is symbolized by the small filled square on the left-hand side. The upper branch representing the screening alternative to colonoscopy has two possible outcomes, both governed by chance. The alternative test can reveal a normal finding or a neoplasm. The probabilities associated with these two outcomes are P and $1 - P$ respectively. In the case of a normal finding, no further testing is necessary. In the case of a positive test outcome, a subsequent colonoscopy becomes necessary. The lower decision branch representing screening colonoscopy results in the same two outcomes and probabilities as in the upper branch but with different implications. No further diagnostic work-up is needed in case of neoplasm or any other positive finding. In summary, the decision tree weighs the higher costs of a colonoscopy against the savings obtained through a cheaper alternative procedure with the occasional need to perform two procedures in patients with positive findings. For the upper branch to cost less than the lower branch:

$$\text{Alternative} + (1 - P) \times \text{Colonoscopy} < \text{Colonoscopy} \quad [13.2]$$

Simple algebraic manipulations yield:

$$\text{Alternative} < P \times \text{Colonoscopy} \quad [13.3]$$

In essence, any alternative test procedure needs to cost less than colonoscopy multiplied by the expected frac-

tion of subjects with normal findings. For instance, expecting 30% of all subjects at age 50 years to harbor polyps and a colonoscopy to cost \$1000, $P = 70\%$ and the alternative procedure $< \$700$.

The usefulness of this type of threshold analysis relates to the fact that it can be similarly applied to many different screening techniques that require a colonoscopy as a follow-up test for their positive results. As indicated above, such screening techniques include FOBT, flexible sigmoidoscopy, and newer stool tests for tumor-specific DNA sequences. It needs to be kept in mind that threshold analysis represents a rather crude, back-of-the-envelope type of calculation that ignores, for instance, the different costs associated with simple colonoscopy vs. polypectomy and the impact of false-positive or false-negative outcomes of the alternative test procedure. Of course, the analysis could be refined by using more detailed assumptions or one could use a more detailed Markov modeling, as done previously to assess the cost-effectiveness of flexible sigmoidoscopy or FOBT [3]. Using a Markov process, we also did not find (MRI or CT) colonography to be a cost-effective method that could presently compete with colonoscopy [24]. However, it is conceivable that further refinements and simplifications of the technique will lower its costs and render it a cost-effective alternative in the future.

Surveillance and prevention in ulcerative colitis

Patients with long-standing extensive ulcerative colitis harbor an increased risk of developing colorectal cancer [25–28]. After 40 years about 30% of all patients with pancolitis have developed colorectal cancer [25–28], compared with a 6% cumulative risk over lifetime for such cancer in the general population [29]. Because of the increased risk of cancer, surveillance colonoscopy in long-standing pancolitis has been widely recommended [30–32]. The rationale of surveillance colonoscopy is to detect cancer at an early stage when treatment is more likely to be curative. Little evidence exists, however, that surveillance is truly efficacious and cost-effective in preventing deaths from colorectal cancer. Considering the obstacles to a clinical resolution, one can again use the techniques of medical decision analysis to assess the feasibility and usefulness of surveillance. However, the values of ACER or ICER would provide little guidance to the clinician, since no other comparative measures of prevention are available to put such parameters in perspective. Instead of expressing the outcome of a simulation in terms of ACER or ICER, a threshold analysis is used similarly to the example given above [33]. The analysis tries to answer the following question: How high does the cumulative probability of colorectal cancer

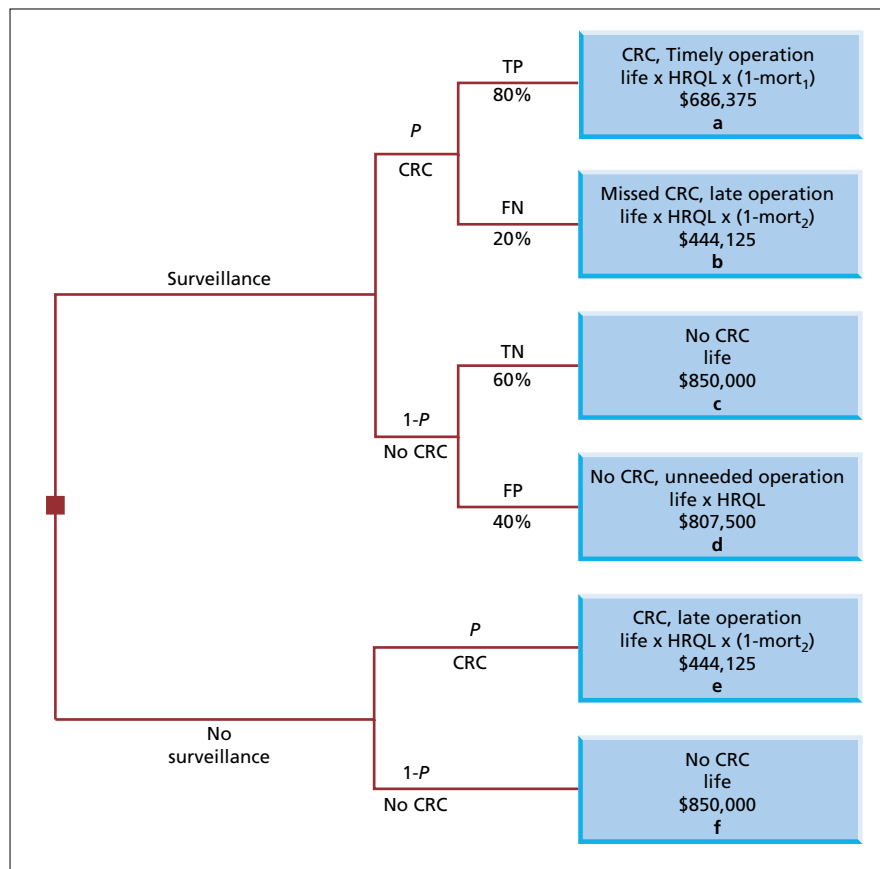


Fig. 13.6 Decision tree for threshold analysis of surveillance in patients with ulcerative colitis. P , cumulative probability of developing colorectal cancer (CRC); TP, true-positive (sensitivity); FN, false-negative; TN, true-negative (specificity); FP, false-positive results of surveillance colonoscopy; HRQL, health-related quality of life (95%); mort_1 (15%) and mort_2 (45%), cancer-related mortality in patients with and without surveillance respectively.

need to be for biannual surveillance to be more beneficial than nonsurveillance?

This question is translated into the decision tree shown in Fig. 13.6. Its structure is explained proceeding from left to right and from top to bottom. The filled square on the left-hand side symbolizes the initial decision for or against surveillance. The chances for or against the development of colorectal cancer are denoted as P and $1 - P$ respectively. In the case of cancer, surveillance colonoscopy plus histology can yield true-positive (TP) or false-negative (FN) test results. Cancers prevented or detected as a consequence of surveillance are associated with proctocolectomy. The mortality ($\text{mort}_1 = 15\%$) reflects the impact of cancers that cannot be prevented through surveillance and proctocolectomy. The life gained becomes reduced by the impaired HRQL after proctocolectomy. The final outcomes of TP and FN surveillance tests are quite similar, except for the higher mortality rate ($\text{mort}_2 = 45\%$) associated with cancers missed during surveillance. Colonoscopy in patients without dysplasia can yield true-negative (TN) or false-positive (FP) tests. Life and its quality remain unaffected by TN surveillance procedures. FP tests lead to an unnecessary proctocolectomy and a reduction in HRQL. The main lower branch of the tree represents the decision

against surveillance. It has only two possible outcomes governed by the probability of developing cancer. In the case of cancer, the outcome is identical to that of a missed cancer as a consequence of FN surveillance tests. Without cancer, the outcome is identical to the outcome associated with TN surveillance tests, i.e. life unaffected by cancer or proctocolectomy.

The decision tree is applied to the example of a 45-year-old patient with ulcerative colitis first diagnosed at age 35. Since the patient's life expectancy is about 34 years, a biannual surveillance program would require 17 colonoscopies at a total cost for surveillance of $17 \times \$1000 = \$17\,000$. Using the human capital approach, the value of life is equated with the average annual earnings multiplied by the life expectancy, i.e. $\text{life} = 34 \times \$25\,000 = \$850\,000$. The HRQL after proctocolectomy is assumed to be 95% compared with 100% of an unoperated healthy individual. A recent study reported a cancer mortality rate of 15% (mort_1) in a population with surveillance as opposed to 45% (mort_2) in a population without surveillance [34]. The sensitivity of colonoscopy in detecting premalignant lesions and preventing cancer-related death is estimated as $\text{TP} = 80\%$, while the specificity is estimated as $\text{TN} = 60\%$ based on data taken from Connell and colleagues [35].

For surveillance to be the preferred management strategy, the upper main branch of the decision tree should result in a higher yield than the lower main branch:

$$- \text{Surveillance} + P \cdot TP \cdot a + P \cdot FN \cdot b + (1 - P) \cdot TN \cdot c + (1 - P) \cdot FP \cdot d \geq P \cdot e + (1 - P) \cdot f \quad [13.4]$$

where a – f are used as short forms to indicate the various outcomes. The cost for surveillance enters the equation with a minus sign, as opposed to the plus sign associated with the benefit of life-years saved. Equation 13.4 can be solved for the probability value of P :

$$P \geq \frac{-\text{surveillance} + (TN \cdot c + FP \cdot d - f)}{(TN \cdot c + FP \cdot d - f) - (TP \cdot a + FN \cdot b - e)} \quad [13.5]$$

Although the formula may look daunting, the P -value is readily calculated on a spreadsheet. A probability of $P = 16\%$ is obtained using the values introduced in the preceding paragraph. This P -value suggests that if the probability for developing cancer exceeds 16%, surveillance would represent a decision preferred over no surveillance. In the present example of a 45-year-old patient with a 10-year history of ulcerative colitis, the cumulative probability of developing cancer over the patient's remaining lifetime of 34 years equals:

$$P = 10 \text{ years} \times 0.5\% + 10 \text{ years} \times 1.0\% + 14 \text{ years} \times 1.5\% = 36\% \quad [13.6]$$

Considering the high risk of developing colitis-related cancer, biannual surveillance appears to be the better medical decision to make. Since the 36% probability of developing cancer exceeds the threshold P -value of 16%, surveillance becomes the preferred management strategy. The strength of the argument in favor of surveillance is directly proportional to the threshold value. A low threshold value would argue strongly in favor of surveillance. Vice versa, a high threshold value that exceeds the lifetime probability of developing cancer would speak against the use of surveillance colonoscopy.

Since the value of life appears as variable in the final outcomes of all six branches in the decision tree shown in Fig. 13.6, the actual costs calculated by the human capital approach exert little influence on the outcome of the analysis. The cost of surveillance pales in comparison with the benefit of life-years saved. Therefore, variations in the cost of surveillance also exert relatively little influence on the threshold probability. However, the outcome of the analysis very much depends on the other assumptions built into the model. It has been suggested, for instance, that HRQL remains largely unaffected by proctocolectomy [36]. Increasing HRQL from baseline 95% to 100% halves the threshold value from baseline 16% to 8%. In the baseline analysis shown in Fig. 13.6, the following set of values were chosen: $\text{mort}_1 = 15\%$, $\text{HRQL} = 95\%$, $\text{TP} = 80\%$. Slight variations lead to a second set of values, such as $\text{mort}_1 = 25\%$, $\text{HRQL} = 85\%$,

$\text{TP} = 70\%$. The resulting threshold value $P = 45\%$ lies outside the cumulative lifetime risk of the patient to ever develop colorectal cancer. The second set of assumptions is by no means extreme and seems to fall well within a reasonable range that might be expected by a widely distributed surveillance program.

As these examples show, one can conceive similarly reasonable sets of assumptions that result either in excessively high or low thresholds. Based on one's preferences, one can use the decision analysis to do both, defend or refute the usefulness of surveillance colonoscopy. To narrow down the possible range of each assumption built into the decision analysis, a better set of data would be needed that can only be obtained through clinical studies. More refined decision models can be envisaged that account for the time-dependent development of dysplastic lesions and their multistep transition into cancer [37]. Instead of comparing the two main branches of Fig. 13.6, one can compare the outcome of two separate Markov chains that simulate the age- and time-dependent occurrence of colorectal cancer. Such more complicated models also consider the transition from dysplasia to cancer, the expenditures arising from medical and surgical therapy, as well as the indirect costs of surveillance. However, a more detailed model provides a similar answer as the present threshold analysis, i.e. the argument in favor or against surveillance depends on the assumptions built into the model, for which definitive data are lacking [37]. The decision analysis shows which factors are most relevant for the success of a surveillance program, but fails to provide a clear-cut answer as to whether such a program would be truly beneficial.

Limitations of CEA

The decision for or against screening and prevention of colorectal cancer depends on many partly interrelated factors. These factors include:

- family history of adenomatous polyps and cancer;
- patient demographics;
- presence of other comorbid conditions;
- incidence and prevalence of colorectal polyps;
- progression of various polyp types and other pre-malignant conditions to cancer;
- sensitivity and specificity of competing diagnostic techniques;
- invasiveness and risks of various diagnostic modalities;
- surgical success at different disease stages;
- adverse effects, disability, and mortality from surgery;
- effectiveness of other treatments;
- availability of medical interventions;
- medical and nonmedical costs;
- natural history, including mortality, of colorectal cancer.

Many of these parameters do not remain constant but vary as the patient ages and the disease progresses. For instance, the sensitivity and specificity of all screening methods improve as the disease progresses from a small mucosal lesion, to polyp, to small and eventually large cancer [38,39].

For the vast majority of associations, sufficiently reliable data do not exist. Different factors contribute differently to the disease and its prevention. Medical decision analysis helps to weigh the contribution of these factors and to choose between competing management options. Because the available evidence is often crude or incomplete, economic and medical decision analyses have to include many assumptions in their models. Although the individual assumption may have a small margin of error, the sheer multitude of assumptions built into a model can render its overall outcome susceptible to large variations. Even if the influence of individual factors is known and clinically well established, their interaction and joint influence often remain untested and unknown. For instance, it is known that colonoscopy is a good technique for diagnosing colon cancers and removing polyps, but less conclusive evidence exists that these single achievements actually prevent cancers or cancer-related deaths [40–42]. Even if screening colonoscopy prevented deaths from colorectal cancer, it would still remain to be proven that such a strategy actually saved lives and extended life expectancy [43,44]. It may well be that patients who are saved from death through colorectal cancer soon succumb to other diseases. Screening itself could be associated with untoward medical or social effects that, in the final balance, completely negate its seemingly obvious benefits [45].

In the review process of decision analyses submitted for publication, reviewers almost invariably suggest additions that make already complex models even more complicated and difficult to appreciate. The inclusion of many less relevant side issues distract from the few important associations. Unfortunately, simple models are often misjudged as being primitive or inconclusive rather than transparent, insightful, or elegant. There is a general failure among medical reviewers to understand that instead of painting a detailed picture of reality, ideal models are supposed to contain a simplified and condensed representation of a medicine that focuses on the few essential parameters. It does not help the clinician to have the complexity of his or her medical reality be replaced by the black box of an overly complicated model whose conclusions have to be taken at face value, because the model has become too large and too detailed to fit the confinements of a journal article. Even experts may find it difficult to disentangle the intricacies of individual models and compare their outcomes [46].

To publish their decision analyses investigators are forced to oversell the relevance of their modeling efforts

and present their outcomes as definitive answers to lingering medical problems. They restrict the ranges tested in the sensitivity analyses or avoid pointing out variables that shift the model out of balance. The investigators make their results appear more conclusive than they really are and advertise them as mathematically derived rigorous evidence for or against a particular medical strategy. Various medical specialists and their professional organizations pursue a political and economic agenda. Gastroenterologists, for instance, are interested in studies that confirm the relevance associated with endoscopic procedures, whereas radiologists want to emphasize the benefit of their imaging techniques, and generalists want to preserve the use of FOBT and flexible sigmoidoscopy as screening methods accessible to the nonspecialist. Rather than look at details of the analysis, CEA are often accepted based on their outcome alone and whether they succeed in confirming a set of preconceived notions. However, medical decision analyses are generally less suitable for implementing a specific policy, but more suitable for highlighting which variables are important in influencing the medical decision or its outcome. It needs to be kept in mind that models only serve as guidance for assessing the potential outcome of a medical strategy. Economic and decision models do not obviate the primacy of clinical data gathered through controlled clinical trials.

Summary

In comparing two competing screening strategies, the following scenarios may arise. If one strategy is cheaper and more effective than the alternative one, the decision in favor of the cheaper and more effective strategy is made easy. The mixtures of more effective but more expensive or less effective but less expensive outcomes are sometimes difficult to decide without a formal cost-effectiveness analysis. However, physicians should not misread a cost-effectiveness analysis as guidance toward the best medical strategy. Compared with no screening, a single colonoscopy represents a very cost-effective screening strategy of less than \$3000 per life-year saved. Repeat decennial colonoscopies save two to three times more lives than a screening program based on a single colonoscopy. The ICER of decennial colonoscopy compared with no screening amounts to \$11 000 per life-year saved. Colonoscopy is also associated with a relatively modest ICER when used in addition to FOBT, i.e. \$11 400 per life-year saved. In screening using flexible sigmoidoscopy, the costs saved on colonoscopies are partly offset by the additional expenses for two procedures in all patients with distal polyps and the higher expenses for cancer care among patients with missed proximal cancers. Economic and decision models are generally unreliable in predicting the exact outcomes

of a specific screening policy, but more suitable for demonstrating which variables are most important in influencing its expected result. Models can only guide in comparing the potential outcomes of competing strategies, but they do not obviate the primacy of clinical data gathered through controlled clinical trials.

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Chapter 14

Hereditary Colorectal Cancer

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Introduction

Colorectal cancer (CRC) is the second most common cause of cancer-related mortality, with approximately 57 100 deaths annually in the USA. The lifetime risk for CRC is about 6% in both males and females [1]. The causes of colon cancer are heterogeneous and include several environmental and heritable factors. Undoubtedly, a complex interaction between these two categories ultimately determines risk. The majority of cancers occurs in patients with no family history and are defined as sporadic cases. However, roughly 10–25% of patients have familial colon cancer as defined by their positive family history. In addition, several well-characterized hereditary syndromes have been identified that confer a higher risk for colorectal cancer. Although such syndromes account for only a small percentage of CRC cases (1–3%), the genetic and molecular mechanisms involved have contributed immensely to our understanding of cancer pathogenesis in general.

The clinician, especially the primary care physician and gastroenterologist, should have a fundamental understanding of familial colon cancer, including hereditary CRC syndromes. For this select group of patients, screening recommendations for CRC and overall management are distinct from those of the general population. Furthermore, the hereditary syndromes have unique phenotypes with additional clinical manifestations, including other types of malignancies. Genetic testing is available for many of these syndromes and offers another tool for the clinician to identify this subset of patients and their families.

Familial colon cancer

A family history of colon cancer is a significant risk factor for the subsequent development of CRC [2]. Several studies have established the risk of CRC in relatives of a patient with colon cancer, and have demonstrated that clustering of cases within families occurs frequently. The risk in a first-degree relative of a person with CRC is approximately the same at the age of 40 as it is for someone in the general population at the age of 50 [3]. First-degree relatives of persons with CRC have a

two- to three-fold increased risk of colon cancer compared to control or population incidence [4–6]. Furthermore, the age of the patient at the time of diagnosis and the number of affected relatives affects the degree of risk. If the patient is diagnosed when older than 55 years, the risk to first-degree relatives is approximately double that of the general population. This risk is three-fold if the patient is between 45 and 55 years and four-fold if younger than 45 years at the time of diagnosis [7]. Likewise, if two first-degree relatives have colorectal cancer, the risk increases by three- to four-fold.

The risk of colorectal cancer is also increased in relatives of a person with colon adenomas, as demonstrated by the National Polyp Study. The risk in siblings and parents of a patient with any adenomatous polyp was 1.78 (95% CI, 1.18–2.67). Again, the age of the person at the time of adenoma diagnosis was also important. The risk of CRC increased to 2.59 (95% CI, 1.46–4.58) if the polyp was diagnosed at a less than 60 years of age compared to an age greater than 60 years [8]. In another study by Pariente *et al.* [9], the odds ratio for all adenomas in first-degree relatives of colon cancer patients compared with controls was 1.5 (95% CI, 1.0–2.4). However, if high-risk adenomas (villous component or size ≥ 1 cm) were considered, the odds ratio increased to 2.6 (95% CI, 1.3–5.1).

Although there is clearly an increased chance of developing CRC in persons with a family history, the specific factors involved in this risk are incompletely understood. Hereditary factors certainly predispose to developing CRC and are probably a major determinant. However, environmental exposures significantly interplay with the hereditary tendency to develop CRC. Hereditary factors appear to make one more susceptible to the deleterious effects of certain exposures.

Which factors and how much each contributes to familial tendency have only partially been elucidated. Environmental exposures of adult life are unlikely to be major determinants of familial CRC risk, although they are certainly important to overall colon cancer pathogenesis. Studies of spouses of persons with CRC, for example, show no increased risk of CRC [10]. By contrast, an analysis of cohorts of twins in three Nordic countries emphasizes the importance of inheritance in

the propensity to develop CRC. In this cohort, colon cancer was only 1 of 3 cancers to show a significant influence by hereditary factors; the remaining 25 cancers appeared to have minimal, if any, contribution from inheritance, and were presumably more dependent on environmental exposures [11]. The study found that inheritance was part of the pathogenesis of colon cancer in 36% of all colon cancer cases. Exposure of family members to common or the same environmental factors accounted for only 8% of familial cases.

According to several kindred studies, the common familial risk probably arises from several low to moderately penetrant susceptibility alleles [12,13]. Several genes and chromosomal loci have already been demonstrated to be involved in the inherited predisposition to CRC. Houlston and Tomlinson [13a] performed a pooled analysis on 50 studies to clarify the impact of individual polymorphisms on cancer risk, and were able to identify three potential candidate alleles that confer an increased susceptibility. These polymorphisms include the adenomatous polyposis coli (*APC-I1307K*) variation, the Harvey Ras-1 variable number tandem repeat polymorphism (*HRAS1-VNTR*), and certain alleles of the methylenetetrahydrofolate reductase (*MTHFR*) gene. The *APC-I1307K* mutation is a mutation in the *APC* gene found in 6% of the general Ashkenazi Jewish population, 12% of this population with CRC, and 29% with CRC and a family history of colon cancer. *APC-I1307K* mutation predisposes to a milder degree of CRC risk compared to that observed in persons with familial adenomatous polyposis, which also arises from *APC* mutations. This mutation predisposition appears to give rise to a phenotype of CRC that is similar to sporadic cases aside from a mild to moderate increased risk [14–16].

Genetic testing is available for the *APC-I1307K* mutation in a person of Ashkenazi Jewish descent with a family history of CRC. Other than this specific population and the established hereditary syndromes (see below), no other routine genetic testing exists to identify persons at risk for colon cancer. Therefore, the clinician must be aware of those at higher risk based on their family history, so effective CRC screening can be implemented. Screening recommendations for persons with a family history of CRC differ from those for the general population; they are more aggressive and begin at younger ages. It must be understood that these recommendations are not based on prospective controlled studies with mortality endpoints since no studies have yet been performed. Based on ethical considerations and the identification of higher risk in families with colon cancer, such future studies may not be accomplished.

Recommendations for CRC screening in the setting of familial colon cancer are based on known risk and the known effectiveness of screening modalities. The recom-

mendations are given in several consensus statements. In 1997 a multidisciplinary expert panel, composed of representatives from several organizations, including the American Gastroenterological Association (AGA), the American College of Gastroenterology (ACG), the American Society for Gastrointestinal Endoscopy (ASGE), the American Society of Colon and Rectal Surgeons (ASCRS), and the American Cancer Society (ACS), established clinical practice guidelines for both CRC screening in the general population as well as those with a familial risk [17]. Recently, the panel established new criteria [17a]. For those with a family history of CRC or polyps, the panel makes specific screening recommendations for other family members depending on who is affected (first-degree, second-degree relatives, etc.), how many relatives are affected and at which ages. For those with at least two first-degree relatives with CRC or a single first-degree relative with CRC or adenomatous polyps diagnosed before the age of 60 years, the panel recommends a colonoscopy every 5 years, starting at the age of 40 years or 10 years younger than the earliest case in the family (whichever comes first). Double-contrast barium enema is another possible option for screening, but the preferred method is colonoscopy. If a first-degree relative is diagnosed with CRC or adenomatous polyps at age 60 years or older, the screening recommendations are the same as those persons at average risk for developing CRC, but beginning at age 40 years. This is also the recommendation for those with two second-degree relatives affected with CRC. Finally, the panel recommends the same screening for CRC as the average-risk population in those with second- or third-degree relatives with CRC.

The ACS also has separate recommendations [18]. In those persons with a first-degree relative with CRC or adenomatous polyps diagnosed before age 60 years or if two or more first-degree relatives had CRC at any age, full examination of the colon should begin at age 40 years or 10 years before the youngest case. The most recent United States Preventive Services Task Force (USPSTF) guidelines give a strong recommendation that all average-risk men and women receive CRC screening starting at age 50 years. They add that early age screening in those with affected first-degree relatives is “reasonable” [18a]. They note that the best evidence for colon cancer screening comes from fecal occult blood test (FOBT) and sigmoidoscopy studies, but that the combination of these two, as well as colonoscopy and barium enema are also reasonable screening approaches in view of the characteristics of these procedures and present evidence. Other groups have made recommendations, but they are similar to both the multidisciplinary expert panel and the ACS. Table 14.1 outlines a composite of the recommended screening interval and ages of implementation for familial colon cancer.

Table 14.1 Colon cancer screening recommendations for persons with familial risk.

Familial risk	Recommendation
Second- or third-degree relative with colorectal cancer	Same as average risk*
First-degree relative with colon cancer or adenomatous polyps diagnosed at age \geq 60 years	Same as average risk, but begin at age 40 years
Two or more first-degree relatives with colon cancer, or a single first-degree relative with colon cancer or adenomatous polyps diagnosed at an age $<$ 60 years	Colonoscopy every 5 years,† beginning at age 40 years or 10 years younger than the earliest diagnosis in the family, whichever comes earlier Double-contrast barium enema may be substituted, but colonoscopy is preferred

* Colonoscopy may be considered, even starting at a younger age, depending on the number and age of second- and/or third-degree relatives with colon cancer.

† An interval of 3–5 years is given by some organizations to allow for families with more severe familial risk.

Inherited syndromes of colon cancer

Although technically considered familial cases, CRC developing in the setting of inherited syndromes represents a unique situation as there is a better understanding of the pathogenesis, genetics, and molecular biology involved. Furthermore, these genetic syndromes have a significant association with several benign and malignant extraintestinal manifestations. Unlike the more common familial colon cancers, genetic testing is available and allows for more effective screening of families at risk.

Familial adenomatous polyposis

Epidemiology

Familial adenomatous polyposis (FAP) is a well-characterized genetic condition with first reports in the literature in 1861 and 1873 [19,20]. It is the most common of the polyposis syndromes—a heterogeneous group of disorders characterized by multiple gastrointestinal polyps occurring in the lumen of the gut. The hallmark of FAP is the propensity to develop hundreds to thousands of adenomatous colon polyps with an inevitable occurrence of CRC if not treated. The prevalence of FAP varies between 1 in 6850 and 1 in 31 250 (2.29–3.2 cases per 100 000 persons) [19,21,22], with both genders affected equally. Historically, FAP accounted for about 0.5% of all CRC cases [21], although currently this number is likely to be lower, probably due to improved screening and prevention of CRC development [22]. Variants of FAP include Gardner’s syndrome, about two-thirds of Turcot’s syndrome families, and attenuated adenomatous polyposis coli (AAPC), also referred to as attenuated FAP (AFAP).

Etiology

FAP occurs in families as an autosomal dominant condition. Disease-causing mutations occur in the adenomatous polyposis coli gene (APC) on the long arm of

chromosome 5 (5q21-q22) [23–28]. Different APC mutations can result in different clinical manifestations as noted below. Over 825 germline mutations have been identified [29]. About one-third of newly diagnosed cases not belonging to a known FAP family represent spontaneous or new APC mutations [19].

The APC gene has 15 exons, coding for 2844 amino acids and a 311.8-kDa protein. Exon 15 comprises over three-quarters of the coding region. The APC protein controls cell proliferation through signalling pathways involved in apoptosis, cell proliferation, colonocyte migration, and, perhaps, chromosomal stability.

Interestingly, the location of the mutation within the APC gene bears on the phenotype of the disease. Depending on the specific mutation, patients can present with differences in polyp burden, location, age of presentation, and extracolonic manifestations. In attenuated FAP (AAPC), mutations are found in the extreme 5’ part of the gene, in exon 9 or in the far 3’ end [30–38]. The most frequent mutation in FAP involves codon 1309. Persons with mutations at this location tend to present at an average age of 20 years, compared to 10 years later in those with mutations between codons 168 and 1580 (excluding 1309) [39]. Those with mutations 3’ to codon 168 and 5’ to codon 1580 present at an average age of 52 years. Furthermore, extracolonic manifestations associate to some degree with the mutation location. Congenital hypertrophy of the retinal pigment epithelium (CHRPE) is observed with mutations between codons 463 and 1387 [40], while it tends to be absent when the mutation is between codons 1444 and 1578 [41,42]. Thyroid cancer is associated with mutations in the 5’ end of exon 15. Studies have also found desmoid tumors to be associated with mutations in specific exons [43].

Clinical presentation

Gastrointestinal manifestations

Currently, most patients with FAP are diagnosed at an asymptomatic stage of their disease due to screening



Fig. 14.1 Multiple pedunculated and sessile polyps seen on colonoscopy in a patient with FAP.



Fig. 14.2 Numerous sessile polyps in the gastric corpus in a patient with known FAP.

efforts. If symptoms do develop, 66% of patients already have cancer. Typical symptoms include rectal bleeding (79%), diarrhea (70%), and abdominal pain (40%), which are uncommon in patients with polyps alone.

A clinical diagnosis of FAP can be made when a patient has 100 or more colonic adenomatous polyps, or less than 100 if the patient has an immediate relative with FAP [19]. Typically, a person will present with an average of 1000 polyps in fully expressed FAP and sometimes up to 5000. In early disease development and AAPC, the polyp number can be significantly less. Polyps usually begin to appear in the second or third decade of life, with an average age of polyp occurrence at 15.9 years (range 8–34) as assessed by prospective rigid sigmoidoscopy [44]. The average age of diagnosis, when the patient presents with symptoms, is 35.8 years (range 4–72) [19].

The typical adenomatous polyp in FAP is small. In fact, even in fully developed cases, more than 90% of polyps are less than 5 mm and less than 1% are larger than 1 cm. Polyps can carpet the entire colonic mucosa (Fig. 14.1) or occur as more distinct, larger lesions. They are distributed throughout the colon, although there is a slight distal predominance. Histopathologic examination of polyps is indistinguishable from sporadic adenomas. There can be villous and tubulovillous architecture, but this is seen far less commonly than tubular adenomas. A unique feature of FAP that is not seen in the general population is the finding of adenomatous epithelial cells in a single crypt called microadenomas [19]. Microadenomas are often found in the biopsy specimens of normal-appearing, flat mucosa. Budding of dysplastic epithelium is also seen as well as aberrant crypt foci, which are identified by staining the colonic wall with methylene blue [45].

Untreated FAP will inevitably progress to adenocarcinoma of the colon. The average age of CRC diagnosis is

39 years. Eighty-seven per cent will develop cancer by the age of 45 years, and 93% by the age of 50 years. Although uncommon before adolescence, CRC has been described in FAP cases as young as 9 years of age [46]. Most FAP colon cancers (84%) are distal to the splenic flexure, which is similar to the distribution of sporadic cancers. Synchronous (41%) and metachronous (7%) tumors occur often. Average life expectancy after the diagnosis of colonic malignancy is 2.6 years. The risk for CRC correlates with polyp burden. Persons with over 1000 polyps are at a 2.3-fold higher risk of CRC compared to those with less than 1000 polyps [47].

Polyps also develop in other parts of the gastrointestinal tract. Gastric polyps occur in 23–100% of FAP patients and are usually nonneoplastic fundic gland polyps [48–51]. On endoscopic examination, gastric polyps are multiple and sessile, 1–5 mm in size, the same color as the surrounding mucosa, and located in the gastric fundus and corpus (Fig. 14.2). They can coalesce to form a matted, irregular mucosal surface. Histologically, the polyps consist of simple hyperplasia of the fundic glands with microcysts. They rarely cause symptoms and rarely progress to malignancy. However, about 10% of FAP patients develop adenomatous polyps in the stomach, typically in the antrum and less so in the body and fundus [49,52]. The lifetime risk of gastric adenocarcinoma is 0.6%, probably as a consequence of adenomatous gastric polyps.

Often of more clinical significance in FAP are duodenal polyps, including ampullary polyps (Fig. 14.3). About 50–90% of FAP patients will develop adenomatous polyps in the duodenum [51], which are often small (1–5 mm), numerous, and located throughout the duodenum, especially in the second and third portions. Some patients have polyps in the periampullary area only. Like colon polyps, duodenal polyps show an adenoma–carcinoma progression and can have villous



Fig. 14.3 Characteristic ampullary tumor in a patient with known FAP.

architecture and high-grade dysplasia. The Spigelman staging system [53] evaluates the severity of duodenal polyposis.

Duodenal cancer usually occurs in the periampullary region and exhibits a lifetime incidence of 3–5% [19,51]. Cancer occurs at an average age of 45–52 years (range 17–81 years) and is one of the leading causes of death in FAP patients who have had a prophylactic colectomy. The typical periampullary location of adenomas and cancers may be related to bile or pancreatic secretions [51,52]. Unlike the case with colonic polyps, the severity and presence of duodenal adenomas has not been consistently shown to relate to the location of the APC gene mutation [51].

Small bowel adenomas can also occur and concentrate in the proximal jejunum (50% of cases) or distal ileum (20% of cases) [54]. Patients can also develop adenomas in the distal ileum after colectomy. Younger patients can develop prominent lymphoid follicles of the distal ileum, which must be differentiated histologically from adenomas. Small bowel cancer is uncommon in any of these situations.

Although the frequency of lesions is unknown, adenomas and cancer can develop in the gallbladder, biliary tree, and pancreas [48,54–56].

Extraintestinal manifestations

FAP also has several important extraintestinal manifestations. Osteomas are benign lesions of bones that often occur in the skull and mandible. The lesions appear as radiopaque lucencies on plain radiographs and are of little clinical importance, except for occasional cosmetic concerns. Osteomas can appear in children before the development of polyposis, but can develop later in life as well [57,58]. Several dental abnormalities have also been described in FAP, including supernumerary

teeth, unerupted teeth, dentigerous cysts, and odontomas [58–60]. Again, these can precede the development of polyposis. The incidence of these dental abnormalities in FAP is 17%, compared to 1–2% in the general population.

Desmoid tumors are benign fibrous growths with an incidence in FAP of 3.6–20% [61–63]. The relative risk of desmoid tumors in FAP compared to the general population is 825 and occurs at an average age of 28–31 years [64]. They may be the first manifestation of disease and, in some families, may be the only finding of FAP. Other than the location of the APC mutation, other risk factors include a family history of desmoids, female gender, and osteomas [65]. Although considered benign, desmoid tumors are a significant cause of morbidity and mortality. Mortality from the tumors is 10–50% with a 10-year survival rate of 63%; they are a common cause of death in those who have had prophylactic colectomy. Desmoid tumors in FAP consist of monoclonal growths of hyperproliferative fibroblastic cells. Tumors are most common in the abdomen, both intraabdominally and within the abdominal wall [62,63]. The most common symptom is abdominal pain, though only a third of tumors cause pain. They do not metastasize; however, tumors can grow and compress structures, such as nerves, blood vessels, and hollow organs, and can erode into bones. Surgery can stimulate the development and growth of desmoid tumors [66].

Congenital hypertrophy of the retinal pigment epithelium (CHRPE), also called pigmented ocular fundus lesions, are dark round areas of pigment of the retina [67], ranging in size from 0.1 to 1.0 disk diameters. They are best seen on slit-lamp examination. Bilateral lesions or multiple lesions (> 4) are relatively specific for FAP (94–100%), but only have a sensitivity of 58–84%. CHRPE can be the earliest clinical manifestation of FAP.

Adrenal adenomas [68,69] are also more common in FAP than in the general population, with an incidence of 7% and 13% in two studies [70,71]. Functioning adenomas and adenocarcinoma have both been reported, although the association with FAP is unclear. Management is identical to that in the general population.

Cutaneous lesions in FAP consist of epidermoid cysts, sebaceous cysts, lipomas, and fibromas [58,72–76]. Epidermoid cysts often occur before puberty and may precede the development of polyposis. Nasal angiofibromas have also been reported in FAP patients [77].

Extragastrintestinal malignancies

Several malignancies not affecting the gastrointestinal tract have been associated with FAP. Hepatoblastoma is an important malignancy in children with FAP. The risk is 800-fold higher than that of the general population

[78,79] and usually develops within the first 5 years of life with a male predominance. Thyroid cancer affects 2% of FAP patients [80], with a relative risk of 7.6 compared to the general population. The average age of diagnosis is 28 years (12–62 years) and there is a female predominance [81]. The characteristic histology is papillary cancer. Pancreatic cancer has also been found to be higher in the FAP population with a relative risk of 4.46 [81] compared to the general population.

Variants of FAP

Attenuated adenomatous polyposis coli (AAPC)

As the name implies, less polyp burden and later onset of disease characterizes AAPC. Usually, there are an average of 30 colonic polyps, though the number can vary widely in different families [36–38,82]. In some families, polyp burden can be minimal—making the diagnosis difficult without genetic testing—but in others, the number can approach those in typical FAP. Polyps have a more proximal distribution in the colon. CRC develops, on average, at age 50 years with a lifetime risk of 80% [37]. Unlike, colonic polyps, upper gastrointestinal polyps are not attenuated [35,36,83].

Gardner's syndrome

The term Gardner's syndrome is mostly of historic interest, though it is still commonly used. Gardner's syndrome is characterized by typical FAP, but with a high propensity to develop extracolonic growths, especially osteomas, fibromas, and epidermoid cysts [59]. With the discovery of the APC gene, it was realized that FAP and Gardner's syndrome both resulted from mutations of that gene. Again, the location of the mutation in the APC gene has an important role in the tendency to develop extracolonic growths [84].

Turcot's syndrome

About two-thirds of Turcot's syndrome patients have germline mutations in the APC gene, giving rise to polyposis as well as central nervous system (CNS) tumors [85]. The other third arise from germline mutations in the DNA mismatch repair genes and are a variant of hereditary non-polyposis colorectal cancer (HNPCC). The CNS tumors in patients with germline APC mutations are typically medulloblastoma-type, anaplastic astrocytomas, or ependymomas [86,87]. By contrast, in patients with germline DNA mismatch repair gene mutations, the tumors are usually glioblastoma multiforme [87]. The relative risk of CNS tumors in FAP is 92-fold [86], and 40% of families with CNS malignancy have more than one family member with tumors.

Genetic testing

Genetic testing for hereditary syndromes serves as a valuable method for screening individuals and their families at high risk for disease. Informed consent is an essential component of genetic testing, and the patient or his/her representative must understand the rationale, meaning, and limitations of testing, including implications for screening and treatment. Genetic counseling both before and after testing should be available.

Most of the inherited syndromes of colon cancer now have available genetic tests. Commonly, these tests use peripheral leucocytes for obtaining DNA. An increasing number of laboratories are offering such genetic tests, and a website lists these available laboratories (<http://www.genetests.org/>). The American Gastroenterological Association (AGA) has established guidelines for genetic testing in hereditary colon cancer [88]. Testing should be utilized in two specific situations: (i) to confirm the diagnosis in an individual clinically suspected of having the disease, and (ii) in at-risk family members. In a particular family, the affected member should be tested first to identify the mutation and then other family members should be screened for that specific mutation. The accuracy of this method is near 100% when a germline mutation is identified in the index case. When no mutation can be identified in the affected member, additional family members should not undergo genetic testing. However, they should still be considered high risk and have appropriate management and screening. If no affected family member is available in a pedigree suspected of harboring the disease, family members can be tested, although the likelihood of an uninformative result is high. In this circumstance, failure to identify a mutation cannot exclude the diagnosis, and family members must still undergo suggested cancer screening.

An APC mutation can be found in 80–90% of FAP families [89]. Generally, individuals with the typical polyp burden of FAP, suspected AAPC, or a first-degree relative of a person with known FAP or AAPC should be offered testing. Several methodologies exist for genetic screening and include protein truncation testing (PTT), linkage analysis, and DNA sequencing. When sequencing is used, single-strand conformation polymorphism testing (SSCP) or similar methods are often employed to narrow the area where sequencing should be done. Sequencing is becoming the preferred method because of its accuracy. With sequencing, once a germline mutation is identified, other family members can be tested for the same mutation. Since the accuracy of testing is so high once a germline APC mutation is identified in a particular family, only those who test positive need appropriate screening for FAP. Genetic testing should be delayed until age 10–12 years, given the potential psy-

Table 14.2 Colon screening recommendations for persons with hereditary syndromes. (Adapted from Burt [90] with permission.)

Hereditary syndrome	Recommendation
Familial adenomatous polyposis*	Sigmoidoscopy annually, beginning at age 10–12 years†
Hereditary non-polyposis colorectal cancer‡	Colonoscopy, every 1–3 years, beginning at age 20–25 years
Peutz–Jeghers syndrome	Colonoscopy, beginning with symptoms or in late teens if no symptoms occur. Interval determined by number of polyps but at least every 3 years once begun
Juvenile polyposis	Colonoscopy, beginning with symptoms or in late teens if no symptoms occur. Interval determined by number of polyps but at least every 3 years once begun
Cowden’s syndrome	Colonoscopy only if large bowel symptoms occur

* Includes the subcategories of FAP, Gardner’s syndrome, Turcot’s syndrome, and AAPC.

† In AAPC, colonoscopy should be used instead of sigmoidoscopy because of the preponderance of proximal colonic adenomas. Colonoscopy screening in AAPC should probably begin in the late teens or early twenties.

‡ Includes Muir–Torre syndrome.

chological affects during the first decade of life and lack of bearing on clinical management [90].

Cancer screening

Appropriate management of FAP patients not only includes surveillance for colon polyps and CRC, but also for other potential malignancies as well as timely referral for prophylactic colectomy. Several studies have shown the benefit of screening and subsequent colectomy in FAP patients [91,92]. In relatives screened for FAP, the mortality from colon cancer is 1.9% compared to 44% in FAP patients who present with symptoms. Screening should be offered to anyone with a genetic diagnosis of FAP or to relatives of those with FAP when genetic testing is inconclusive or not available [88]. Guidelines for screening suggest annual sigmoidoscopy beginning at age 10–12 years [90]. The interval can be increased each decade and revert to suggested screening for the general population at age 50 if no polyposis is found. If screening begins at a later age, then colonoscopy is the preferred modality for the first examination. Likewise, if surgery is delayed for greater than a year after polyposis develops, then annual colonoscopy should be instituted. In AAPC, polyps are predominantly proximal and, thus, colonoscopy should always be used. In this condition, screening can be delayed until the late teens or mid twenties. Table 14.2 outlines the screening recommendations for CRC.

After surgery, adenomas and cancers may develop in the rectum if a subtotal colectomy with ileorectal anastomosis is performed, or in the ileal pouch if a total colectomy with ileoanal pull-through is done [93,94]. Screening the ileal pouch should occur within 2 years after surgery and then every 6 months to 3 years, depending on the polyp burden [94a]. For the rectal remnant, screening with sigmoidoscopy should happen every 3–6 months, depending on the rate of adenoma recurrence.

Because of the higher incidence of duodenal cancer and, to a lesser degree, gastric cancer, the upper gastrointestinal tract should also undergo periodic examination. Although, routine screening has never been shown to improve outcome, the theoretical advantage makes this recommendation reasonable. The general recommendation is to begin screening at age 20–25 years, though some recommend screening at the initial time of diagnosis and earlier in those with a family history of duodenal cancer at young ages. Upper endoscopy should be done with a side-viewing endoscope to facilitate examination of the duodenal papilla.

Screening for other malignancies [90] includes annual thyroid examination beginning at age 10–12 years, periodic head CT or MRI in patients with a family history of CNS tumors, annual liver palpation in the pediatric patient at risk, periodic examination of the small bowel (enteroscopy or radiography) if extensive duodenal polyposis is found, and consideration of abdominal computed tomography every 3 years to examine the pancreas, small bowel, and adrenals. Table 14.3 summarizes screening recommendations. Except for the colon, the screening recommendations are empirical, based on risk. Further knowledge of the disease natural history may change these.

Treatment

Colectomy is the definitive treatment for patients with FAP before the development of CRC, and should be considered once polyps emerge. Most centers defer surgery until after high school if the polyp burden is minimal. Surgical options include subtotal colectomy with ileorectal anastomosis or total colectomy with mucosal proctectomy, ileal pouch construction, and ileoanal pull through. Subtotal colectomy, which is a single-stage procedure and has less morbidity, is an option for those with AAPC and those with a family history of no or few rectal polyps [95,96].

Table 14.3 Risks and screening recommendations for extracolonic cancers in the inherited syndromes of colon cancer. (Adapted from Burt [90] with permission.)

Syndrome	Screening recommendations
<i>FAP</i>	
Duodenal or peri-ampullary cancer	Upper GI endoscopy (including side-viewing examination) every 1–3 years, start at age 20–25 years
Pancreatic cancer	Possibly periodic abdominal ultrasound after age 20 years
Thyroid cancer	Annual thyroid examination, start age 10–12 years
Gastric cancer	Same as for duodenal
CNS cancer, usually cerebellar medulloblastoma (Turcot's syndrome)	Annual physical examination, possibly periodic head CT in affected families
Hepatoblastoma	Possibly liver palpation, hepatic ultrasound, α -fetoprotein, annually, during first decade of life
<i>HNPCC</i>	
Endometrial cancer	Pelvic examination, transvaginal ultrasound and/or endometrial aspirate every 1–2 years, start at age 25–35 years
Ovarian cancer	As for Endometrial cancer
Gastric cancer	Upper GI endoscopy every 1–2 years, start at age 30–35 years
Urinary tract cancer	Ultrasound and urinalysis every 1–2 years, start at age 30–35 years
Renal cell adenocarcinoma	
Biliary tract and gallbladder cancer	No recommendations given
Central nervous system (usually glioblastoma)	No recommendations given
Small bowel cancer	No recommendations given
<i>PJS</i>	
Stomach, duodenum	Upper GI endoscopy every 2 years, start at age 10 years
Small bowel	Annual hemoglobin, small bowel X-ray every 2 years, both start at age 10 years*
Breast cancer	Annual breast examination and mammography every 2–3 years, both start at age 25 years
Pancreatic cancer	Endoscopic or abdominal ultrasound every 1–2 years, start at age 30 years
Uterine	Annual pelvic examination with pap smear and annual pelvic ultrasound, both start at age 20 years
Ovarian cancer	
Adenoma malignum (cervix)	SCTAT† tumors (females), in almost all women with PJS
Sertoli cell tumor (males), unusual	Annual testicular examination, start at age 10 years; testicular ultrasound if feminizing features occur
<i>Juvenile polyposis</i>	
Gastric and duodenal cancer	Upper GI endoscopy every 3 years, start in early teens (mainly to avoid complications of benign polyps)
<i>Cowden's syndrome</i>	
Thyroid cancer	Annual thyroid examination, start in teens
Breast cancer	Annual breast examination, start age 25 years; annual mammography, start age 30 years
Uterine and ovarian cancer	No recommendations given

* Interval may be lengthened if polyps not found, to avoid excess irradiation.

† Sex cord tumor with annular tubules.

Nonsteroidal antiinflammatory drugs (NSAIDs) and cyclooxygenase-2 (COX-2) inhibitors have some utility in the management of FAP. Several studies have shown regression of colonic adenomas with the NSAID sulindac, as well as the COX-2 inhibitor celecoxib [97–100]. The latter has FDA approval for use in rectal adenoma regression in those patients who have had a subtotal colectomy. A recent study suggested that sulindac may have a role in regression of polyps in the remaining rectal segment in patients who had undergone subtotal colectomy, making further endoscopic management and

resection of polyps easier [101]. However, the use of sulindac as primary prevention in the development of adenomatous polyps in patients with FAP has not been shown to be effective [88].

Duodenal adenomas may also require management and definitive therapy [51]. Removal of duodenal polyps should be considered when they are large (≥ 2 cm) or exhibit advanced histology—villous architecture or high-grade dysplasia. Options for treatment include endoscopic ablation or polypectomy, surgical polypectomy, duodenectomy, or the Whipple procedure. Endoscopic

therapy is appropriate for large, single, pedunculated polyps, while surgery is indicated for larger, sessile polyps with advanced histology. Endoscopic papillectomy for ampullary adenomas should be performed when obstructive symptoms occur or for advanced histology [102–105]. Multiple sessions are sometimes required, and the recurrence rate is fairly high. Other therapies under investigation include chemoprevention and photodynamic therapy.

Desmoid tumors are a particular therapeutic challenge in FAP. Surgery is usually indicated for extraabdominal and abdominal wall tumors secondary to symptoms [62,63], cosmetic issues, or risk to adjacent structures. Less than half will recur with this approach. For intra-abdominal desmoid tumors, however, surgery is often difficult or impossible. Medical therapies include sulindac and tamoxifen, an antiestrogen. A response of more than 50% can be seen with both of these options [106,107]. Chemotherapy is also an alternative for unresectable cases.

Hereditary nonpolyposis colorectal cancer

Epidemiology

Hereditary nonpolyposis colorectal cancer (HNPCC) is another inherited syndrome with a high lifetime risk of CRC. Like FAP, HNPCC is associated with several other clinical manifestations, but, unlike FAP, CRC usually develops in the absence of polyposis. The syndrome was first described as a syndrome of CRC in the setting of gastric and endometrial tumors [108]. The syndrome was initially called Cancer Family Syndrome and later Lynch syndrome; currently, the most commonly used term is HNPCC. HNPCC accounts for approximately 1–3% of colon cancer cases, depending on the patient population studied [109–111]. However, in a recent population-based study from Utah and California, HNPCC accounted for only 0.86% of CRC cases, based on identification of germline mutations of DNA mismatch repair genes (MMR) [112].

Etiology

Individuals inherit HNPCC in an autosomal dominant fashion. The genetic defect is a germline mutation in any one of the five DNA mismatch repair genes (MMR), although over 95% of germline mutations involve hMLH1 or hMSH2 [113,114]. Additionally, mutations in two of the MMR genes, PMS1 and PMS2, previously thought to be pathogenic in several HNPCC families, have come into question. Mutations in another MMR gene, MSH6, occur in a small fraction of families but result in a somewhat different phenotype (see below).

Typically, an individual inherits one mutant allele and retains one wild-type allele. With time, the wild-type allele inactivates through somatic mutation or so-called loss of heterozygosity [115]. In the general population, germline mutations in the DNA MMR genes are not common; however, Farrington *et al.* [116] found that 28% of young CRC patients (< 30 years old) had a pathogenic mutation in either hMSH2 or hMLH1 genes. The role of DNA MMR proteins is to repair replication errors, which commonly occur during cell division. When mutations exist in the MMR genes, replication errors persist and accumulate through repeated cell divisions. This is manifested by microsatellite instability. DNA microsatellites are segments of DNA found throughout the human genome composed of sequences of repeating DNA bases. Microsatellite instability (MSI) exists when there are multiple microsatellite errors. MSI is typical of almost all CRC arising in the setting of HNPCC, in contrast to only 15% of sporadic colon cancers. In sporadic cases, MSI usually occurs by a different mechanism of DNA MMR inactivation. Interestingly, MSI is found in the colon cancer tissue, but not in the surrounding mucosa. MSI testing can be performed on colon cancer tissue in an individual suspected of having HNPCC, adding a diagnostic tool to identify families at risk for this syndrome (see below).

Clinical presentation

The phenotype of HNPCC has many differences compared to FAP. The lifetime risk of developing CRC is about 80%, with an average age at diagnosis of 44 years [113,114,117]. Unlike FAP, patients typically have few adenomatous polyps. The distribution of both polyps and cancers favors a proximal location in the colon, with about 60–80% of cancers developing proximal to the splenic flexure [118]. Furthermore, 45% of persons with HNPCC will have synchronous or metachronous CRC within 10 years of resection [119]. In comparison to sporadic polyps, polyps in the setting of HNPCC develop at a younger age, are larger than age-matched controls, and tend to exhibit a more advanced histology [120]. The cancerous tissue has a peritumoral lymphocytic response or a Crohn's-like pattern [121,122]. Stage-for-stage, HNPCC patients with CRC have better survival compared to sporadic cases [123].

Like FAP, there are extracolonic manifestations of the syndrome, particularly several malignancies. Persons with HNPCC are at greater risk for cancers of the genitourinary system, biliary system, central nervous system, small bowel, and stomach [124–127]. The highest risk exists for endometrial cancer (43–60% lifetime risk), gastric cancer (13–19% lifetime risk), and ovarian cancer (9–12%). There is also a reported higher risk of pancreatic, laryngeal, breast, and hematopoietic malignancies

Table 14.4 Amsterdam criteria for the diagnosis of HNPCC.*Amsterdam criteria I*

- 1 Three or more relatives with histologically verified colorectal cancer, one of whom is a first-degree relative of the other two; FAP should be excluded
- 2 Colorectal cancer involving at least two generations
- 3 One or more colorectal cancer cases diagnosed before the age of 50

Amsterdam criteria II

- 1 Three or more relatives with histologically verified HNPCC-associated cancer (colorectal cancer, cancer of the endometrium, small bowel, ureter, or renal pelvis), one of whom is a first-degree relative of the other two; FAP should be excluded
- 2 Colorectal cancer involving at least two generations
- 3 One or more cancer cases diagnosed before the age of 50

[118,128]. Other than the varied malignant phenotypes, HNPCC patients have a paucity of other syndromic manifestations. Café au lait spots, sebaceous gland tumors, and keratoacanthomas can be found, though the latter two are more commonly found in the Muir–Torre variant of HNPCC [128].

Clinical criteria have been established for the diagnosis of HNPCC. In 1990, the International Collaborative Group on HNPCC established research criteria for the diagnosis of HNPCC [129]. These classic or Amsterdam I criteria specified that at least three relatives had to have CRC, with all of the following criteria being met: (i) one relative should be a first-degree relative of the other two; (ii) at least two successive generations should be affected; (iii) at least one CRC should be diagnosed before the age of 50; (iv) FAP should be excluded; and (v) tumors should be verified by pathologic examination. In response that these criteria were too stringent, particularly for clinical applications, the Amsterdam II criteria were developed [130]. These criteria are similar to the original ones; however, instead of CRC only, all potential malignancies related to HNPCC were included (cancers of the colorectum, endometrium, small bowel, ureter, and renal pelvis). Table 14.4 summarizes the Amsterdam criteria for the diagnosis of HNPCC.

Variants of HNPCC*Muir–Torre syndrome*

The Muir–Torre syndrome is characterized by several different cutaneous manifestations in addition to the malignancies of HNPCC. These include sebaceous adenomas and epitheliomas, basal cell epitheliomas, keratoacanthomas, and sebaceous carcinomas. The latter are usually found on the eyelid. This syndrome typically arises from mutations of the *hMSH2* gene.

Turcot's syndrome

As already mentioned, about a third of Turcot's syndrome families arise from mutations in the MMR genes. These patients usually will manifest typical findings of HNPCC together with CNS glioblastomas. Interestingly, the 5-year survival rates for glioblastomas in these families appear to be longer than those for sporadic glioblastomas [86].

MSH6 syndrome

Mutations in the MSH6 gene are uncommon, but can give rise to a characteristic syndrome. Persons with this mutation have an endometrial cancer risk of about 60% and a lower risk of CRC compared to typical HNPCC (about 40%). At least in some families, there is a later onset of tumor diagnosis.

Genetic testing

Unlike FAP, which often has a distinct, easily identifiable phenotype, HNPCC is more difficult to clinically diagnose; therefore, genetic testing has an additional role in HNPCC. The same general approach for genetic testing in FAP can be applied to HNPCC [88]. Again, the person most likely to have the mutation should be tested. Typically, this would be the youngest person with colon cancer in a family that meets the Amsterdam criteria. If the mutation is identified in a family, then other family members can be screened for that mutation, and those that are positive need appropriate cancer screening as described below. However, if the mutation is not identified, all members in a family with suspected HNPCC need cancer screening. Genetic testing should commence at age 20–25 years. The laboratory methods for genetic testing are similar to FAP and include PTT, SSCP, and sequencing. Sequencing, often preceded by SSCP or similar methods, is the most commonly used approach.

The ability of genetic testing to identify and exclude families accurately is inferior to testing in FAP. In one study of families meeting the Amsterdam criteria, testing for a mutation in the MMR genes identified only 49% of the families [131]. Because of the fear of excluding too many families with HNPCC, the Amsterdam criteria were modified as noted above. Also, other approaches have been established to include more families into appropriate screening, even though the Amsterdam criteria are not met. Using MSI testing of tumor tissue in a patient with a strong family history of CRC is one such approach. Since almost all colon cancers in the setting of HNPCC have MSI [113], those patients with MSI-positive tumors can then be offered specific genetic testing for MMR mutations. MSI testing identifies families

Table 14.5 Modified Bethesda criteria for MSI testing in colorectal cancer.

-
- 1 Individuals with cancer in families that meet the Amsterdam criteria
 - 2 Individuals with two HNPCC-related cancers, including synchronous and metachronous colorectal cancers or associated extracolonic cancers
 - 3 Individuals with colorectal cancer and a first-degree relative with colorectal cancer and/or HNPCC-related extracolonic cancer and/or a colorectal adenoma; one of the cancers diagnosed at age < 45 years, and the adenoma diagnosed at age < 40 years
 - 4 Individuals with colorectal cancer or endometrial cancer diagnosed at age < 45 years
 - 5 Individuals with right-sided colorectal cancer with an undifferentiated pattern (solid/cribriform) on histology diagnosed at age < 45 years
 - 6 Individuals with signet-ring-cell-type colorectal cancer diagnosed at age < 45 years
 - 7 Individuals with adenomas diagnosed at age < 40 years
-

with HNPCC depending on the population studied. In those families fulfilling the Amsterdam criteria, MSI testing is positive in 81% [132–135]. By contrast, in families suspected of having HNPCC, but not meeting Amsterdam criteria, positive results occur in 36% [134–137].

A suggested approach for HNPCC screening is to first identify families at high risk and then perform appropriate testing. Certainly, those meeting the Amsterdam criteria would qualify and should have direct testing for MMR mutations. Because not every family with HNPCC meets the Amsterdam criteria, another set of criteria, called the Bethesda criteria [138], has been developed to assist with identifying appropriate indications for MSI testing (Table 14.5). An efficient approach is to proceed directly to genetic testing if any one of the first three criteria of Bethesda are met [139]. Alternatively, MSI testing can be done on the CRC tumor tissue, if available, and proceed to genetic testing if this is positive. Additionally, MSI testing can be done on CRC tumor tissue if any person with young age or family history of colon cancer is present. Genetic testing for MMR mutations would then be done only if MSI is positive.

Cancer screening

Screening for cancers should be offered to at-risk family members in pedigrees meeting the Amsterdam criteria, as well as those with a known genetic mutation consistent with HNPCC [90]. Because of the incidence of proximal tumors, colon cancer screening should include colonoscopy beginning at age 20–25 years, or 10 years earlier than the youngest case in the family (whichever is first), and repeated every 1–2 years. Screening other potential sites of cancer development is recommended,

but is not based on clinical trials. Recommendations for gastric cancer screening are upper gastrointestinal endoscopy every 1–2 years beginning at age 30–35 years. For uterine cancer screening, pelvic examination, transvaginal ultrasound, and/or uterine aspirate should be performed every 1–2 years starting at the age of 25–35 years. Recommendations for screening for urinary tract cancers suggest beginning at age 30–35 years and entail annual ultrasound and urinalysis. Other cancer screening guidelines are even less well established. Tables 14.2 and 14.3 summarize the screening recommendations for malignancies in HNPCC.

Treatment

Specific medical therapy for HNPCC does not exist. Surgical intervention, specifically subtotal colectomy, is indicated when a patient either develops colon cancer or when an advanced adenoma is diagnosed that cannot adequately be removed with endoscopic techniques. Prophylactic colectomy in patients with known MMR mutations is not clearly indicated and is a matter of debate. When dysplasia is found in the uterus, hysterectomy should be performed.

Peutz–Jeghers syndrome

Epidemiology

Peutz–Jeghers syndrome (PJS) is a syndrome characterized by hamartomatous polyps in the gastrointestinal tract and distinct mucocutaneous pigmentation [140]. There is an associated risk of both gastrointestinal and nongastrointestinal malignancies. About 1 in 120 000 live births are afflicted with PJS.

Etiology

PJS is an autosomal dominant genetic condition, and is known to arise from a mutation in the *STK11* gene (also called *LKB1*), which is located on chromosome 19p [141–145]. The gene codes for a serine/threonine kinase that is involved in the p53 apoptosis pathway [146]. Several types of mutations can occur in the *STK11* gene, including frameshift mutations and deletions, but all of them lead to loss of activity. About 50% of cases are familial, and the rest are presumed to be isolated cases representing new mutations. Mutations in the *STK11* gene are found in about 60% of apparent inherited cases and in 50% of isolated cases [147].

Clinical presentation

Like the other inherited colon cancer syndromes, PJS is associated with other gastrointestinal and extraintestinal



Fig. 14.4 Several duodenal polyps in a patient with PJS.

manifestations, including several malignancies. By far the most distinguishing manifestation of PJS is mucocutaneous lesions. In over 95% of patients with PJS, melanin pigment spots occur on the lips or buccal mucosa. Pigment spots may also be found on the face, forearms, palms, soles, perianal area, and, rarely, on the intestinal mucosa. Pigmented spots on the lips usually cross the vermilion border, and are darker and more clustered compared to the common freckle. Lesions appear in infancy and begin to fade at puberty, though the perioral lesions, particularly those on the buccal mucosa, often persist into adult life.

Clinical diagnosis can be made in the setting of mucocutaneous lesions together with characteristic gastrointestinal polyps (Fig. 14.4). The average age of diagnosis is 22 years in men and 26 years in women [147], though about a third of patients present within the first decade of life. Typically, symptoms result from complications of gastrointestinal polyps, which occur in 88–100% of patients. Polyps are found throughout the gastrointestinal tract with a frequency as follows: small bowel, 96%; colon, 27%; stomach, 24%; and rectum, 24% [147]. They begin to grow in the first decade of life and usually become symptomatic in the second or third decade. Polyps range from 0.1 to 3 cm in size and can be sessile or pedunculated. Characteristically, polyps have a lobulated appearance endoscopically. On histology, these polyps are nondysplastic with a normal appearing mucosa appropriate for the area in which the polyp is found. The muscularis mucosae extends as branching fronds in the polyp, giving an arborizing pattern that is sometimes described as “pseudoinvasion.” Adenomatous and, subsequently, cancerous changes may occur in PJS polyps, and are probably the source of much of the small bowel cancer in this disease [144,147–149]. Polyps can ulcerate, infarct, bleed, or cause intussuscep-

tion with intestinal obstruction and cause much of the morbidity and surgical intervention of PJS.

After the age of 30, malignant complications become the major concern. By the age of 65 years, about 93% of PJS patients will have some kind of malignancy—either intestinal or extraintestinal [147,150–152]. The most common gastrointestinal cancers include colon, with a lifetime risk of 39% and presenting at an average age of 46 years, and pancreatic, with a lifetime risk of 36% and presenting at an average age of 41 years. Gastric and small bowel cancers occur less frequently. Nongastrointestinal malignancies include breast (54% lifetime incidence), ovarian (21% lifetime incidence), Sertoli cell tumors (9% lifetime incidence with 10–20% becoming malignant), and lung (15% lifetime incidence).

Genetic testing

Genetic testing is available for patients suspected of having PJS based on family history or characteristic clinical presentation. Only about 50% of families with clinical PJS, however, will have a *STK11* germline mutation [153], suggesting other possible genetic etiologies in disease pathogenesis. Again, the same principles of genetic testing apply to PJS as they do to FAP and HNPCC.

Cancer screening

Colon cancer screening should begin in the late teens and consists of colonoscopy at least every 3 years or sooner, based on findings [90]. For pancreatic cancer, either endoscopic ultrasound or transabdominal ultrasound should be done every 1–2 years starting at age 30 years. Radiography of the small bowel should commence at age 10 years and be repeated every 2 years. Because of the high risk of breast and ovarian cancer, mammography every 2–3 years and annual breast examinations should begin at age 25, and annual pelvic examinations with or without uterine washings should start at age 20 years. For males, testicular examinations should begin at age 10 years. Cancer screening recommendations are outlined in Tables 14.2 and 14.3. All of the screening in PJS is empirical and based on risk, but provides a rational approach pending definitive clinical trials.

Treatment

Treatment focuses on preventing both benign and malignant complications of gastrointestinal polyps. Removal of polyps is indicated when they are greater than 0.5–1.0 cm in size. Surgery is often necessary to remove large polyps in the small bowel or when colonic polyps are difficult to manage endoscopically.

Juvenile polyposis

Epidemiology

About 1 in 100 000 individuals have juvenile polyposis (JP), a syndrome characterized by multiple juvenile polyps of the gastrointestinal tract with associated risk of several malignancies and certain extraintestinal manifestations [154–157]. Juvenile polyps are found in about 2% of children, and must be distinguished from JP because of the clinical significance of the latter.

Etiology

Like the other inherited colon cancer syndromes, JP is an autosomal dominant genetic disorder. About half of JP families have a mutation in either the SMAD4 gene (also called the DPC4 gene) on chromosome 18 or the BMPR1A gene on chromosome 10 [158–160]. Most families (38%) have a mutation in the BMPR1A gene, with only 15% having a SMAD4 mutation. The remaining families have an unknown genetic basis for their disease, suggesting other potential candidate genes. The SMAD4 protein is involved in the transforming growth factor beta (TGF- β) signalling pathway, and the BMPR1A gene product is a serine-threonine kinase type 1 receptor, which also belongs to the TGF- β receptor superfamily.

Clinical presentation

The clinical criteria for the diagnosis of JP include: (i) at least five juvenile polyps in the colorectum; (ii) juvenile polyps throughout the gastrointestinal tract; and (iii) any number of juvenile polyps in a person from a family with known JP [161]. The average age of diagnosis is 18.5 years [162]. Juvenile polyps are most common in the colon, though they can occur anywhere in the gastrointestinal tract. Size of polyps ranges from small, sessile lesions to large (> 3 cm), pedunculated ones. Endoscopically, polyps are usually round, reddish, and smooth (Fig. 14.5), though larger polyps can appear multilobulated. Often, they have a white exudate on their surface. Histologically, the polyps contain cystic spaces filled with mucin, and the surface mucosa is nondysplastic with abundant lamina propria. Characteristically, there are elongated, benign cystically dilated glands that lack a smooth muscle core. Polyps usually appear in the first decade of life and can number anywhere from dozens to several hundred. Most patients will become symptomatic within the first two decades of life, presenting with rectal bleeding, abdominal pain, passage of tissue per rectum, and intussusception—all complications of polyps.



Fig. 14.5 Hamartomatous polyps at the splenic flexure in a patient with JP.

Colon cancer incidence ranges from 9% to 68%, though the latter figure probably is more accurate based on more recent studies [153,153a,156,158,161,163]. The average age of cancer diagnosis is 34 years (range 15–68 years). Cancers are thought to arise from adenomatous tissue within the juvenile polyp. Other cancers include malignancies of the stomach, duodenum, biliary tree, and pancreas [164].

Benign manifestations of JP have also been found. The exact incidence in JP has been difficult to discern, as several other distinct syndromes with juvenile polyps overlap with JP, including Cowden's syndrome and Bannayan–Ruvalcaba–Riley syndrome. Congenital abnormalities, including those of the heart, gastrointestinal, genitourinary, and central nervous system, have been described [164]. Hypertelorism and macrocephaly have also been associated with JP [165].

Genetic testing, screening, and treatment

Genetic testing for JP has recently become available. Testing should be performed in individuals suspected of having the disease and family members at high risk. Because of similar phenotypes, genetic testing allows differentiation from Cowden's syndrome.

Cancer screening should include both upper gastrointestinal endoscopy and colonoscopy beginning in the late teens [90]. The screening interval can be 3 years if no polyps are found, but annually once polyps are found (Tables 14.2, 14.3).

Colectomy should be considered when polyps are difficult to control or when advanced histology is found. Likewise, partial or complete gastrectomy may be necessary for large or advanced gastric neoplasia.

Cowden's syndrome

Cowden's syndrome (CS) is now known to exhibit some increased colon cancer risk, and also includes

hamartomatous polyposis that can be confused with the above syndromes. Also, extraintestinal malignancies are characteristic of the disease, and are important to recognize and screen [157,166–168]. CS occurs in approximately 1 in 200 000 individuals, though the condition is probably underdiagnosed.

The genetic basis of CS has been identified as germline mutations in the PTEN gene, a tumor suppressor gene [169–172]. About 80% of persons fulfilling the clinical criteria for CS will have a PTEN, while only 10–50% of people not meeting the criteria will have one [171,173]. A variant of CS, Bannayan–Riley–Ruvalcaba syndrome (BRR), also arises from mutations in PTEN, but only 50–60% of patients with BRR are found to have a PTEN mutation [174]. Genetic testing is available for CS and BRR.

The clinical manifestations of CS include multiple gastrointestinal hamartomas with a distribution as follows: stomach, 75%; esophagus, 66%; colon, 66%; and duodenum, 37% [175]. In the esophagus, the polyps are actually glycogen acanthosis, which are white, flat elevations [176]. In the remainder of the gastrointestinal tract, the hamartomas are of several different types, including the most common, juvenile polyps, but also lipomas, inflammatory polyps, ganglioneuromas, and lymphoid hyperplasia. A characteristic feature of the juvenile polyps in CS is the neural elements contained in the polyps. Colon cancer risk is elevated compared to the general population, albeit only mildly, with one study finding a 9% CRC risk.

Patients are at risk for extraintestinal malignancies, specifically thyroid cancer (usually follicular, but sometimes papillary) in 10%, breast cancer in 25–50% of females with reports of cases in males as well, endometrium in 2–5%, as well as kidney, ovary, lung, retina glioma, and melanoma [167,177].

Other manifestations of CS include several cutaneous features. In fact, multiple facial trichilemmomas are a classic feature of the disease. Persons also tend to develop verrucous skin lesions of the face and limbs and cobblestone-like hyperkeratotic papules of the gingiva and buccal mucosa. By the third decade of life, 99% of patients will have mucocutaneous features of the disease [167]. Congenital defects have also been described, including hypoplastic mandible, a prominent forehead, a high-arched palate, macrocephaly, and mental retardation. Many patients (50%) will develop thyroid goiters, and some will develop early uterine leiomyomas, hemangiomas, lipomas, lymphangiomas, meningiomas, and neurofibromas. Diagnostic criteria for CS have been established [178].

BRR is a variant of CS that includes typical CS as well as macrocephaly, delayed psychomotor development, lipomatosis, hemangiomatosis, and pigmented macules of the glans penis [179]. Lhermitte–Duclos disease is a condition with benign hamartomatous overgrowth of

ganglion cells in the cerebellum. Recent investigation disclosed that nearly all cases of this disease occur in the setting of CS [180–182].

No specific screening recommendations exist for gastrointestinal malignancy in CS, although at least average-risk screening should be performed. Annual thyroid examinations should start at age 18 years and annual breast examinations at age 25 years, with annual mammography at 30 years. Annual skin examinations for melanoma and annual urinalysis for renal cell carcinomas should also be performed, as well as annual suction biopsies of the uterus, commencing at age 35 years (Table 14.3).

Summary

Although the majority of CRC occurs as sporadic cases, a significant portion has a familial tendency. Obviously, genetics have an integral part in these cases, but the environment, likewise, is a major determinant of lifetime risk. Identification of families at high risk based on family history is essential, as no universal genetic testing is available. Specific colon cancer screening recommendations have been established to guide clinicians in identifying and initiating intensified screening in appropriate patients and families. As our understanding of the genetic basis of familial risk increases, genetic testing will hopefully supplement our ability to manage patients in this high-risk category.

The known hereditary colon cancer syndromes have contributed significantly to our knowledge of cancer pathogenesis. Although they comprise a small proportion of CRC cases overall, they are important disorders to understand and identify. Since colon cancer is not the only potential malignancy in these conditions, awareness of other cancers and initiation of appropriate screening will likely improve outcomes. Furthermore, the arena of genetic testing is fully applicable to this population and offers an excellent tool to aid in the identification of families with hereditary colon cancer syndromes.

Both the primary care provider and gastroenterologist are important in identifying the patient groups at increased risk of CRC. With knowledge of the etiology, clinical presentations, and appropriate cancer screening and treatment options, clinicians can have a significant impact on the quality of life as well as mortality in persons and families with familial risk for CRC.

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Chapter 15

Complications

James Church

Introduction

Over the last three decades, advances in endoscope design, bowel preparation, and the array of instruments and techniques available have made colonoscopy one of the safest of invasive procedures. Complications and adverse effects still happen of course, but their frequency is low. The purpose of this chapter is to describe the range of complications that can happen during colonoscopy, to show what their expected frequencies may be, and to provide some advice on how to prevent and how to manage them. A discussion of some general principles that apply to complications of colonoscopy is worthwhile.

Risk management

The basis of risk management in a medical setting is to define the risks that apply to each patient for any procedure, and then to consider the benefits to be achieved by that procedure in the light of those risks. Patients are told about the balance of risks and benefits that apply in their own particular situation and participate in the decision-making process that flows from this balance. This is informed consent. For example, a patient with severe chronic obstructive respiratory disease and a positive fecal occult blood test needs a colonoscopy but is at risk of cardiac and respiratory complications from oversedation. That patient must understand that sedation will be light if it is given at all. The endoscopist realizes that technique must be gentle and takes steps to adapt to this need. Other scenarios may be a patient with a recent myocardial infarction, where the need for a screening colonoscopy can be deferred until the patient's cardiac status is stable, or a patient on coumadin who presents for surveillance, in whom the coumadin may not need to be stopped unless a significant polyp is found. Minimizing risk by adapting the clinical approach to the patient is an important aspect of reducing complications. Assessing risk on the basis of a careful history and examination is essential to this process.

The dilemma of teaching

The technique of colonoscopy is learned practically, not theoretically, and although simulators are becoming more realistic in offering a close to reality learning experience, there is no way to avoid supervised patient experience. Both Geenen *et al.* [1] and Fruhmorgen and Demling [2] have shown that complication rates of colonoscopy are inversely related to the experience of the examiner. The teacher is thereby faced with a dilemma. Trainees need to work through difficult situations to learn the techniques required, yet patients must not be put at increased risk just for the purposes of training. If the trainee is not allowed to attempt difficult examinations, skills will not be readily acquired, but patient safety is paramount. Patients who have had a sigmoidectomy present an opportunity for novice colonoscopists to perform comfortable, minimal risk examinations. At the other end of the spectrum of difficulty is the elderly patient with severe diverticulosis or a fixed sigmoid loop, when the novice may require considerable assistance from the trainer.

Putting the literature into perspective

Several factors must be considered when reading reports of complications of colonoscopy to allow a helpful interpretation of the data. The design of the study is a key to the applicability of the results. A retrospective, or multi-institution or multiendoscopist survey will not give accurate incidence rates but will show the range of severity of the problem. A single endoscopist or single unit study will not show the range of the problem, but will usually report overoptimistic results as most data come from expert units. A case report may be interesting and illustrative of an approach to the particular problem it describes, but it does not allow the authors or their readers to make generalizations based on one or a few patients.

The date of the study is as important as its design because several factors that influence colonoscopy complications have changed over the years. The range and quality of available endoscopes and endoscopic instruments has improved significantly, allowing gentler and

more efficient examinations. Furthermore the effectiveness of bowel preparation, sedation and analgesia is better and the average experience level in endoscopy units has moved well into the “expert” range. Balancing this maturation of experience is a willingness of experts to take on riskier cases. The likely outcome of complications has also changed with time as advances in antibiotics, anesthesia technique and surgical options (i.e. laparoscopy) have made treatment more effective and less risky. Therefore a consideration of the risks of diagnostic and therapeutic colonoscopy must be based on today’s realities, and not rely too much on old, perhaps irrelevant data.

Mortality

The worst complication of any procedure is the unexpected, unanticipated death of the patient. Risk management is important in minimizing mortality, considering whether the colonoscopy should be done at all, whether to persist with a difficult examination in an elderly, frail patient or whether to remove a small cecal polyp in an 80-year-old. Selection of patients for colonoscopy should reflect such decision-making. Elective examinations are contraindicated in critically ill patients, or patients with a limited life expectancy. However even under the best of circumstance patients sometimes die from the complications of colonoscopy. In 1983 Macrae *et al.* reported a mortality rate of 0.06% in a series of 5000 consecutive examinations [3], and in 1994 Jentshura *et al.* reported a mortality rate of 0.015% [4]. Most deaths occur after serious complications (perforation, hemorrhage) in patients with serious comorbidity. Waye *et al.* summarized 12 reports describing 165 perforations out of 99 539 diagnostic colonoscopies and 76 perforations out of 18 659 therapeutic colonoscopies [5]. The overall mortality was 5/83 725 (0.006%). As shown in this chapter, death can occur from any serious complication of colonoscopy, from the electrolyte imbalance caused by sodium phosphate prep to the cardiac events brought on by hypoxia from oversedation, to the sepsis that may follow perforation and the blood loss that can occur with hemorrhage. Prevention and correct management of these complications will minimize mortality.

Complications of bowel preparation

A clean colon is a prerequisite to a thorough colonoscopy, and there is no alternative to flushing the stool out of the colon. Bowel cleansing regimens are designed to do this in such a way as to be effective in most patients without being too unpleasant or severe. However, aspiration in elderly patients has been described [6] and vomiting is quite common [7,8]. Various techniques to improve passage of the liquid and to reduce the amount

that is drunk have been published and are covered in detail in Chapter 18. The phosphosoda preparation is potentially more dangerous than polyethylene glycol (PEG), as the lavage fluid is drawn out of the patient’s interstitial space into the colon by the hyperosmotic phosphosoda. Dehydration is routine, so patients are encouraged to drink water liberally with their preparation. Hookey *et al.* recently reviewed 26 studies of liquid sodium phosphate bowel preparation that included 2496 patients [9]. There were no major prep-related adverse reactions. A review article described 29 patients who did have serious adverse reactions to sodium phosphate lavage, including symptomatic hypocalcemia, hypokalemia, hypernatremia, hypotension, and acute renal failure. Thirteen of these cases were having colonoscopy: two patients died. Sixteen cases had sodium phosphate for other reasons and four died. Most of the patients suffering significant adverse effects either had a dose that was higher than recommended, or had conditions that may have predisposed them to having a problem (e.g. chronic renal failure, bowel obstruction or ileus, preexisting dehydration, or electrolyte imbalance). The authors of the review concluded that sodium phosphate lavage was safe as long as appropriate exclusions for comorbidity were followed and the recommended dose limits obeyed (2×45 mL doses given 5–12 h apart). The increased compliance found with the smaller volume preparations [10] makes sodium phosphate an attractive first choice, as long as patients have normal renal and cardiac function and are not taking diuretics.

Complications of intubation

Complications can occur during both intubation or extubation of the colon. Usually, most traumatic damage is done on the way in and most therapeutic damage is done on the way out. Some complications, such as perforation, can be done either way. This section will focus on complications due to traumatic intubation. The most serious of these is perforation.

Perforation

The reported incidence of traumatic perforation can be very low, 3/82 416 (0.004%) colonoscopies reported by Sieg *et al.* [11], and 0.02% of 8473 diagnostic colonoscopies reported by Wexner *et al.* [12]. Waye *et al.* [5] reviewed 10 series reported from 1974 to 1994 in which 165 perforations occurred during diagnostic colonoscopy (0.17%), with individual series rates ranging from 0 to 0.86%. Wexner *et al.* [12] reviewed 27 series reported between 1975 and 2000, including 276 202 patients. The average rate of perforation (including both diagnostic and therapeutic exams) was 0.2% and the range was 0.033–0.81%. Wexner’s review also shows

that perforation rates halved since the 1980s, falling from an average of 0.34% in the five series reported in the 1970s and 0.33% in the nine series reported in the 1980s to 0.16% in the 14 series reported in the 1990s.

Traumatic perforation may occur because of direct scope trauma, splitting of the bowel at a stricture or by the sideways pressure of a loop, or pneumatic dilation to pressures high enough to perforate. Most perforations occur in the sigmoid colon, probably as a result of a tear in a fixed loop. Pushing the end of the scope through the bowel wall is uncommon, especially in healthy bowel. Uno and Morita [13] created such a situation in surgically resected bowel and found that at pressures of 2–3 kg/cm² the muscularis propria ruptures first followed by a split in the serosa. Tearing of the mucosa is the last event in the sequence and produces the hole. Exerting this degree of force in a clinical situation is very unlikely. The other common cause of perforation is a pneumatic blowout in the right colon, when the pressure of insufflated air is unrelieved [14]. Perforations can also occur from biopsy, and Foliente *et al.* [15] reported five cases of cecal perforation in elderly patients (mean age 79.6 years), three of which were due to routine cold biopsy. The distended cecal wall can become extremely thin in elderly patients, making biopsy potentially dangerous. Biopsies should be directed to the mucosa overlying a muscular fold if possible, especially in the cecum of elderly patients.

Prevention of traumatic perforations

Ideal colonoscopic technique is gentle, unhurried and efficient, using an economy of action and minimizing loops [16]. “Pushing through” or “sliding by” are high-risk maneuvers and should be used as a last resort. Pain is a sign to stop pushing and find an alternate approach to a situation. It is surprising how many reports of traumatic complications of colonoscopy describe the examination as “uneventful” or “easy insertion”, yet there is splenic rupture, colonic perforation, or some other catastrophe. Perhaps the definition of “uneventful” or “easy” needs to be reevaluated in these circumstances. Colonoscopists may also need to accept that sometimes there will be an incomplete exam. Because completeness “to the cecum” is the most commonly used measure of colonoscopic expertise (inappropriately so), there is a tendency to get there “at all costs.” Sometimes the cost may be a perforation. As colonoscopy becomes more commonly performed, safe technique becomes increasingly important.

Patients with diseased colons are more likely to have a perforation and so the incidence of perforation in completely normal colons is small. Colonoscopists must be aware of situations where the risk of perforation is increased:

- 1 Severe diverticulosis with muscular hypertrophy and a narrow sigmoid where the colonoscope may become impacted in the sigmoid. A proximal pneumatic blowout may occur as insufflated air distends the right colon, although the scope does not advance. The use of CO₂ as an insufflating gas [17] in this situation may not prevent the perforation, but the gas will be absorbed more rapidly than will room air. A pediatric colonoscope is less likely to become impacted.

- 2 Severe Crohn’s colitis, ischemia, acute (sealed) diverticulitis, and deeply invasive cancer may weaken the colonic wall so that it gives way under unusually minor stress. This includes direct forward trauma from the tip of the scope, or, more commonly, a tear in the side of the colon on the apex of a loop due to stretch. Strategies to adopt include avoiding use of “slide by” in a diseased colon, use of a pediatric colonoscope, avoiding loops, and abandoning the examination.

- 3 Intraoperative colonoscopy, or any colonoscopy done under general anesthetic, removes the role of pain as a warning sign to stop pushing. In the unconscious patient, there is a temptation to push through loops with more force than would ordinarily be used. There are few data that speak to this concern, and those that are available report safety in very small numbers of patients [18]. Endoscopists performing colonoscopy in patients under general anesthesia should use the same loop-avoidance techniques as they would use in awake patients.

Sometimes patients need to be colonoscoped in the immediate postcolectomy period. The most common indication is bleeding, although postoperative distension may also be an indication. Cappell *et al.* [19] stated that such examinations are safe although they reported on only 52 patients.

Recognition of perforations

Causing a perforation during colonoscopy is unfortunate, but failing to recognize that a perforation has occurred, or to acknowledge the possibility, may be disastrous. Perforation of a clean, well-prepared colon is much easier to repair than a perforated colon containing stool, surrounded by fecal contamination and sepsis. Most traumatic perforations are immediately obvious [20]. Either the peritoneal cavity is visible through the endoscope, or the patient’s abdomen becomes grossly distended, with or without pain. If either situation occurs, the examination must be immediately stopped. A markedly distended abdomen, usually with loss of liver dullness to percussion, is an indication for an immediate abdominal X-ray. Free intraperitoneal gas may mean a perforation, or at least a split in the colonic muscle and serosa that has allowed air to escape through the porous mucosa. The clinical circumstances of the colonoscopy will usually alert the endoscopist to the

possibility that an injury occurred. If a pneumatic “split” in the colonic wall is likely, a water-soluble contrast enema will show whether there has been a frank perforation [21]. A surgical consultation is routine, and the decision for surgery is based on the likely cause of the perforation, the state of the bowel (diseased vs. normal), and the comorbidity present in the patient. For traumatic perforations the threshold for surgery should be low [20].

Extraperitoneal perforations

Sometimes the colonic perforation is on the mesenteric side of the colon. When escaping air passes into the mesentery it may then travel to and through the retroperitoneum [22] into the mediastinum. Often a small amount of free air can be seen in the peritoneal cavity on X-ray, after it has leaked through the peritoneum. Retroperitoneal air can track up into the neck and present with crepitus [23], or it can enter the chest cavity and cause life-threatening pneumothoraces [24]. Retroperitoneal perforations can usually be treated with intravenous antibiotics and observation.

Treatment of perforations

Almost all traumatic perforations need surgical repair, because they are often ragged and large. This is in contrast to postpolypectomy perforations where some may be managed conservatively. The largest series of colonoscopic perforations has been reported by Garbay *et al.* [25], who reviewed the outcome of 183 colonoscopic perforations, collected from 54 French medical centers over 12 years. Eighty of the patients were over 70 years of age. Sixty-eight patients had perforation during a therapeutic examination. Clinical details of the patients are listed in Table 15.1. In general, surgical options include simple suture repair in patients with small holes and minimal contamination and a normal bowel, resection and primary anastomosis in patients with abnormal bowel or a large ragged hole, and colostomy in patients who are sick, with extensive contamination and major comorbidity. Sometimes a repair may be protected by diversion if factors associated with a risk of anastomotic leak are present (e.g. malnutrition, chronic steroid therapy, anemia or extensive blood loss, diseased but unresectable bowel). The advantage of this approach is that closing the loop stoma is much less of an operation than re-laparotomy to close a primary Hartmann procedure. The range of surgical procedures reported by Garbay *et al.* is shown in Table 15.1. Their mortality rate was 12%, and was significantly related to medical comorbidity and the size of the perforation. Seventy-seven patients had postoperative complications, of whom 23 needed a reoperation. Both mortality and morbidity may be

Table 15.1 Clinical aspects of a large series of colonoscopic perforations [25].

Clinical aspect	No. (%)
Diagnosis	
Immediate	75 (42%)
Delayed 1 h to 42 days	100 (56%)
Presentation	
Peritonitis	76
Pain without peritonitis	55
Septic shock	5
Generalized sepsis	3
Bleeding	1
Miscellaneous	6
Plain abdominal X-ray	
Pneumoperitoneum	116
Retroperitoneum	6
Normal	17
Patients operated within 6 h of endoscopy	(48%)
Size of perforation	
< 2 cm	73 (49%)
> 2 cm	76 (51%)
Site of perforation	
Rectum	12
Sigmoid	132
Left colon	15
Transverse colon	6
Right colon	15
Small bowel	2
None found	2
Surgeries	
Suture closure	59 (32%) (20 with stoma)
Resection	88 (48%) (53 with stoma)
Exteriorization	33 (18%) (33 with stoma)
Other	3 (2%) (2 with stoma)

reduced by the use of minimally invasive techniques to treat perforations [26–28]. One of the biggest series is by Wullstein *et al.* [29], who also classified perforations according to size. Five of the seven patients were treated by closure of the perforation or laparoscopic resection. There was no mortality, little morbidity, and most patients went home within 5 days of surgery. An even less invasive way of treating colonic perforation was recently described by Mana and colleagues [30], who used clips applied through the colonoscope to seal a small sigmoid perforation.

The decision to treat a perforation nonoperatively is the result of a careful evaluation of the clinical circumstances, and rests on the presence of a well-prepared clean colon with minimal bacterial contamination of the peritoneal cavity. Other essentials are a small or sealed perforation, normal bowel and a patient with good healing capacity and an intact immune system. Seow-Choen *et al.* [31] reported five such patients, four of whom had a therapeutic colonoscopy. All presented with pain from 2

to 12 h after colonoscopy and four had pneumoperitoneum. All responded to conservative therapy. Damore *et al.* [32] reviewed the literature and found that 58 of 196 (30%) perforations from 12 series were managed conservatively. Orsoni *et al.* [20] attempted conservative therapy in 21 out of 48 cases but needed to operate on eight. Four of five cases of traumatic perforations managed conservatively ultimately needed surgery. The lessons from these experiences are that some small perforations from polypectomy can be managed conservatively under close observation with surgery for any deterioration, or even failure to improve. Traumatic perforations usually need urgent surgery. Pneumatic split of the serosa splits can be distinguished from true perforation by water-soluble contrast enema [21].

Intraluminal bleeding

Bleeding is an usual complication of diagnostic colonoscopy. Dafnis *et al.* [33] reported no cases in 4677 colonoscopies, Waye *et al.* [5] found 38 cases in their collective review of 51 378 diagnostic colonoscopies (0.07%), and in the report of Wexner *et al.* of 13 580 colonoscopies, there was no case of bleeding without biopsy [12]. Of the 10 cases where bleeding did occur, five followed hot biopsy, four were after snare polypectomy, and only one case followed cold biopsy. Kavic and Basson [34] reviewed five studies of colonoscopic complications and found 26 cases out of 101 397 diagnostic colonoscopies, most following biopsy. By contrast is the frequency of postpolypectomy hemorrhage occurring in 284 out of 14 951 cases. Significant bleeding from a cold biopsy in a patient with normal coagulation is only likely to occur when a vascular structure is biopsied, such as an hemangioma, an arteriovenous malformation, or a prominent mucosal vein. Cold biopsy forceps will rarely reach deep enough into the submucosa to damage the submucosal arteries. An arteriovenous malformation rarely needs to be biopsied. It is either treated or left alone. Biopsy should also be avoided in patients with coagulopathy or with portal hypertension.

Extraluminal bleeding

Bleeding from outside the colonic lumen can also occur during or after colonoscopy, but not be visible, and if it continues will present at some time after the procedure has been completed. The most common cause is damage to the spleen, but mesenteric lacerations, tearing of adhesions, and retroperitoneal bleeds have been reported.

Splenic trauma

Splenic injury has been described in several case reports and small series [35–48]. Various mechanisms have been

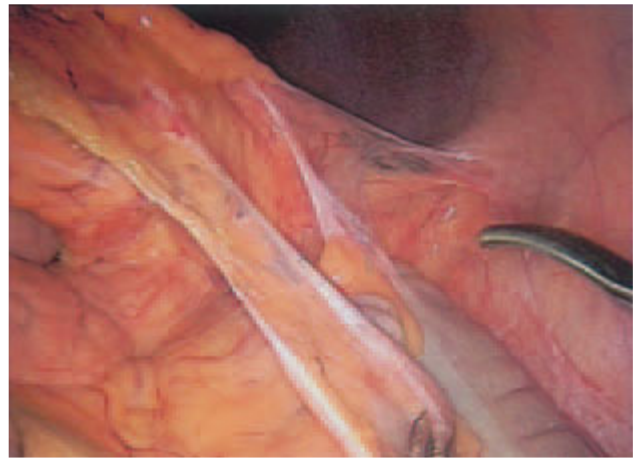


Fig. 15.1 Close anatomic relationship of spleen to splenic flexure Courtesy of Dr C. Delaney.

proposed to account for the injury, including simple tearing of the splenic capsule by traction on the splenicocolic ligament, direct trauma to the spleen by a loop of colon, and excess fragility of the spleen due to splenomegaly. There is an intimate anatomic relationship between the spleen and the splenic flexure of the colon that raises the question of why the spleen is not damaged more often (Fig. 15.1). Ahmend *et al.* [46] reviewed 17 cases of splenic rupture secondary to colonoscopy and found that all presented with abdominal pain, usually within 24 h of the examination. Only half were anemic (8/17), but 13 had an elevated white blood cell count. CT scan made the diagnosis in seven, laparotomy in six, ultrasound in one, and angiography in one. Treatment was conservative in four patients and required splenectomy in 11. Stein *et al.* [47] describe treatment of a splenic injury at colonoscopy with embolization, a technique that has been used in cases where the rupture was due to trauma.

Tse *et al.* [48] postulated that the spleen may be at more risk when the patient is supine than when the patient is in the left lateral position. A high degree of awareness of the possibility of splenic rupture must be maintained and no patient complaining of postcolonoscopy abdominal pain can be ignored. The differential diagnosis includes perforation as well as splenic rupture. An X-ray of the abdomen, complete blood count and, if necessary, abdominal CT scan should lead to the diagnosis. Treatment can be conservative if the patient is stable and is followed closely. Signs of progressive or ongoing bleeding call for action; usually splenectomy.

Mesenteric damage

Mesenteric laceration caused by colonoscopy is a rare phenomenon. Hernandez *et al.* [49] reviewed the literature in 1999 and found only three reported cases, each



Fig. 15.2 Serosal tear in the sigmoid colon seen at surgery the day after a preoperative colonoscopy (From [16] with permission).

one associated with a splenic tear. Their own case was an isolated incident that caused significant abdominal pain and a drop in hematocrit. CT scan made the diagnosis and laparotomy was required for ligation of a bleeding artery. Yoshimura and Sasaki [50] reported a similar case except that the bleeding was retroperitoneal, coming from an artery on the left psoas muscle. It is likely that subclinical damage to the mesentery occurs more often and is responsible for the relatively common post-colonoscopy abdominal pain that lasts a few days and then spontaneously disappears. Sometimes damage is noticed at laparotomy after a preoperative colonoscopy has been performed (Fig. 15.2).

Complications in other organs

There have been a few case reports describing unusual cases of rare complications. These have been listed comprehensively in reviews by Waye *et al.* [5] and Kavic and Basson [34]. They include cases of postcolonoscopy priapism [51], small bowel obstruction [52,53], mesenteric ischemia [54], cecal volvulus [55,56], acute pancreatitis [57], appendicitis [58,59], cholecystitis [60], and small bowel perforation [61]. Adhesion obstruction and strangulation of the terminal ileum can occur hours or days after an apparently uneventful colonoscopy [52,53]. In patients with a mobile cecum colonoscopy can affect the anatomy of the bowel and could predispose to an obstruction or a volvulus. A case of mesenteric ischemia presenting 3 days after colonoscopy in an 89-year-old man [53–56] is unlikely to have been directly related to the endoscopy, although dehydration from the preparation may have potentiated a low-flow state. Vender *et al.* [58] reported three cases of postcolonoscopy appendicitis out of approximately 8000 colonoscopies over 2 years. They speculated that the cause could be preexisting disease in the appendix, barotrauma from overdistension,

pushing a fecolith into the appendix, or direct intubation of the appendix. Thomas and Mitre [57] suggest that their case of pancreatitis was due to direct pressure of the colonoscope on the pancreas, an unlikely and unprovable hypothesis. Milman and Goldenberg [60] describe two cases of cholecystitis that closely followed colonoscopy, and speculate that the dehydration caused by bowel preparation may have precipitated the attacks. The cases of small bowel perforation and colonoscopy implicate severe adhesions in the etiology of the damage, although “additional pressure to negotiate the sigmoid colon” is noted in one case [61]. The true incidence of an association between such entities and colonoscopy can never be known. In some cases the association may be coincidental.

Cardiopulmonary complications

Vasovagal reaction

Shore *et al.* [62] have suggested that anxiety, the sight of blood or body tissues, visceral pain and a warm, crowded environment may set the stage for a vasodepressor (vasovagal) reaction. Vasovagal reactions do occur during colonoscopy, and in one study were the second most common complication after bleeding (J. Church, unpublished data). The initial presentation is a slowing of the heart rate, down as low as 30 beats per minute. Hypotension, sweating, pallor, and a feeling of impending fainting can accompany this. Often the vasovagal reaction happens during intubation of a tightly looped sigmoid colon, suggesting that tension on a tight sigmoid mesentery may stimulate the vagal nerve and slow the heart rate [63,64]. In a prospective study of 228 consecutive colonoscopies, Herman and colleagues [65] defined vasovagal reaction (rather liberally) as a fall in heart rate either below 60 beats per minute or a drop of more than 10% of baseline for more than 5 min, or a fall in blood pressure to less than 90 mmHg systolic or less than 60 mmHg diastolic; 37 of 223 patients fulfilled these criteria. The only differences between the patients who had a “reaction” and those who did not were a higher dose of midazolam (4.6 mg vs. 3.9 mg, respectively) and more moderate to severe diverticulosis (43% vs. 16%). Treatment of the reactions included increased fluids (24%), naloxone (5%), and atropine (5%). The authors did not stop any procedure because of the reaction and no adverse sequelae followed. Isolated hypotension without bradycardia is more likely to be due to dehydration, potentiated by the combination of benzodiazepines and narcotics. A true vasovagal reaction, defined by profound bradycardia, responds to discontinuation of the vagal stimulation by withdrawing the colonoscope. Hypotension due to oversedation or dehydration is treated with intravenous fluids and narcotic antagonists.

Hypoxia and cardiac events

Although serious cardiac events such as infarction and arrest during or after colonoscopy are rare (0.012% [66]), changes in the EKG have been described and include arrhythmias, ST segment depression or elevation, ventricular tachycardia, and ventricular fibrillation [67–69]. These changes are likely to be due to epinephrine release stimulated by anxiety and pain. Their clinical effect is determined by the cardiac status of the patient and the level of oxygen desaturation during the procedure. The incidence of hypoxia is related to the amount of sedation given to the patient but may occur in unsedated patients, as shown by Eckhardt *et al.* [70] who reported 24 cases out of 2384 patients undergoing unsedated colonoscopy, none of which lasted longer than a minute and none of which were treated. Three patients suffered a “severe vasovagal reaction,” two sedated and one unsedated. In this study the only predictor for adverse cardiopulmonary events was impaired physical status. Ristikankare *et al.* [71] compared cardiopulmonary complications in patients grouped according to sedation and found significant decreases in oxygen saturation and blood pressure in patients receiving a mean of 2.9 mg midazolam but no serious cardiac events occurred. Yano *et al.* [72] found that the risk of oxygen desaturation was significantly greater in patients over the age of 60, compared to those younger than 60 years, despite a reduced dosage of midazolam in the elderly patients. The combination of a narcotic and a benzodiazepine is particularly potent in causing hypoxia and hypotension. The potential sequelae of oxygen desaturation were demonstrated by Holm *et al.* [73] who reported that two patients had EKG evidence of myocardial ischemia and one had runs of extra systoles. Extrapolating the results from these small studies to routine practice is unwise, as they may not reflect the general experience, where clinically significant cardiac complications of colonoscopy are rare. However all patients undergoing colonoscopy should have pulse and oxygen saturation monitoring and those with a significant cardiac history should have an EKG monitor.

Even patients within 3 weeks of a myocardial infarction usually tolerate endoscopy well. Cappell [74] reported on 18 such patients who underwent lower gastrointestinal endoscopy for bleeding. Three of the 18 patients had unstable cardiac disease at the time of endoscopy, and two had complications: one developed second-degree heart block and premature ventricular contraction 3 h after sigmoidoscopy while another developed an asymptomatic bradycardia during colonoscopy, leading to an aborted procedure. None of the more stable patients had any cardiac events, showing that a recent infarction is not an absolute contraindication to colonoscopy. Of course it is not an ideal time for

the examination and if an exam must be done, close monitoring and involvement of the cardiology service is necessary.

Patients with severe chronic obstructive pulmonary disease are at risk of hypercapnia if they are oversedated, and may have a respiratory arrest if pain and distress levels rise. Such patients should have very little sedation if any, and increasing distress is an indication to stop the examination.

Anxiety reactions

Sometimes patients begin colonoscopy in a heightened state of anxiety, regardless of premedication with a benzodiazepine. Such patients are so anxious that they may complain of pain on rectal intubation. Tachypnea can lead to tetanic contraction of the hands and numbness of the face. If the examination must be performed, it can be rescheduled under general anesthesia.

Infectious complications of colonoscopy

Colonoscopy provides the potential for infection to occur in the patient by introduction of organisms with the colonoscope, by translocation of endogenous organisms into the bloodstream, or by seeding of organisms on to non-biologic implants, and in the endoscopist by contamination with infected bodily fluids. In 1985, Kelley *et al.* [75] reported subclinical bacteremia in 35% of patients undergoing colonoscopy and endotoxemia in 50%, showing that colonoscopy could result in translocation of bacteria and toxins from the lumen into the circulation. Berger *et al.* found subclinical endotoxemia in 21 of 32 patients having colonoscopy and bacteremia in one. Recent studies demonstrate a low incidence of bacteremia during colonoscopy (2–4%). The rate of infectious complications of colonoscopy is considerably lower than this, possibly because the enteric flora subject to translocation during colonoscopy do not usually cause infective endocarditis. Cases of peritonitis have been reported in patients with cirrhosis [76,77] and in peritoneal dialysis [78], but these cases do not indicate that routine antibiotic prophylaxis is needed. Llach *et al.* [79] reported that colonoscopy does not induce significant bacteremia in cirrhotic patients with or without ascites. Only a few cases of endocarditis following colonoscopy [80] have been described, and prophylaxis for high-risk cardiac conditions is recommended at the endoscopist’s discretion on a “case by case” basis (see Chapter 19). Introduction of an infectious agent into a patient through a contaminated colonoscope or endoscopic instrument is a concern of both the endoscopic community and the general public. The risk of this happening has been estimated to be 1 in 1.8 million [80]. Transmission of *Salmonella* species by colonoscope has

been reported [81,82] as have *Klebsiella*, *Enterobacter* and *Serratia* infections [83]. Until 2000, there has been no report of HIV transmission but one case of hepatitis B and two of hepatitis C have been described [80].

Preventing infectious complications

Cleaning, disinfecting and sterilizing (see Chapter 28)

Standards for the cleaning of endoscopes are now widely published, involving the types of solutions, routines, and methods to be used [82,84–87].

Antibiotic prophylaxis

The American Society for Gastrointestinal Endoscopy has published Guidelines for antibiotic prophylaxis in endoscopy in 1995 [88].

Protection of the endoscopist and endoscopy assistants

Measures to avoid contact with potentially contaminated body fluids (such as gowns, gloves, goggles, and masks) and the use of plastic/nonrecapped needles should be standard in endoscopy units, and should minimize the risks of staff acquiring an infection. All patients should be treated as potential carriers of a bloodborn pathogen [89], and all endoscopy units need to comply with communicable disease guidelines.

Incarceration of the colonoscope

The colonoscope may become trapped in the colon under two circumstances: a hernia and a tight, tortuous sigmoid colon. Koltun and Coller [90] and Leisser *et al.* [91] describe the situation in patients with an inguinal hernia where the scope could not be removed by simply pulling from the anus. In one case, the large loop of the scope in the hernia sac was maintained by the examiner's fingers while the scope was removed [90]. Incarceration in a tight sigmoid colon is more difficult to remove, with time, an antispasmodic, and warm water irrigation [92] all being parts of the solution.

Complications of therapeutic colonoscopy

Postpolypectomy bleeding

Bleeding occurs after polypectomy because a submucosal artery is either not sealed at all or the seal is broken later. This can happen after both snare excision and hot biopsy. Postpolypectomy bleeding is classically described as immediate or delayed, however immediate bleeding is usually considered as part of the poly-

pectomy. The chances of immediate postpolypectomy bleeding can be minimized by some of the strategies described below. The rate of secondary bleeding is not under the control of the endoscopist. Reviews of the incidence of postpolypectomy bleeding quote rates of 0.66–3.4% with a mean of 1.2% [5,13]. Not all polyps are at an equal risk of bleeding: risk factors include the following:

Location

Polyps particularly at risk for bleeding seem to be right sided [93], possibly because the bowel wall is thinner here and submucosal arteries are closer to the snare or zone of coagulation. Submucosal arteries may be more numerous in the right colon, although there are no data on this point.

Size and shape

The incidence of bleeding after removal of large polyps (> 2 cm) was summarized by Waye *et al.* [5] at 5.4%. The larger the amount of tissue enclosed in the snare the greater the chance of picking up submucosal arteries, and so piecemeal polypectomy should take pieces no bigger than 2 cm in one bite. Pedunculated polyps with a thick stalk are also a high-risk situation [3] and can be injected with 1 : 10 000 epinephrine prior to polypectomy.

Patient factors

Patients on anticoagulants, including coumadin, aspirin, and platelet inhibiting agents, or patients with a coagulopathy are at risk of bleeding. Colonoscopy with polypectomy in these patients is a "high-risk" procedure (American Society for Gastroenterology, ASGE). ASGE Guidelines [94] state that in patients with a high risk of thromboembolism warfarin must be stopped 3–5 days before the procedure, and consideration should be given to the use of heparin while the INR is subtherapeutic. When the risk of thromboembolism is low, warfarin is stopped as before but no heparin is necessary. Colonoscopists should communicate with vascular medicine or internal medicine colleagues to determine the best course of action in each patient.

ASGE Guidelines also state that there is no evidence to show that aspirin and other NSAIDs increase the risk of postpolypectomy bleeding.

Technique

Hot biopsy is just as likely if not more likely to cause bleeding as snaring, despite the smaller size of polyps treated in this way [95,96]. The zone of coagulation

produced by hot biopsy cautery is directed downwards into the submucosa, where it can damage the wall of submucosal arteries resulting in delayed hemorrhage when the area of thermal injury sloughs. This contrasts to the cautery produced by a snare, which is directed parallel to the mucosa, and will not damage submucosal arteries unless they are included in the pedicle.

Preventing postpolypectomy bleeding

Choosing your battles

The decision about which polyp to remove and which to refer to surgery is an individual one, based on the experience and confidence of the endoscopist. Alternatives include referring a difficult polyp to a different endoscopist or referring the patient to a surgeon.

Stop anticoagulants (see Chapter 20)

Coumadin should be stopped at least 5 days before polypectomy. Patients on coumadin should have a normalized INR before the procedure. The patient's cardiologist, primary physician or vascular specialists can help determine the risks of stopping anticoagulation, and whether heparin or low molecular weight heparin is necessary as an interim measure.

Good technique

Detailed technical advice can be found in Chapters 35 and 36. However it is wise to use pure coagulation current at all times, and close the snare slowly. Hot biopsy technique should be reserved for polyps that are too awkwardly placed for a snare, and too large to be completely removed by cold biopsy.

Preinject with saline or 1 : 10 000 epinephrine

Lifting a polyp on a bed of saline increases the distance from the base of the polyp to the submucosal arteries. This is effective in minimizing the risk of bleeding and should be almost routine in large (> 2 cm) cecal and ascending colon polyps. Use of epinephrine makes immediate bleeding even less likely but may not prevent a secondary hemorrhage.

Treating postpolypectomy bleeding

Consent (see Chapter 4)

Part of the consenting process is to warn patients of the possibility of postpolypectomy hemorrhage. This involves making sure that the patient is not planning any trip that would make urgent care inaccessible for the

next 2 weeks. Patients living more than 2 h away from the treating institution should be given a copy of the colonoscopy report with clear descriptions of the site and method of the polypectomy. If necessary the polypectomy should be deferred.

Immediate bleeding (see Chapter 47)

The quickest and most effective way to stop immediate bleeding from the polypectomy site is to inject the area with 1 : 10 000 epinephrine. If the polyp was pedunculated the stalk can be resnared and held for several minutes. Other thermal modalities can be applied.

Delayed bleeding

Delayed postpolypectomy hemorrhage can occur from 1 to 15 days after polypectomy. Regardless of the precautions taken against it, postpolypectomy hemorrhage can occur in any patient, although it is more common in large right-sided or rectal polyps. Often the bleeding has stopped by the time the repeat colonoscopy is done, but if it has not the bleeding site is injected with 1 : 10 000 epinephrine and treated by a thermal or mechanical modality.

Perforation

Perforation of the colon may occur during or after polypectomy because the coagulation current causes full-thickness necrosis of the colonic wall. Sometimes a section of normal colonic wall is inadvertently included in the snare and coagulated along with the polyp. It is wise to compare the apparent thickness of the tissue enclosed in the snare with the diameter of the stalk or polyp as seen on the screen. Snare excision of a diverticulum or an ileocecal valve can also lead to perforation.

Perforation can occur immediately after polypectomy if a full-thickness piece of colonic wall has been removed, or late if a necrotic patch of colon sloughs out (Fig. 15.3a,b). The incidence of postpolypectomy perforation ranges from 0.08% to 0.69% with a mean of 0.35% per polyp and 0.41% per patient having polypectomy [5].

Prevention of perforation

All technical aspects of polypectomy are important in preventing perforation. The placement of the snare is important in allowing the mucosa to be lifted away from the underlying muscle. The fat in lipomas is a poor conductor of electrical current requiring a dangerous amount of current for their removal. Cancers invade the colonic submucosa and sometimes the muscle, leading to full-thickness wall resection when they are

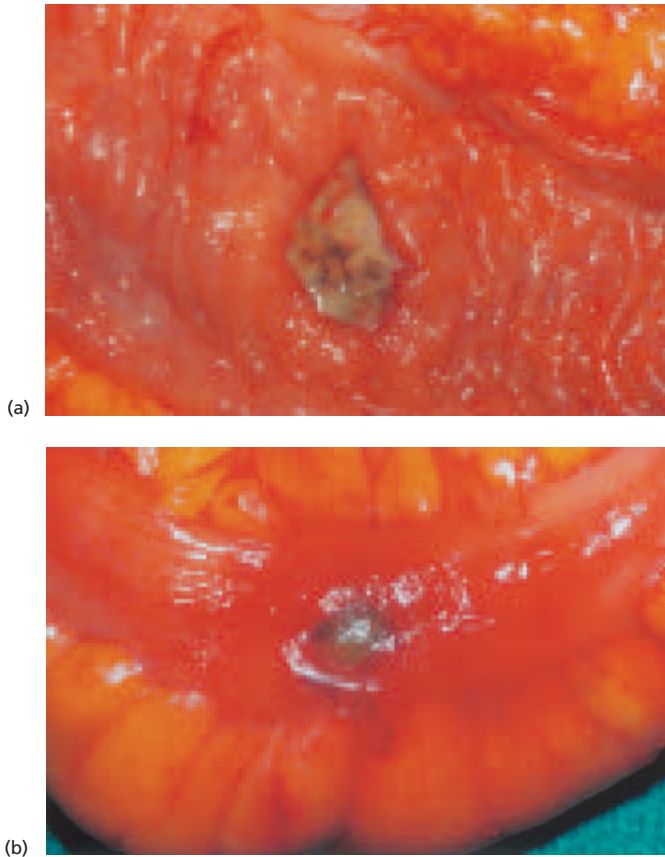


Fig. 15.3 (a) Mucosal aspect of snare polypectomy of small polypoid cancer, the patient had elective surgery 4 days later (with permission). (b) Serosal aspect of polypectomy site in (a) showing full-thickness necrosis (From [16] with permission).

removed (Fig. 15.3a,b). The cecal wall can be very thin and prone to perforation with standard amounts of current. Saline or adrenalin infiltration under polyps will raise them away from the colonic wall and make cautery safer.

Treatment of perforation

Successful treatment of postpolypectomy perforation depends on early diagnosis and appropriate decision-making. Unusual abdominal distension or delayed onset of abdominal pain warrants investigation with abdominal examination and X-ray. The presence of peritonitis mandates laparotomy. Free intraperitoneal gas means there has been perforation or at least thinning of the colonic wall, but does not necessarily indicate surgery unless there is also peritonitis. Without peritonitis, bowel rest and intravenous antibiotics are often effective. Early perforations are less clinically harmful as fecal contamination is minimal. At surgery, simple closure is a realistic option. Late colonic perforations are rarely amenable to closure and usually require resection.

Postpolypectomy syndrome

In the presence of thermal injury to the muscular layers and serosa, the patient may present with all the classic signs and symptoms of a colonic inflammatory process such as caused by appendicitis or diverticulitis, except that in the postpolypectomy patient, the inflammation is thermal, not infectious. Such patients sometimes present with localized pain, tenderness and fever with or without signs of peritoneal irritation. This occurred in 9 of 777 polypectomies (1%) reported by Waye *et al.* [95], with all cases resolving on antibiotic therapy. Hospitalization and treatment with intravenous antibiotics and bowel rest is usually successful in resolving such symptoms within a few days.

Impaction of snare in polyp

If a snare enters a polyp deeply with coagulation current and the endoscopist desires to abandon the resection and remove the wire loop, the snare may be stuck and not retrievable. The easiest way out of this situation is to cut the handle off the snare, remove the colonoscope over the snare, pass the colonoscope again, and resect the polyp head piecemeal until the original snare can be retrieved. Alternatively one can wait until the incarcerated snare is expelled from the rectum as the enclosed portion of polyp sloughs off. Other solutions are available (see Chapter 36).

The missed lesion (see Chapter 30)

Colonoscopy is not a perfect examination. The “miss rate” of adenomas varies according to size from 27% for diminutive adenomas to 6% for large adenomas [97]. Cancers are missed, usually because they are not reached [98] but sometimes because they are mistaken for colitis or ischemia.

Lesions can be missed because they are not seen in an incomplete exam, not seen because they are covered by stool, not seen because of their low profile, or not seen because of their awkward position in a flexure of the colon. It is important to examine all the colon completely, including the traditional “blind spots” of the cecum under the ileocecal valve, the hepatic and splenic flexures, and the low rectum. Incomplete colonoscopy must be followed up with air contrast barium enema, CT colography, or a repeat colonoscopy. A poor preparation in which parts of the mucosa are not seen needs to be followed by another examination with a better preparation. Lesion detection rate can be optimized by a careful withdrawal, as suggested by Rex who showed that the rate of missed adenomas was related to time of withdrawal [99]. The implications of missing a lesion can be minimized by warning the patient that colonoscopy is not

perfect, and by asking the patient to return if symptoms persist [100].

A related concern is the inaccurate localization of significant colonic pathology. This can have a disastrous effect on surgery as shown by Hancock and Talbot [101]. When resection of a colonic lesion is to be done laparoscopically, three- or four-quadrant tattooing may be necessary to prevent removal of the wrong section of bowel. Even with an open resection, on-table colonoscopy may sometimes be needed to make sure the correct section of colon is removed with adequate margins.

Summary

Colonoscopy is a complex process that offers several opportunities for misadventures and complications. The continuing increase in demand for colonoscopy as a way of screening for colorectal cancer, diagnosing colorectal disease, and treating colorectal mucosal lesions means that complications are certain to occur with increasing frequency. An awareness of common complications, a routine to minimize or prevent them and a familiarity with the treatment options, and how to apply them is an essential part of every colonoscopist's practice.

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Chapter 16

Standardization of the Endoscopic Report

Michel M. Delvaux

The rapid development of computer technology has dramatically modified the management of medical data. Data processing in digestive endoscopy has become, over the last decade, one of the major challenges for the discipline. Interest has grown as the use of computers together with electronic endoscopes has allowed the capture of images of high quality to illustrate the report [1]. Electronic endoscopes are currently used in most endoscopy units for colonoscopy, which have also experienced other significant advances including magnifying endoscopes, improvement of image quality, and the availability of new therapeutic options, for example hemostatic clips and stents for colonic strictures.

Over the same period, computer technology has grown at a tremendous rate and the decreasing price of hardware has made it accessible to all endoscopists. The ability to input data in a standardized computer format constitutes a unique opportunity for developing cooperative studies sharing data issued from multiple endoscopic units. The CORI project in the USA has nicely demonstrated that the use of a common software in several endoscopy units supports such cooperative studies [2]. Unfortunately, standardization of endoscopic data is far from being achieved in current practice. Exchange of data between existing systems is difficult and standard data formats have so far not been widely accepted by the community. The text description of findings is the most important part of the information to be shared between the physician performing the endoscopic procedure and the referring physician. For the past several years, attempts have been made to standardize the endoscopic report and the format of endoscopic data. Previous initiatives aimed at developing common software have failed in spite of support by national societies [3]. Recent efforts have concentrated on the development of standard formats allowing easy exchange of data between systems. At the turn of the 21st century, two efforts of standardization deserve particular attention, as they actually enable standardization of endoscopic reports and data exchange. The Minimal Standard Terminology (MST) has been designed as a “minimal” list of terms that could be included within any computer system used to record the results of a gastrointestinal endoscopic examination [4]. It followed the initial attempt by

Maratka to systematize nomenclature in digestive endoscopy [5]. On the other hand, image file formats used for endoscopic images are the same as those adopted for digital cameras, i.e. TIFF, JPEG . . . most of time including a certain level of data compression. A standard format has been proposed for radiology images, the DICOM (Digital Imaging and Communication in Medicine), which now also includes a supplement for visible light—color—pictures [6].

In this chapter, we will describe the process of data management in digestive endoscopy with respect to the use of data standards and their implementation in software, and then will discuss more specific issues that relate to colonoscopy.

Type of data managed in an endoscopy unit

The performance of an endoscopic examination requires that data be provided and managed before the procedure in order to generate other data, as shown in Figure 16.1. Data acquired before the procedure include scheduling in the unit, the demographic data, and the clinical history, as well as the results of other tests. These data, when recorded in a computer system, are managed in the *hospital information system* (HIS). Input of data into the system is not performed in the endoscopy unit, except when the patient is admitted directly to the unit for a specific procedure. A link therefore needs to be established between the HIS and the *endoscopy information system* (EIS) to avoid duplicate data entry and decrease the risk of error between data recorded in the two systems.

The endoscopic procedure itself generates data of two types. Historically, the text description has been the only data that was included in the endoscopic report, and was often handwritten or dictated. The endoscopic report was the only method for transmitting the results of the procedure to the physician managing the patient. The American Society for Gastrointestinal Endoscopy provided guidelines for the content of this endoscopic report, with a list of the necessary items that should be present (Table 16.1) [7]. The hope was to develop *public domain software* for computer-based reporting systems;

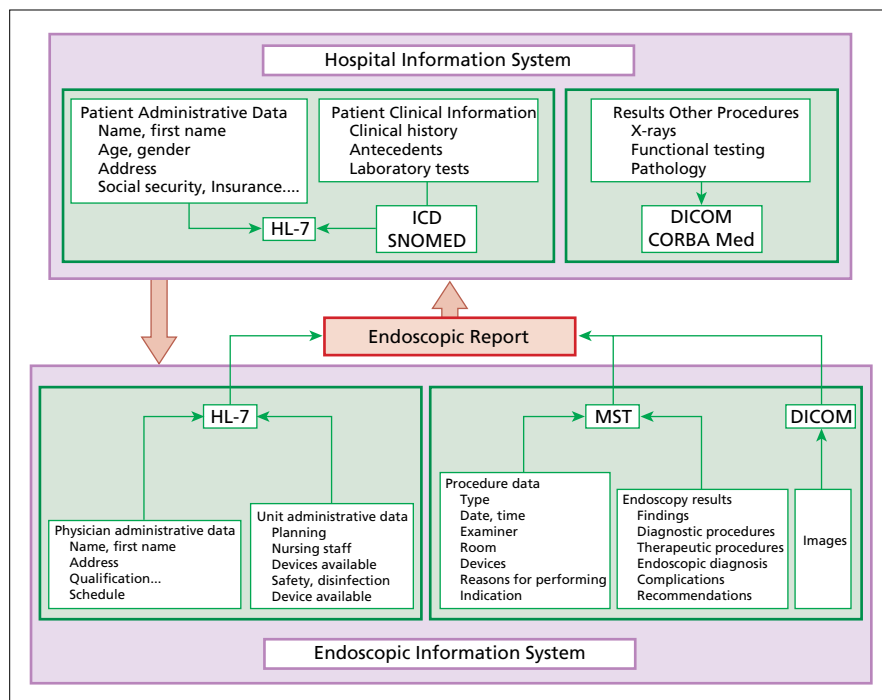


Fig. 16.1 Datasets to be managed in the endoscopic information system and relationship with the hospital information system. For each set of data, standard data formats are configured. MST, Minimal Standard Terminology for Digestive Endoscopy.

Table 16.1 Structure of an endoscopic record.

1	Patient demographic data
2	Date of procedure
3	Endoscopist
4	Type of endoscopic examination performed
5	Instruments used
6	Reasons for examination
7	Medication details (anesthesia, anesthesiologist, analgesia, sedation, . . .)
8	Anatomic extent of examination
9	Limitation(s) of examination
10	Findings and specimens obtained
11	Endoscopic diagnosis
12	Therapeutic interventions and results
13	Notation of images captured
14	Complications
15	Discharge arrangements
16	Comments
17	Results of biopsies and other late tests
18	Final diagnosis.

this initiative failed. Currently, data input into the recording system varies widely from unit to unit: hand-written or dictated reports are the most common methods of entering data, most of which is based upon the use of natural language. Shifting to a computerized recording system imposes to some extent the use of a structured language that can be analysed and handled by the application database (see below).

The development of videoendoscopes and the use of personal computers has allowed the capture of high-

quality endoscopic images and their inclusion in the endoscopic report [8,9]. Images captured in endoscopy are obtained from visible light, like regular colored photographs. Video sequences are also recordable but require much more space on digital recording devices and in general, their use remains limited to the endoscopy unit itself, as they are not routinely exported to the patient's file. There is no doubt that an accurate documentation of endoscopic procedures with images from the examination would dramatically improve the quality of the report and move endoscopy towards a more regimented presentation of the results.

Organization of the data in an endoscopic database

Several types of endoscopic databases have been proposed. However, the most effective one is the "object-oriented" database of the relational type. The database is in fact made of several separate folders where data are stored according to type. One patient whose demographic data are stored in one file can undergo several examinations and for each of them, a separate file will be created. Each examination will contain both text and images, the latter being stored in another folder, so that an examination can include an unlimited number of images (Fig. 16.2). The software of the database is organized in a way that allows it to retrieve data from the different files to build an "object" composed of the dataset relevant for a given examination and send it to the screen or the printer. Figure 16.3 shows the structure of an

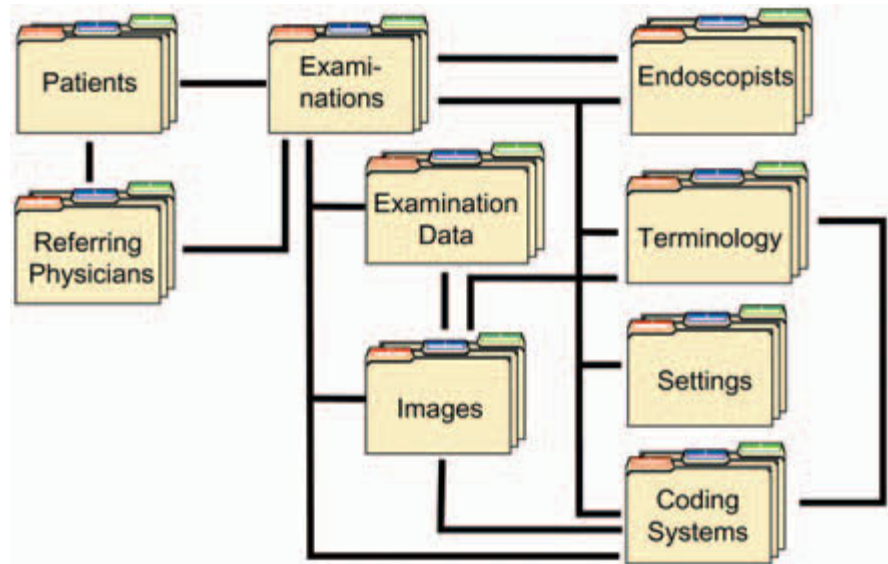


Fig. 16.2 Architecture of a relational database showing the various files that contain the data and the multiple relationships that can be established between them.

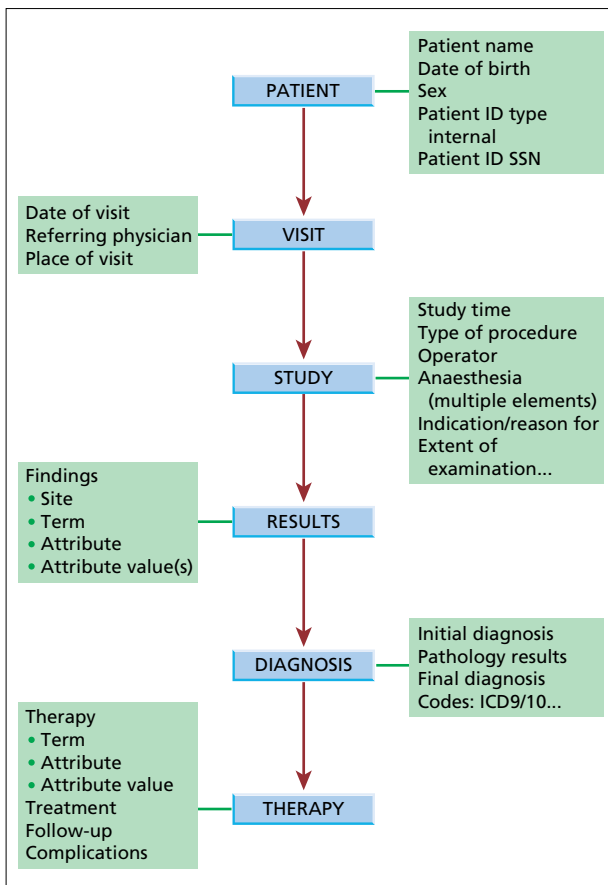


Fig. 16.3 Organization of the data elements belonging to the endoscopic report in a structured object that can be used as a model for standardization of the dataset.

object that would contain all the information needed to describe an endoscopic procedure, which will then be included in the endoscopic report.

The Minimal Standard Terminology for standardization of the endoscopic report

Background and principles

The initial attempt to systematize endoscopic nomenclature was done by Z. Maratka and published as the “OMED” (Organisation Mondial d’Endoscopy Digestif) Terminology [5]. Despite the clever design, acceptance was very low in the endoscopic community and it was never implemented in practical reporting systems. Following an initiative of the European Society of Gastroenterology, an endoscopic report project started in cooperation with the American and Japanese Societies for Gastrointestinal Endoscopy [10]. The major aim of the project was to devise a “minimal” list of terms that could be included within any computer system used to record the results of a gastrointestinal endoscopic examination. It was decided that the terms selected must have wide acceptability and provide a means for recording the findings in the majority of examinations performed. Excessive detail was to be avoided and rare findings were to be recorded using “free text” fields. Each term was selected on the basis that it would be expected to be used in at least 1 out of 100 consecutive examinations. The only terms included that did not fit this criteria were descriptive terms that could be found only in certain areas of the world (e.g. parasites), where they might be relatively common.

To facilitate implementation and allow a more complete description of observations, when necessary,

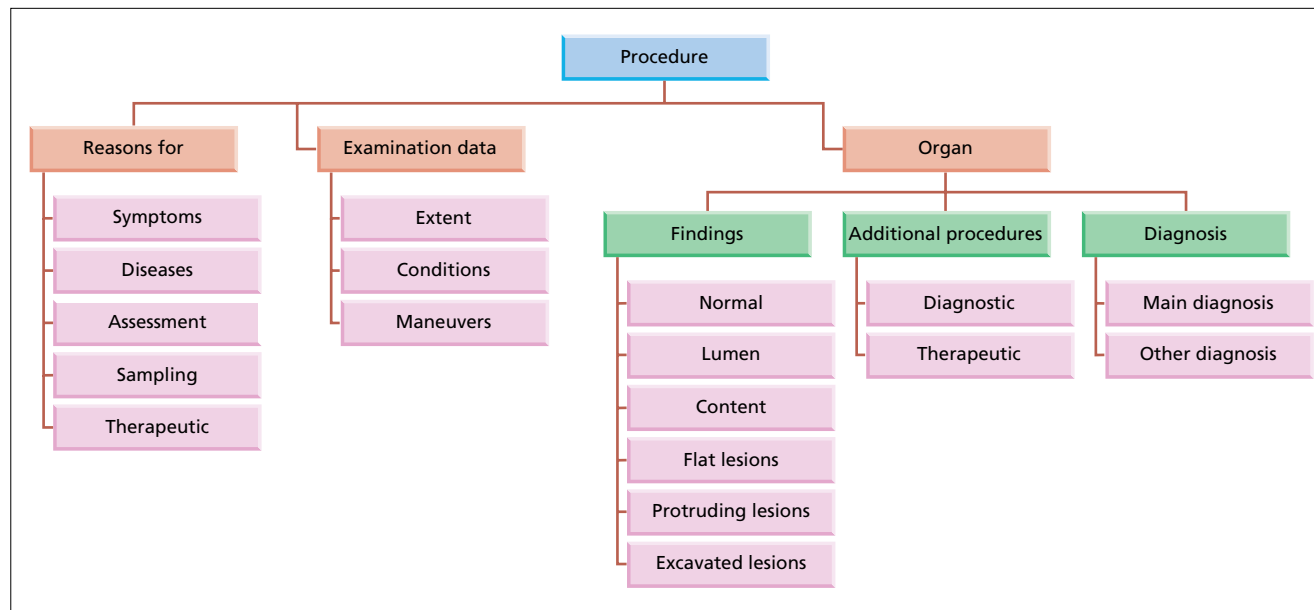


Fig. 16.4 Organization of the Minimal Standard Terminology and hierarchy of terms as they are displayed in the tables. This hierarchy follows the logical pathway used by endoscopists to build an endoscopy record.

qualifying attributes which provide additional detail were attached to the above terms. The attributes are a list of descriptive concepts such as size, number, extent, etc. . . . for which there are a series of values appropriate to that item. Every described lesion has a location on a list of sites relevant to the organ being examined. By this construction the lists of terms with their modifiers and qualifying attributes, translate the report into a structured language.

Structure of the MST and sections of the endoscopic report

The Minimal Standard Terminology is structured to contain lists of terms that cover the main types of endoscopic examinations, i.e. upper GI endoscopy, colonoscopy and ERCP, with an additional complementary list of Therapeutic Procedures that might be performed (Fig. 16.4). These lists contain terms that define concepts describing the medical fields of the endoscopic report:

Reasons for examination

The lists of terms describing the reasons why an endoscopy is performed are presented as “reasons for performing an endoscopy.” The concept is broader than the one of indications, as some examinations may have been performed for reasons that are not accepted as indications. An “indication” is used to define the reason for

an endoscopy, which complies with generally accepted standards of practice. There may be reasons for an endoscopy which are not indications. For example, a patient may want to undergo annual colonoscopy for colorectal cancer surveillance even though there is no prior history of polyps or family history of colon cancer. The reason for colonoscopy is to exclude a tumor but there is no agreed indication.

Extent of the examination

This section refers to the characteristics of an examination, and is defined as the anatomic extent of the procedure. A limit of the examination is defined as any limitation that impedes adequate execution of the procedure. It is recognized that there is some overlap in the concept of extent and limit. The intent of this section is to convey in an explicit manner those characteristics of the examination that affect the completeness of the examination, as well as any limitations that prevent a complete examination and will include any maneuvers necessary to execute a complete examination. For colonoscopy, if the cecum is reached, then the anatomic site “cecum” specifies the extent of examination. The quality of bowel cleansing is a major factor for the quality of the procedure, especially when small and flat lesions are sought. Poor preparation is considered a limit of the examination.

Findings

Findings cover the description of observations made during an endoscopic procedure, without necessarily linking them to a diagnosis. It is important to distinguish

“elemental” or single lesions that are described individually, versus diffuse abnormal patterns that contain several elemental lesions and that constitute a finding by themselves. In the colon, an example would be colitis with an ulcerated mucosa associated with ulcers, congestion, friability, and hemorrhage. Terms used to describe functional changes, such as contractility and elasticity of the wall, increased or decreased peristalsis, functional narrowing or extrinsic distortion, have been excluded from the MST, as they were considered to be too subjective and imprecise to aid in making a diagnosis. In addition, these terms are too open to misinterpretation for use in any multicenter studies. Particular attention has also been given to avoid synonyms and terms which in daily practice were observed to overlap frequently and lead to unnecessary detailed descriptions. As an example, the original OMED terminology proposed many terms describing a stenosis such as stenosis, stricture, narrowing, compression, obstruction have been discarded and the unique term “stenosis” has been selected.

Endoscopic diagnosis

This indicates the diagnosis, single or multiple, that the endoscopist feels is most likely on the basis of macroscopic findings. This is not necessarily the final diagnosis, which takes into account the findings of any additional procedures performed such as biopsy/cytology. The diagnostic list has been split into two parts: (i) main diagnoses, ordered by expected prevalence; (ii) other (rarer) diagnoses listed alphabetically. The decision on which list a particular diagnosis appears is based upon the expected frequency of this finding in a routine clinical context. This “diagnosis” could be used to implement a “conclusion” field within any report generated. Such a conclusion would be based on a synthesis of all of the findings recorded. This is particularly true when a number of different lesions are described, such as colonoscopy of inflammatory bowel disease. It should be possible to record a “negative conclusion” as well as a positive one. It is often as important to record that a fea-

ture is not present as it is to describe what is found; for example, the failure to find any sign of bleeding when a patient presents with an apparent gastrointestinal bleed. It is suggested that it be possible to qualify a diagnosis by “certain,” “suspected,” “probably not present,” and “definitely excluded.”

Therapeutic and diagnostic procedures

This section is intended to describe the additional maneuvers that are undertaken in the frame of an endoscopic procedure to either increase its diagnostic yield by sampling tissue or biological fluid from the examined gut segment or treat a disease with an endoscopic technique.

List of terms for colonoscopy and difficult terms

Lists of terms in the MST have been customized to the pathology specific to each gut segment, according to the frequency of lesions and the particular relevance of pathological conditions. To facilitate the implementation of endoscopic reporting software, the terms have been classified under headings that cover large categories of lesions found in each section (Table 16.2). Headings have been defined according to the relationship of lesions to the intraluminal findings in or on the mucosa, which is always examined during an endoscopy.

Table 16.3 shows the list of terms that have been selected for description of findings in the colon. Some of the terms proposed in this list will be difficult to use in the way that is intended, since surveys performed during the development and the validation phases of the MST have shown they were used with a wide variability in meaning or that multiple synonyms were used. On the other hand, the selection of a term had to take into account the need for a very precise descriptive word and the acceptability of these words among physicians from different countries with different native languages. The following terms appeared difficult to use in view of the results of the validation studies (see below) and deserve further explanation:

Table 16.2 Major headings for grouping of terms in the structure of the MST.

1. Normal	Should be used if the organ has been entirely examined and everything is normal
2. Lumen*	Contains all terms regarding an abnormality of the size of the organ, any deformity, compression, and evidence of previous surgery
3. Contents	Terms describing the presence of various materials within the organ
4. Mucosa	Terms describing patterns of the mucosa that are mainly diffuse and may involve all the mucosa of one limited area. These terms are not applicable to individual lesions
5. Flat lesions	Terms to be used for individual lesions which are in the plane of the mucosa
6. Protruding lesions	Terms to be applied to lesions growing above the plane of the mucosa
7. Excavated lesions	Terms to be applied to lesions whose surface is beneath the plane of mucosa

* This heading also includes some terms classified under “Wall” in the OMED terminology.

Table 16.3 List of terms, attribute and attribute values describing the findings at the level of the colon.

Headings and terms	Attributes	Attributes values	Sites*
<i>Normal</i>			
Normal			Site(s)
<i>Lumen</i>			
Dilated	Site(s)		
Stenosis	Appearance	Extrinsic Benign intrinsic Malignant intrinsic	Site(s)
	Length (cm)		
	Traversed	Yes/No	
Evidence of previous surgery	Type	Colocolonic anastomosis Ileocolonic anastomosis Coloanal anastomosis Ileoanal anastomosis Colostomy	Site(s)
	Suture material visible	Specify	
<i>Contents</i>			
Blood	Kind of blood	Red Clot Hematin (altered blood)	Site(s)
Foreign body			Site(s)
Parasites			Site(s)
Exudate			Site(s)
Stool			Site(s)
Stent	Type	Specify	Site(s)
<i>Mucosa</i>			
Vascular pattern	Appearance	Normal Increased Decreased	Site(s)
	Extent	Localized Segmental Diffuse	
Erythematous (hyperemic)	Extent	Localized Segmental Diffuse	Site(s)
Congested (edematous)	Extent	Localized Segmental Diffuse	Site(s)
Granular	Extent	Localized Segmental Diffuse	Site(s)
Friable	Extent	Localized Segmental Diffuse	Site(s)
	Bleeding	Yes: spontaneous Yes: contact bleeding No	
Ulcerated mucosa	Continuity	Discontinuous Continuous	Site(s)
	Bleeding	Yes No	
	Stigmata of bleeding	Yes No	
Petechiae	Number	Few Multiple	Site(s)
Pseudomembrane	Extent	Localized Segmental Diffuse	Site(s)

Continued

Table 16.3 (cont'd)

Headings and terms	Attributes	Attributes values	Sites*
Melanosis	Extent	Localized Segmental Diffuse	Site(s)
<i>Flat lesions</i>			
Angioectasia	Number	Single Few Multiple	
	Size [†]	Small Medium Large	
	Extent	Localized Patchy Diffuse	
	Bleeding	Yes No	
	Stigmata of bleeding	Yes No	
<i>Protruding lesions</i>			
Polyp(s)	Number	If less than 5, specify If more than 5: specify if many or multiple	Site(s)
	Extent [‡]	Localized Segmental Diffuse	
	Size	In mm	
	Pedicle**	Sessile Pedunculated	
	Bleeding	Yes No	
		Stigmata of bleeding	
Pseudopolyps	Extent	Localized Segmental Diffuse	Site(s)
Lipoma	Size	Small Medium Large	Site(s)
Tumor/mass	Diameter	mm	
	Size	Small Medium Large	Site(s)
	Length	Diameter in mm In cm	
	Type	Submucosal Fungating Ulcerated Infiltrative Fron-d-like/villous	
	Obstructing	Partial Complete	
	Circumferential	Yes No	
	Bleeding	Yes: spurting Yes: oozing No	
	Stigmata of bleeding	Yes No	
Hypertrophy anal papillae			
Hemorrhoids	Bleeding	Yes No	

Continued overleaf

Table 16.3 (cont'd)

Headings and terms	Attributes	Attributes values	Sites*
Suture granuloma	Number	Single Few Multiple	Site(s)
Condylomas			
Excavated lesions			
Erosion	Number	Single Few Multiple	Site(s)
	Extent	Localized Segmental Diffuse	
	Bleeding	Yes No	
	Stigmata of bleeding	Yes No	
Aphtha	Number	Single Few Multiple	Site(s)
	Extent	Localized Segmental Diffuse	
	Bleeding	Yes No	
	Stigmata of bleeding	Yes No	
Ulcer	Number	Single (Solitary) Few Multiple	Site(s)
	Size	Largest diameter in mm	
	Bleeding	Yes: spurting Yes: oozing No	
	Stigmata of bleeding	Yes No	
Scar	Number	Single Multiple	Site(s)
Diverticulum	Number	Single Few Multiple	Site(s)
	Opening	Small Large	
Fistula			Site(s)
Anal fissure ^{††}			

* Site recording should mainly be multiple for colonic findings.

† Size in this case could also be given in mm for small angiectasia.

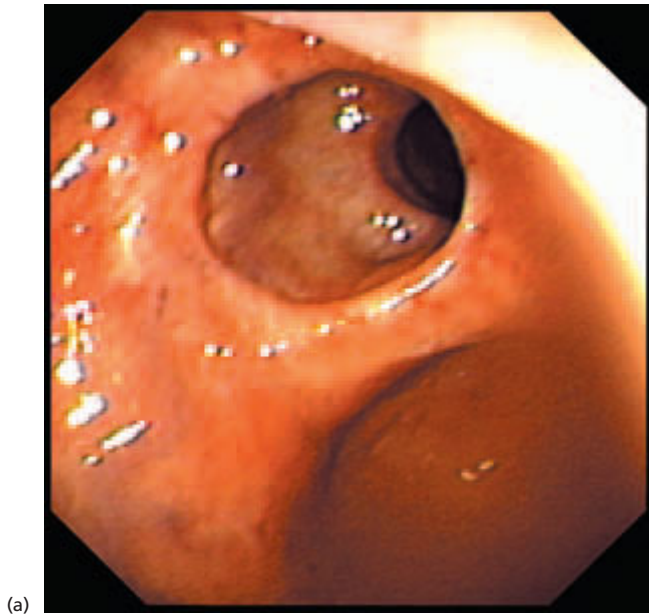
‡ This attribute will apply only when describing multiple polyps.

** In case of multiple polyps, the application would allow the recording of multiple entries.

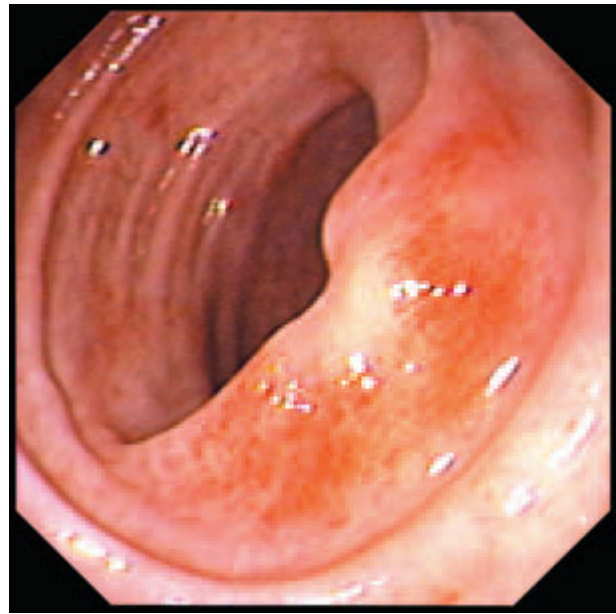
†† Fissure is the preferred term instead of erosion which could be confused with colonic erosions.

• *Stenosis* is replacing several descriptions of a narrowed segment of the gut, like “narrowed,” “strictured,” “stenosed,” “compressed” (Fig. 16.5). The same term has been used to describe the narrowing of a sphincter which either prevents the passage of the endoscope or requires force to traverse it. Functional terms such as

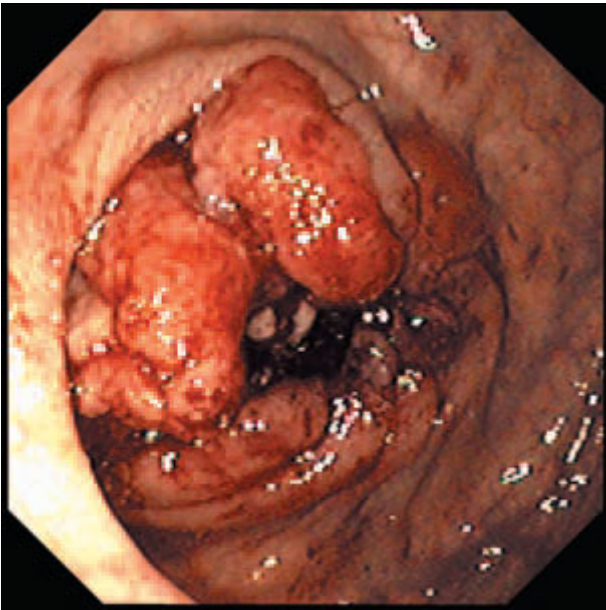
“spasm” have been avoided because of their subjective nature. Once a stenosis has been described it is qualified by attribute values: “extrinsic,” “intrinsic benign,” or “intrinsic malignant,” based on the probable cause. In the case of an extrinsic compression, where actual stenosis of the lumen does not occur, for example



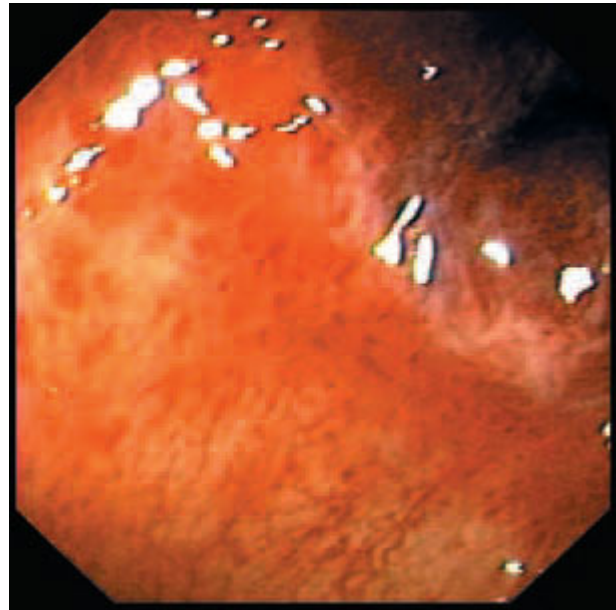
(a)



(a)



(b)



(b)

Fig. 16.5 Example of colonic stenosis from a benign process (a) or a malignant process (b).

the aortic prominence, the term “stenosis” should not be used.

- *Red mucosa, erythema, congested mucosa, hyperemia* were used to define roughly similar lesions or mucosal patterns. Instead of these ambiguous terms, two terms were selected: *erythematous mucosa*, defined as either a focal or diffuse reddening of the mucosa without any other modification, and *congested mucosa*, defined as a combination of erythema with an edematous, swollen or friable mucosa (Fig. 16.6). Due to the large overlap between these terms, it was agreed that hyperemia was equivalent to erythema and edematous was equivalent to

Fig. 16.6 Erythematous mucosa in the colon, defined as an increased redness of the mucosa, due to an increase in its hemoglobin content because of increased blood flow (a). This should be distinguished from a congested mucosa, defined as a swelling of the mucosa due to an increase in the thickness of the mucosa, occurring most often in association with an inflammatory process where permeability of cell membranes is altered and the extracellular osmolarity is modified (b).

congested mucosa. Therefore, these words could be used as an alternative but not added simultaneously to the number of terms used.

- *Erosion, aphtha* are frequently used to describe similar lesions. In the original OMED terminology, the term *erosion* had been avoided because it was considered to be

imprecise and required histologic confirmation; *aphtha* had therefore been the preferred term. However, the term erosion appears to be in such common usage in many languages that it was included amongst the minimal standard. *Erosion* is defined as a small superficial defect in a mucosa, of a white or yellow color, with a flat edge. This may bleed, but the term should only be used when the mucosa is clearly seen and is not covered by blood clot (Fig. 16.7).

In the colon, it was decided to retain the term aphtha, as it was agreed that aphthae were identified more frequently in this area and were recognized as a diagnostic feature of Crohn's disease. In this context, aphthae are defined as yellow or white spots, surrounded by a red halo and frequently with a spot in the center. Aphthae are frequently seen within a congested or erythematous mucosa and are often multiple (Fig. 16.7).

- *Tumor, mass* are regarded as synonyms that comply with local habits in some parts of the world. The word tumor is preferred to describe any lesion which appears to be of a neoplastic nature but without any attempt to say whether it is benign or malignant. It is not used for small lesions such as granules, papules, etc. . . . , nor for other protruding lesions such as polyps, varices, or giant folds. The conjoint ASGE review had difficulty with this term as, in the USA, a patient might assume that a tumor is a malignant lesion. For this reason, it has been agreed that the term mass could be used as an equivalent term when needed.

- *Angioectasia* has been selected as a generic term encompassing both telangiectasia and angiodysplasia. This is because there are no precise visible diagnostic criteria that will allow one to distinguish between these two lesions. This term can also be applied to congenital and acquired vascular malformations within the mucosa of the gastrointestinal tract.

- *Scar* is preferred to the term *fibrosis* as the latter implies a histologically confirmed process. The cicatricial aspect of the mucosa after healing of an ulcer or following a therapeutic maneuver (e.g. injection sclerosis, laser photocoagulation) seems to fit better with this word.

- *Occlusion, obstruction*, although frequently regarded as synonyms, should be used more distinctly, as *obstruction* means blockage of a tubular structure by an intraluminal obstacle (e.g. foreign body) while *occlusion* implies complete closure of the lumen by an intrinsic lesion of the wall (e.g. fibrosis from a healing process). Although obstruction and occlusion can be either partial or complete, the use of these two terms was felt to be confusing and created difficulties when translated into other languages. For the colon, the use of the term obstruction is restricted to the presence of an exophytic tumor in a tubular organ that partially or completely occupies the lumen of a gut segment.



(a)



(b)

Fig. 16.7 Erosions of the rectal mucosa (a) and typical aphthae shown in (b).

- *Ulcerated mucosa* is defined as an endoscopic pattern, made of multiple ulcers frequently joining each other and diffusely distributed over a gut segment, usually the rectum (Fig. 16.8). Mucosa between the ulcers appears congested, friable, and swollen. It is emphasized that this term should be used only in the case of a diffusely ulcerated mucosa when the endoscopist distinguishes this concept from "ulcers" that are multiple (Fig. 16.8). However, it is recognized that the use of this term needs to be evaluated in prospective trials, in order to better define its meaning and whether it is a distinct concept from the term ulcer.

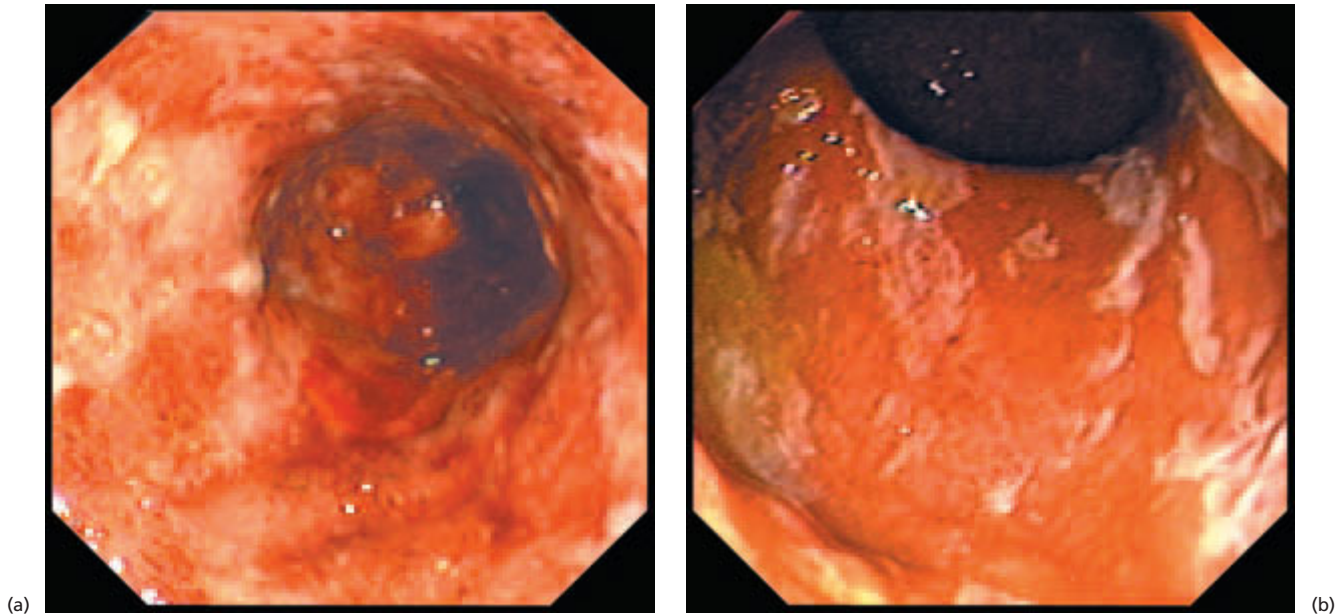


Fig. 16.8 Example of an ulcerated mucosa (a) involving the rectum in a patient with ulcerative colitis. An ulcerated mucosa does not necessarily lead to that diagnosis and this term should not be used in the presence of multiple well-delineated ulcers, separated by areas of almost normal mucosa (b).

Validation of the Minimal Standard Terminology

Validation of the MST has been performed in two multicenter studies, one undertaken in Europe and one in the USA [11,12]. Six thousand two hundred and thirty-two reports were analysed, including 1743 colonoscopies in the European study [11]. Overall, terms originally contained in the MST could describe fully 91.0% of all examinations where “reasons for” were described, 99.5% of examinations where “findings” were described, 95.8% of all examinations containing descriptions of “endoscopic diagnosis,” 98.9% of examinations containing descriptions of “additional diagnostic procedures,” and 94.8% of examinations containing descrip-

tions of “additional therapeutic procedures.” Free text fields were used in the other cases (less than 5% of cases in average).

Data on over 17 000 procedures were analysed in the US study, to determine the utilization of the MST [12]. Detailed data have been obtained from esophago-gastro-duodenoscopies, colonoscopies, and ERCPs and are presented in Table 16.4.

Advantages of the use of the Minimal Standard Terminology for the edition of endoscopic reports

The use of a structured language for the endoscopic reports flows from requests by users, i.e. the endoscopists. The users need to become familiar with the structure of the MST language and modify their reporting technique, in order to transfer the concepts they ordinarily use in natural language into the elemental data of an MST-driven report. MST has designed the nomenclature based on data models that will meet the actual situations where the users are working.

Table 16.4 Results of the testing in the US MST Lexicon Testing Project: total number of examinations and findings.

Examination type	Number of examinations	Number of abnormal findings	Number of findings described with MST	% findings described with MST
All	17 426	33 115	31 079	94
EGD	8136	20 310	19 030	94
Colonoscopy	8296	11 310	10 614	94
ERCP	994	1495	1435	96

EGD, esophago-gastro-duodenoscopies; ERCP, endoscopic retrograde cholangiopancreatography.

The modeling of a structured language as a basis for standardization

An endoscopy report can be thought of as a file which contains a series of documents defined by the needs of practice and filled in with the data generated during a procedure. A standardization process supposes that all the data elements that can be potentially introduced in an endoscopic report are considered and integrated in the model. A model integrating these data elements must be comprehensive for the user, and the data must be introduced in the database in a logical way and then retrieved to build up the report. Therefore, when all the data elements have been identified, a coherent grouping of these elements must be created. The MST lists provide these data elements. As DICOM has integrated all data elements related to medical images in a standardized list of fields [6], MST attempted to utilize a similar interdependent message/terminology architecture. This effort will soon be available as the SNOMED-DICOM microglossary for digestive endoscopy that will enable the creation of templates for the endoscopic report and suggest value-sets for the coded entry of the various fields in the report [13]. This structuring of the data presupposes a detailed analysis of the data elements and their relationship to each other. Based on the results of this analysis, the model is proposed as a logical integration of data along the same path as taken by the endoscopist building a report in natural language (Fig. 16.3).

Using structured language offers the possibility of integration of all the data elements in an "object," i.e. a set of data that is organized in a rigid framework which can be shared and understood by different systems. These objects can then be easily transferred from one system to another. Moreover, these objects can be easily retrieved from databases because relational databases currently used in medical informatics are more and more built as "object-oriented" databases. Another advantage of this database architecture is that data can be retrieved as structured subsets in a fast and secure process.

Clinical benefits for the use of a structured language

Although the advances in endoscope technology have allowed the production of high-quality video images to be transmitted, captured and stored by modern high-speed integrated circuits, image documentation and reporting has not progressed so fast. However the constant increase in the use of computers for the management of medical data has induced a strong need for the standardization of the data to be exchanged. Standardization means the coding of the data in a common format that can be read by multiple information systems, operated on different platforms. This goal is achieved by actions like the DICOM or HL-7, but goes far beyond

medical needs; image formats like JPEG, TGA, and TIFF have been developed for purposes other than medicine, however a medical image without the relevant associated data is of no value [14]. Thus, the need for standardization of medical text data has become stronger over the last decade.

The use of structured reports in endoscopy, based on a structured language like MST will allow statistical analysis of databases, not only derived from the coded data using rigid coding systems like ICD but also on the complete data. Indeed, in a database structured with the MST, not only the terms themselves can be analysed but also the attributes and attribute values can be quantified. The analysis of the data will thus be more detailed. The advantage for clinical research is obvious: standardization of the data in digestive endoscopy will support multicenter trials, will overcome the problems of multilingual data recording in cooperative studies, and will promote outcomes research. The latter point will become very important in the near future. Advances will result only from the analysis of large sets of data and will be based on the evaluation of the following features: (i) adequacy of data descriptions according to observations; (ii) measurement of appropriateness of diagnostic and therapeutic decisions made for the patient; (iii) precise description of technical approaches to diseases; and (iv) multidisciplinary understanding and management of the diseases. All these actions require an integration of medical data, initially at the level of each specialty but also as exported of data from the specialized unit, (i.e. the endoscopy unit) to the integrated care unit through the hospital information system. Large standardized systems have failed in the past to cover the whole range of medical data. This justifies the use of SNOMED to attempt validation of microglossaries in specialty related domains and to integrate these microglossaries at a high level, making them intermeshed by a common structure [15].

Future trends and maintenance of the Minimal Standard Terminology

The future is represented by two main lines of actions: one will be devoted to the maintenance of the MST with respect to evolution of knowledge and practice and to its preservation from inconsistent changes during wider use. The second line will ensure the flexibility of the MST and its possible adaptation to specific situations.

Maintenance of the MST is a longstanding activity that must be integrated in the frame of a scientific society, but it must be an open process that will ensure responsiveness to new developments. Recently, the representatives of OMED, ESGE, and ASGE have met and decided, with the cooperation of some Japanese colleagues, to set up an editorial board for the MST. This board will have

an international dimension and will care for the tasks related to MST, in close cooperation with the various scientific societies. The MST editorial board will be responsible for the maintenance of the subsequent versions of MST, the adaptation of it to new practice, and the release of these versions. The main task of the board will be to promote the use of the MST and to establish relationships with the national societies for gastrointestinal endoscopy, supporting the production of accurate translation in the national languages and the organization of educational events to teach the community how to use MST. Moreover, the editorial board will have to disseminate the MST amongst software developers and to encourage them to implement it in their applications. The editorial board is producing guidelines for a conformance statement to be used by software developers to obtain official recognition that they have properly implemented the MST. This would actually support its dissemination.

Standardization and exchange of images in digestive endoscopy

Over the last decade, informatics in medicine has developed tremendously. Two important areas of advance have been identified that converge with the documentation of endoscopic procedures, i.e. the documentation, storage and transmission of radiological data and the development of specific information systems for hospitals, integrating data from various sources, i.e. the hospital information systems (HIS). These systems suppose integration of data produced by different systems or obtained by different procedures: radiology, endoscopy, pathology, clinical data . . . The development of applications in these fields has from the beginning raised the problem of standards.

Standardization of image format has been for many years driven by radiologists because they had the technical possibility of handling digitized images far before other specialities. However, when technical advances introduced digitized images in endoscopy practice, the need for a standard to allow the exchange of images between various systems has led to the consideration of the possibility of adapting the DICOM system for the exchange of color pictures generated during endoscopic procedures. Initially produced as "*an endoscopy supplement*" to DICOM 3.0, the scope of this supplement has quickly been extended to other modalities producing images in *visible light* (VL) like ophthalmology, dentistry, and pathology [16].

Production of digital endoscopic images

Only electronic video endoscopes provide endoscopic images of high resolution that support digitization and use in computers. Video endoscopes create analog

images from a video signal stream of voltage changes, measured every few microseconds, to turn the continuous signal into a discrete one. This procedure is called sampling. At the same time, the computer quantifies each of the measured values into a numerical value, to turn the analog signal into a digital one. These two processes, sampling and quantifying, transform the continuous analog signal into a discrete digital signal, which can then be stored in the memory of the frame grabber board. The accuracy of the digitization process depends on the frequency of the measurement and the maximum numerical value, which is available for the storage of a measured value. To obtain images of accurate quality for clinical use, the frame-grabber board needs to capture images with a true display of colors and resolution of the details provided by the video endoscope. A good result is obtained with a frame-grabber card that digitizes each of the three color signals red, green and blue with an accuracy of 256 values (2^8 bits), which sums up to a total of $256 \times 256 \times 256$ (~16.8 millions) colors. This is called the color depth of the system and is actually better than the color resolution of the human eye, which is able to distinguish about 7 million different colors. Once a numerical value is acquired, it is stored in the matrix of the memory of the frame-grabber board then the next value is acquired. The memory of the frame grabber allows the storage of one or of multiple images.

Because of the size and shape of the CCD chip located at the tip of the endoscope, the full video screen is usually not used to display the endoscope image. Depending on the manufacturer and the type of endoscope, typical digitized images are built up from about 400×400 to 600×400 pixels, i.e. 160 000–240 000 pixels in total. In view of the fact that the CCD chips in video endoscopes rarely have more than 30 000 light-sensitive elements, it is obvious that the resolution of the digitized image exceeds the resolution of the CCD. The limitation of the resolution in a digitized endoscopic image is based on the maximum resolution of the CCD and the transfer of video signals through wires, but not on the resolution of the frame-grabber board. The file size of an uncompressed image depends on the area in pixels multiplied with the color depth, for example $400 \times 400 \times 24 = 3\,840\,000$ bits. The usual unit for file sizes in a computer is Byte, and 1 Byte equals 8 bits. In our example, the image of 3 840 000 bits would take 480 000 Bytes, or if we divide the number of bits by 1024, the file size is converted to kiloBytes (also kByte or KB). In this example, the file size is then 468.75 kBytes. Using compression algorithms, the size can be reduced by the factor 2–10, without any or significant loss of image quality, depending on the compression method. For instance, the compression type that can be selected is based on the compression algorithm that was initially developed by the Joint Photographers Expert Group (JPEG) [17],

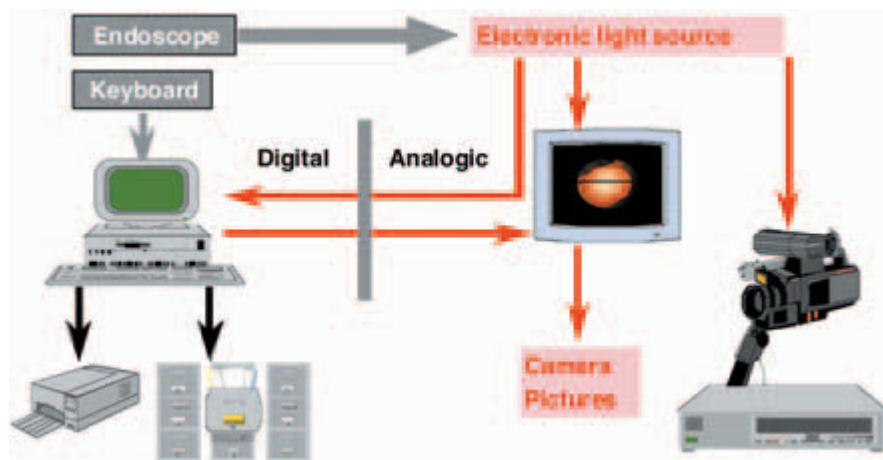


Fig. 16.9 Process of digitization of endoscopic images in an endoscopic workstation including an electronic videoendoscope and a computer equipped with a frame grabber card for capture of images. This computer can be further linked to the hospital network to make the images captured during endoscopic procedures available in the hospital information system.

who evaluated a compression algorithm that takes into account that the human eye is more sensitive for brightness changes than for small color changes. Therefore the compression algorithm reduces the color information more than the brightness information in the image. Although the compression algorithm loses some information, it is optimized for “real world” photos and especially appropriate for images with a relatively small number of different colors, without extremely sharp edges, i.e. high levels of contrast, and without too many small details of different colors. Endoscopic images fully fit into this frame since they contain a limited color spectrum and no sharp contrast areas.

Management of endoscopic images in computer systems

When an image has been captured by the frame-grabber board, it must be transferred to the storage device where it will be hosted. To save the image information, it is transferred from the frame-grabber card through the bus of the computer system to its RAM (the operating memory of the computer) and from there to storage on mass media, for example floppy disks, hard disks, magneto-optical disks, or CD-ROM/DVD media (Fig. 16.9).

Transfer of endoscopic images with the DICOM protocol

The DICOM protocol organizes the transfer of images between computers based on different operating systems. Thereby, the DICOM protocol ensures the following features [6]:

- promotion of communication of digital image information, regardless of equipment and/or manufacturer producing this image;
- facilitation of the development and expansion of picture archiving and communication systems (PACS) that can also interface with other systems within the HIS;

- creation of diagnostic information databases that can be interrogated by a wide variety of devices geographically distributed.

To achieve these goals, the DICOM standard organizes the data describing each image and the text data of the examination to which it belongs into an entity that is called an object (see above). This object is made of various data that are each identified with a specific header telling the computer what kind of data is stored. Data are organized in three levels, depending on their importance for a proper reading of the file. Mandatory data are those that need to be present for any image, for example the content of each pixel that composes the image or the total number of pixels. Conditional data are required only in some circumstances, for example the name of the patient or his/her identifier in the hospital information system that are required only when a nominative report needs to be created. Optional data are regarded as not necessary for the accurate transfer of the data and left to the particular requirements of a given application, for example the patient’s address and insurance numbers will only be used in specific applications but are not part of an endoscopic report as such.

The structure of the DICOM standard, whatever the type of image exchanged between systems, is based on the model of *distributed processing*. Distributed processing has at least two processes sharing information, each doing its own processing but relying on the functionality of each other. An example can be seen in the endoscopy unit. The endoscopic workstation, placed in each endoscopy room, generates images. These images must be stored somewhere and they also need to be displayed on the computer of remote clinical units on request of the clinician. Image acquisition, storage and remote control are distinct services, based on the information contained in the images. The different processes on which these services are based are distinct, can be performed by different systems but share the same information.

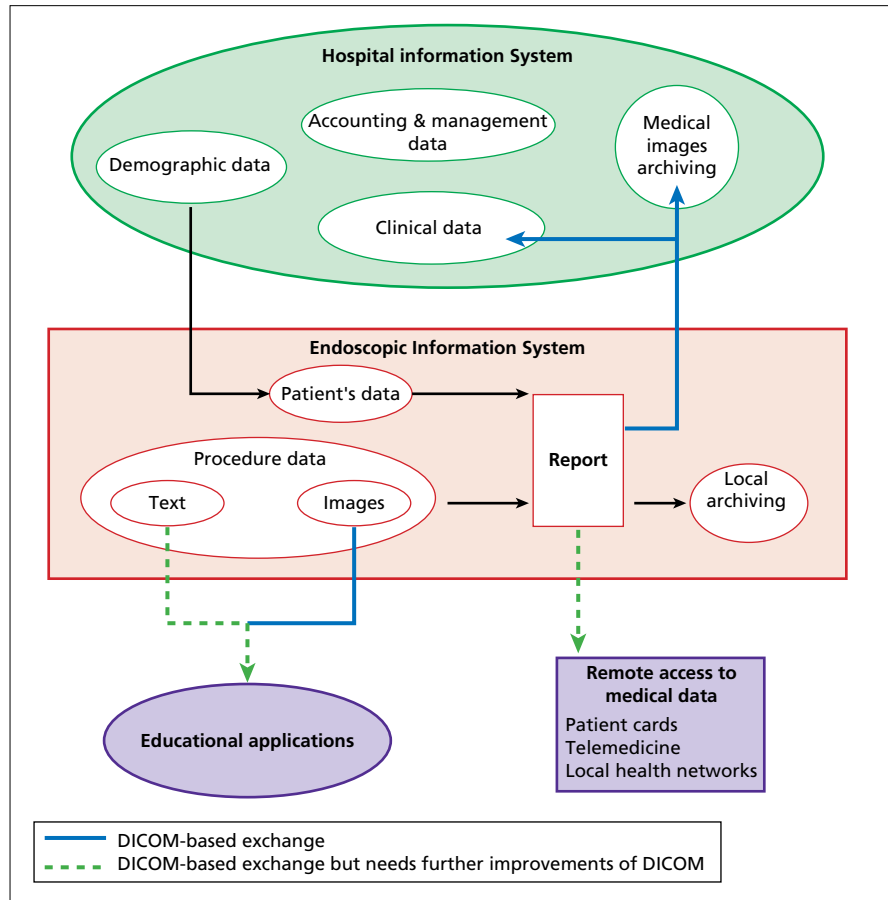


Fig. 16.10 Schematic representation of the pathways along which data are transferred between the endoscopy unit and the other components of the hospital information system or for utilization of the data for various services inside the endoscopy data management system.

In this scenario, which is called a distributed process, the application generating the images or displaying them is strongly decoupled from the communication process, which coordinates data transmission between systems and compensates for the different ways in which data are internally represented on different systems (Fig. 16.10). Hence, the role of each system must be clearly defined. The most important distinction is the one defining the role of “server,” i.e. the application that offers functionalities to others, and the role of “client,” i.e. the application that uses the functionalities generated by others. These relationships are managed under the TCP/IP protocol that basically organizes relationships between servers and clients, for example on the Internet. Once the roles have been defined, the systems must organize the information they want to share. This information is defined by the context of the service implemented. In our example, the storage of images in large reference databases will not require the same information as the display of the image in the clinical unit. However, if the clinical unit wants to retrieve images from the large database, the information used by each of these processes must be consistent and this is achieved by the definition of a global context to which each process will refer to organize information.

The information exchanged is organized in objects, i.e. the information related to one object of the real world, for example, the patient, the image, the procedures, are distinct objects which each contain a number of data fields. These *Information Object Definitions* (IOD) are divided into normalized IODs containing a single information entity or composite IODs containing multiple information entities. Then, the system must link different objects. In our example of the endoscopy unit, the patient (an IOD) may undergo a procedure (another IOD) which will generate multiple images (image IODs). This is typically a composite IOD, which is organized in successive layers, so that at the end, an object is created containing the whole information plus the relevant links. The whole object represents a *service* that is generated by the server application or *service class provider* and that will be used by the client application or service class user. Table 16.1 shows the object that can be generated during an endoscopy procedure. The datafields that are included in this object are not specific to endoscopy but some of them have a particular importance in the case of endoscopic color pictures.

Finally, the DICOM organizes the actions performed on the images. These actions are called *service elements*. These elements determine the operations allowed on

information objects, like *Get*, *Move*, *Store*, *Delete* . . . Service elements can be organized in service groups. The whole procedure results in an encoded dataset that organizes the Byte stream during the exchange between systems. The way of encoding is defined by the transfer syntax which is part of the work done by the service provider. However, the service user or client must be able to recognize this syntax.

Although the general principles of the DICOM can be quite easily understood, the implementation in data management systems has been delayed because of the complexity of the data to be managed and the difficulty in creating the link between the various systems. These problems have recently been solved with the development of Internet technology and the use of the XML language. In that format, data are described in a *Definition Type Document* (DTD) that describes all the data elements that are needed for a specific action or service. The DTD is an easier way of organizing the data elements contained in the IOD (see above).

Use of endoscopic images in clinical practice

Various scenarios have been investigated for the clinical use of digitized endoscopic images. The obvious advantage is the production of a complete endoscopic report associating text data and images. Insertion of images in the endoscopic report supposes that it will be produced by a computerized report generator. Moreover, this report must be transferable to the hospital information system to be included in the patient file that is contained in the database of the hospital information system.

Production of computerized endoscopic reports will also foster several clinical applications, including outcome studies, quality assurance processes, and large multicenter trials. Such achievements will become successful when endoscopic manufacturers and software developers integrate computers and electronic endoscopes in actual endoscopic workstations. Software applications must have a user-friendly interface, be built on a modular model, allowing customization to various types of practice. On the other hand, future applications need to integrate the new standards for data formats and ensure compatibility with existing software. DICOM is an example of the possibility of a successful reporting/imaging initiative as it was born from the joint activity of the manufacturers of radiology equipment and pushed forward by the strong willingness of the scientific associations of radiologists. In digestive endoscopy, a similar momentum is needed to hasten the process of computerization of data management. Technical solutions exist but their implementation has been delayed for various reasons. The wider use of electronic endoscopes and the challenge of endoscopy with other imaging techniques constitute a unique opportunity to make it happen.

Summary

The imaging possibilities offered in digestive endoscopy have dramatically improved over the last decade due to the use of electronic endoscopes and their interface with computers. The data generated during an endoscopy procedure include images and text. The rapid growth of computers for data management in medicine requires that these data be stored in standard formats which are the basis for a proper exchange of information between systems.

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Chapter 17

Reporting and Image Management

Lars Aabakken

Introduction

Gastrointestinal endoscopy is a visual clinical discipline. All examinations, findings, descriptions, and recommendations are based on the images created during the endoscopic examination. In interventional work, the images are the sole guiding material for correct procedures. The traditional mode of reporting these images has been a written report. This report ideally contains the description of what is seen, followed by an expert interpretation of the significance of the findings. The conclusion is typically a diagnosis, with or without a qualifier of confidence.

This model for reporting is not necessarily ideal. The imaging that is the basis for the interpretation of findings should be available as a part of the report. The lack of report imagery in endoscopy results from lack of technical feasibility not of clinical utility. Thus, with the rapid dissemination of image-enhanced reporting systems, the inclusion of report images should be a prerequisite. This chapter deals with some of the issues that text and image reporting generate. It also covers the present status of terminology and standardization in this area.

Text report

Report elements

The endoscopy report is the core means of communication for the endoscopist, and it should be meaningful to endoscopists, general gastroenterologists, and referring practitioners alike. It is also a legal document that may be scrutinized in a court of law to determine if the standard of care has been fulfilled. This combination of audiences calls for a mixture of information, where the various elements of the report are of varying importance to the different readers.

No formal statement has been made concerning the requirements of a complete endoscopy report. However, a certain general structure prevails in most centers, and the ensuing elements and the description thereof is endorsed by a majority of the endoscopic community.

Patient demographics

The full name, birth date, medical record number, or other unique identifier should be included initially and should be easily recognizable (in bold type). The name (minimum) should be repeated in the header of all additional pages of the report in order to avoid misplacement of orphan pages. In a hospital context, the inclusion of an identifying barcode may be useful for efficient paper handling.

Referrer information

The referring unit/physician is typically identified as the addressee of the report. However, all the receivers of the report should be listed in each copy of the report. This is important for ensuring that all the units involved with the patient know who received the pertinent information and, even more importantly, who did not. This is a vital step in avoiding patients becoming lost to follow-up.

Endoscopist

The attending and fellow endoscopist, as well as other doctors attending the procedure, should be included in the report. Even though the fellow typically formulates the report, it is usually important for the reader to realize who was responsible for the interpretations and recommendations presented. In a complex case where the surgeon and possibly the radiologist are summoned, this information should be included as well; alternatively, this information can be detailed in the interpretation/conclusion part of the report.

Indication/clinical history

The reason for the procedure should be clearly stated in the report. This may be a suspected illness, work-up of a specific symptom, follow-up of a known disease with or without sampling, or screening purposes. There is a subtle difference between indication and reason for the procedure, since indications may have implications for

reimbursement. A reason for a procedure, on the other hand, has both clinical and practical implications.

In this section, a concise clinical history is also of value. It serves to put the endoscopic procedure and findings in a context even for readers unfamiliar with the specific patient. There is no need for a complete medical history, but issues of relevance to the endoscopy are important. This includes symptoms/signs and previous work-up of the disease in question. It also includes other diagnoses or problems that are of potential relevance to the endoscopy, e.g. in the context of possible complications. Diabetes, cardiopulmonary problems, anxiety disorders, and hemorrhagic diathesis are a few examples of possibly relevant diagnoses that can be explicitly stated as part of the endoscopy report or reported in a separate history section. This will show the reader that the procedure was done only after a thorough evaluation of all aspects of the particular patient.

Informed consent/disclaimer

The endoscopy report should state that information about the procedure was given to the patient and, to some extent, what that information was. In many countries written informed consent is required prior to the procedure and referral to such a document will be sufficient. Most lawsuits after mishaps are based on the patient's perceived lack of information of possible complications, and written documentation is vital to document the standard of care. In special cases, e.g. a high-risk dilation procedure, a specific account of the discussion with the patient is even more helpful.

Sedation

Drugs given as a part of the procedure should be documented within the endoscopy report. This includes the type of drug, dose, and time and route of administration. The effect of the drug is of interest (e.g. response to midazolam) partly for the follow-up of the patient but also as guidance for future procedures in the same patient. An important piece of information that should be recorded is the odd patient with an adverse reaction to midazolam who becomes agitated.

Technical information

Technical aspects of the procedure are important for interpretation of the procedure, indication for repeat endoscopy, and again as guidance for other endoscopists seeing your patient in the future.

The colonoscopy report should include type and effect of the cleansing procedure, and the ability to visualize the mucosa adequately. In the case of incomplete cleansing, the level of adequate cleansing (if any) should be

noted to enable a more specific repeat study. The completeness of the endoscopy is recorded, including any uncertainty about it and the reason for incomplete study. Even the choice not to enter the distal ileum should be noted; the reason may be perfectly valid (polyp screening). In the case of particular difficulties in passing the instrument, the specific solutions should be included in the report. It is possible that these solutions may need to be repeated at a later date.

Findings

The description of findings is the core information of the report. An objective, systematic, and detailed account of what was seen, or not seen, is the main result of your procedure. This may sound simple but there are caveats. 1 Findings should be described completely and objectively, based on features that are visualized not interpreted. To achieve this, a standardized terminology is an excellent tool (described later). Mixing objective features and interpretation is very easily done, but all interpretative comments should be reserved for the Impression section. Thus the expert reader can more easily evaluate your findings.

2 Documentation of normal findings and/or lack of pathology may be important. For example, the normal retroflex appearance of the anorectal transition is vital in patients with unexplained anemia.

To ensure this type of completeness, the report should be constructed systematically. Most computer software reporting programs automatically offer a template that ensures all segments are described, but in a free text dictation setting omissions may easily occur. In this case, the question "Was it really specifically looked for?" remains unanswered for the reader.

Impression

This section summarizes the findings described above, including interpretation based on the endoscopic appearance and additional information about the clinical setting (e.g. immunosuppression or hemorrhagic diathesis). For nonexpert readers, this will be the main piece of information that allows them to make sense of the specifics of the endoscopic procedure. The distinction between findings and impressions may appear artificial, but adhering to this structure allows the endoscopy report to be a versatile piece of information useful for expert and novice reader alike.

Conclusion and recommendations

The conclusion should summarize the Impression section, with a tentative diagnosis, recognizing the lack of a path report, etc. It should also offer a recommended course of action for the referring doctor responsible for

the follow-up of the patient. If the findings require repeat endoscopy, the timing and arrangements for this should be explicitly stated in order to ensure that all involved parties are informed.

Diagnoses and procedures

Most reporting templates require the entry of formal diagnoses and procedures, including the appropriate codes. ICD-10 codes are used most frequently, although there are inherent shortcomings in using a pathology-based coding system to describe a visual study like endoscopy. Sometimes the discrepancy is nonexistent, e.g. in the case of a hiatal hernia. Other findings may be more equivocal, e.g. esophageal erosions in a patient with severe immunosuppression. In this case, only the pathology report will allow an accurate ICD-10 code to be entered, long after the endoscopy report is finalized and dispatched.

Images as part of the report

The increasing availability of digital endoscopic images is paving the way for their role in standard reporting of endoscopic procedures. Accompanying a textual description of a finding with one or more pictures of the same finding, together with a location diagram, significantly enhances the value of the report, particularly for other endoscopists who may interpret the images independently. Also, in the setting of repeat endoscopies for follow-up of a finding, the ability to compare the appearance of a lesion with previous images is invaluable for determining any progress or healing.

Color images require specialized printers, increasing the cost of preparing the endoscopy report. A possible option is to print images on a separate sheet of paper, while the standard text report is printed on regular non-color laser printers. With the further development of cheaper color laser technology, this problem will probably diminish.

Free text vs. structured input

Traditionally, the endoscopy report was dictated into the general medical record, similar to surgical procedures or consultation notes. This model is still prevalent, at least in Europe, and it is efficient and convenient for the endoscopist.

Even in dedicated endoscopy reporting systems, unstructured input is the rule rather than the exception. Some systems require some degree of uniformity of the text, i.e. separating clinical history from findings and impressions, entering the endoscopist's name in a separate box. This model allows the endoscopist maximal flexibility in the descriptions, lesions and impressions being described in natural language.

In the context of endoscopy reports produced as a document describing the procedure in the individual patient, free text is a good choice but there is the strong possibility that key elements of the report may be omitted.

The digital revolution

Initially, the mere view into the intestine was a revolution. However, the revolution was a very private one, conveyed through the eyepiece of the endoscope, without the ability to share or store the endoscopic view. Endoscopists had little or no means of communicating what they saw, apart from the written endoscopy report, which was an interpretation of the images. Twin eyepieces and mountable cameras were steps in the right direction, allowing discussion and exchange of image information, but these were cumbersome gadgets with limited dissemination.

The introduction of video-based imaging systems created a host of new opportunities. The eyepiece was replaced with the greatly enhanced viewing experience of a large monitor screen, enabling the endoscopic examination to become a shared experience with colleagues and assistants. In addition, still image printers could be connected for paper prints of important findings.

The video signals received and processed in the endoscopy equipment can also be stored electronically, as captured electronic images or digital video. In combination with other existing technologies, this enables access and use of endoscopic images far beyond what was previously feasible.

The increasing availability of electronic image capturing systems opened up new ways of documenting procedures. Where the reader was previously confined to the endoscopist's concept of a "large ulcer", "profuse bleeding", or "moderate inflammation" in a text report, the addition of images allows better understanding of what is actually found. This development parallels what radiologists have been doing for a long time: relating their diagnostic considerations directly to recorded image material.

The ability to share information in text and image permits everyone to understand what endoscopists are talking about. The need to label our findings with medical terms has emphasized the need for language standardization; everyone must mean the same thing when using the same words. The content of a written report will only be of value if the "image-to-word" coding algorithm is the same. The task of establishing a common language of gastrointestinal endoscopy has been taken on by the World Organization of Digestive Endoscopy (OMED) and also by the European and US societies for endoscopy.

Once the words are in place, there is a need to structure information as well. The endoscopy report should be composed in a standardized way, similar to what we

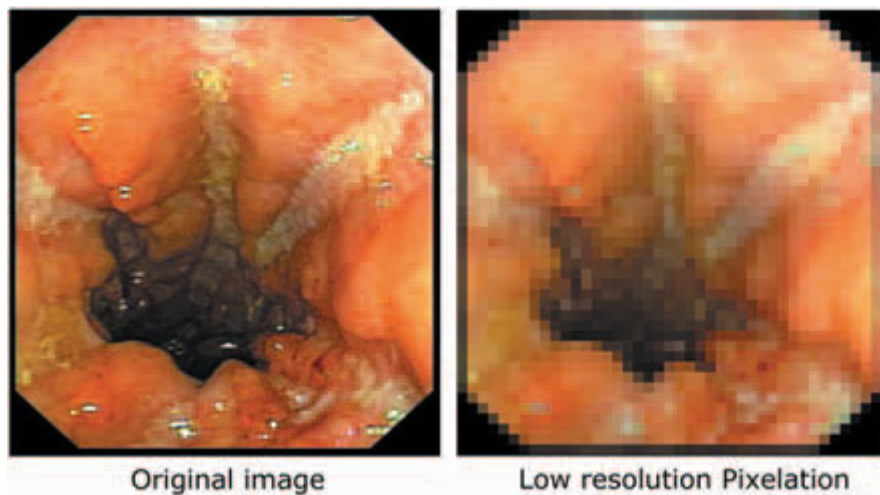


Fig. 17.1 Difference between (a) higher (100 dpi) and (b) lower (10 dpi) resolution. Pixelation is clearly seen at lower resolutions. The same phenomenon is seen if a picture is zoomed beyond its generic resolution.

have come to expect in the medical history and physical findings of a patient on admission. The introduction of computerized reporting systems for endoscopy mandates a structured report. The use of these systems for statistical analysis requires rigorous coding.

The digital revolution in endoscopy laboratories has the potential to change the way endoscopists work and communicate, offering great improvements in the service to the patient and referring doctors. However, this advance requires a nontrivial investment of money, time, and thought on the part of the endoscopist. This section deals with some of these issues.

Digital imaging

Imaging the gastrointestinal tract using a videoendoscope requires several steps: illumination by fiberoptic light transmission, surface reflectance, magnification, charge-coupled device (CCD) conversion of the reflected light to an electrical signal, reconstruction of the signals to an image, and projection on to a monitor. Personal computers with image capture boards and network capabilities permit these images to be captured, stored, printed, and transmitted.

Pixel density

Pixel density (sampling density) is the number of pixels into which an image is divided by the frame grabber. The greater the number of pixels per unit area, the higher the resolution of the image (Fig. 17.1).

File size

The final size of an uncompressed image is calculated simply by multiplying width (in pixels) by height by color depth. Thus a VGA-resolution 24-bit image

(typical for an endoscopic image) would be $640 \times 480 \times 8 \times 3 = 7\,372\,800$ bits, or about 900 kilobytes (kb) (1 byte = 8 bits). File size affects storage requirements, display delays, and transfer times, and becomes important in the everyday use of images. Transferring a 900-kb image with a 28.8-kb modem requires 4.3 min, and a 1-Gb disk drive would be filled with 1100 such images [1]. Thus, all the factors determining file size should be considered in order to optimize the composition of endoscopic images.

In some clinical situations resolution is not important, e.g. a large mass or a pedunculated polyp may be easily identified as such even at low resolution. On the other hand, subtle findings such as the granularity of the mucosa or disruption of the vascular pattern may require a higher pixel ratio. It is also of interest how the image will be used. To show the image on a computer screen, the resolution of the screen determines the optimal resolution (e.g. SVGA); however, printing via a high-quality printer (e.g. glossy prints for a journal manuscript) requires a higher resolution, typically two to three times screen requirements.

At present, there is definitely an upper limit to the resolution feasible for endoscopic images. The CCD chip in the tip of the endoscope has a pixel resolution in the SVGA range. Thus, even if we had capture boards with higher resolution, the image quality would only be marginally better (Fig. 17.2). However, high-resolution endoscopes are being developed that may change this situation.

File compression

For practical purposes, uncompressed images are almost a relic of the past. With the increasing utility of network-based and Internet-based computer applications, the need for smaller files is indisputable.

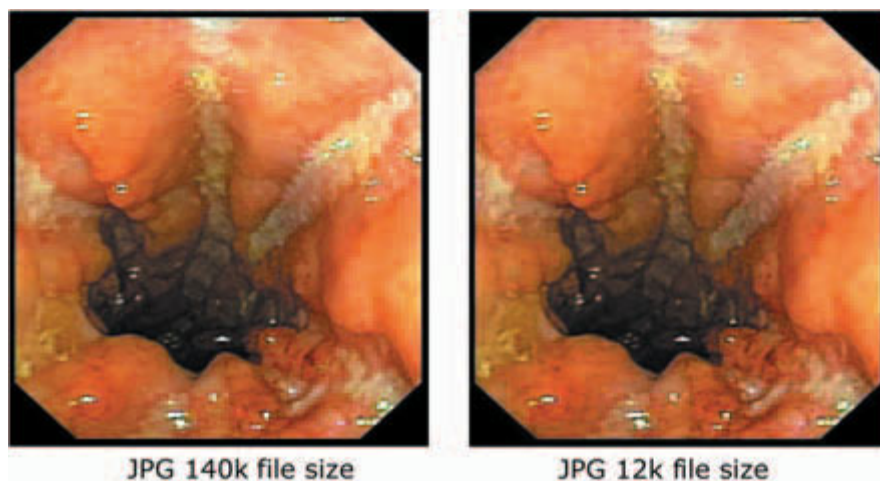


Fig. 17.2 Compressing a typical endoscopic image from 140 kb (already compressed from around 800 kb) to 12 kb is hardly noticeable.

File compression is a computational processing technique that effectively reduces the size of a file, removing redundancies in large binary datasets. Full-motion video requires a frame display rate of 30/s. If each frame is 0.5 Mb, then 1 s of digital video contains 15 Mb of data. Disk storage would be rapidly exceeded and image transmission even on high-speed networks would be slow. Compression is measured as a ratio of the size of the original data divided by the compressed data.

There are two general categories of compression techniques: lossless and lossy. *Lossless compression* techniques preserve all the information in the compression/decompression process. This may be vital for compressing documents or computer program files but these techniques can only achieve moderate compression ratios, which may not be sufficient for medical images, especially radiologic gray-scale images. However, when images are used as a means of primary diagnosis, they require lossless compression, storage, and transmission. Most picture archiving and communication systems (PACS) use lossless compression but require high-end hardware and dedicated high-speed networks.

For the purpose of practical archival storage and transmission of medical images, compression ratios of 20 : 1 or higher are required. In order to achieve this amount of file-size reduction, *lossy compression* techniques need to be employed. Lossy compression implies that some information is lost in the compression/decompression process, but algorithms can be designed to minimize the effect of data loss on the diagnostic features of the images.

JPEG compression is one of the three file formats used for graphical images on the World Wide Web, the others being GIF (Graphical Interchange Format) and PNG (Portable Network Graphics). JPEG files have the advantage of remaining 24-bit true-color files during compression, while GIF files are limited to 8-bit color (256 colors). The PNG file format shows promise as a lossless compression method for the Web but has not yet

gained acceptance at this time. The issue of standard Web formats is an important one because an increasing number of relevant software solutions rely on browser technology for screen display.

There is one final note about JPEG and gray-scale images in general. While color images using JPEG can typically achieve compression ratios of 10 : 1 to 20 : 1 without visible loss and can compress 30 : 1 to 50 : 1 with small to moderate defects, gray-scale images do not compress by such large factors. Because the human eye is much more sensitive to brightness variations than to hue variations, JPEG can compress hue (color) data more heavily than brightness (gray-scale) data. A gray-scale JPEG file is generally only about 10–25% smaller than a full-color JPEG file of similar visual quality. However, the uncompressed gray-scale data is only 8 bits/pixel or one-third the size of the color data, so the calculated compression ratio is much lower. The threshold of visible loss is often around 5 : 1 compression for gray-scale images, substantially different from color images [1].

JPEG 2000 and beyond

The importance of image handling and compression for Internet applications creates a huge momentum for development. The JPEG working group has developed a new standard, which is only just becoming available (accepted as an ISO standard December 2000). This standard is called JPEG 2000, with the file extension .jp2. This standard offers a host of advantages over the existing JPEG standard, the most significant being lack of pixelation at high compression rates and significantly more effective compression.

Although the file size of individual endoscopic images is not a major issue at this point, we should keep in mind that when the display and transfer of large numbers of images and videos becomes a significant part of our daily work-flow, even minute delays for every picture will have an impact. Thus the continuing search for more

efficient file compression will be of major significance for medical imaging. PACS development currently suffers from the high cost of high-end workstations and networks to handle huge image datasets.

DICOM

Digital imaging and communication in medicine (DICOM) is a standard for imaging that contains very specific information about the images, as well as the images themselves. DICOM relies on explicit and detailed models of how the “things” (patients, images, reports, etc.) involved in imaging operations are described, how they are related, and what should be done with them. This model is used to create an Information Object Definition (IOD) for all the imaging modalities covered by DICOM.

An Information Object is a combination of Information Entities and each Entity consists of specific Modules. A Service Class defines the service that can take place on an Information Object, e.g. print, store, retrieve. In DICOM, a Service is combined with an Information Object to form a Service/Object Pair (SOP). For example, storing a computed tomography (CT) scan or printing an ultrasound is an SOP pair. A device that conforms to the DICOM Standard can perform this function. Thus, in a DICOM-conforming network the devices must be capable of executing one or more of the operations the SOP definition prescribes. Each imaging modality has an IOD. The result is that different imaging modalities, such as CT, magnetic resonance imaging, digital angiography, ultrasound, endoscopy, pathology, imaging workstations, picture archiving systems, and printing devices, can be networked and execute a high level of cooperation. In addition, these imaging networks can be connected to other networks found in a hospital or facility.

It is not sufficient to define a standard. It is also necessary to develop a mechanism to enable vendors and purchasers to understand whether the system conforms to the standard. DICOM defines a conformance statement that must be associated with specific implementation of the DICOM Standard. It specifies the Service Classes, Information Objects, Communication Protocols, and Media Storage Application Protocols supported by the implementation. The conformance statement is provided by the vendor and identifies the system capabilities.

DICOM in gastrointestinal endoscopy

The American Society for Gastrointestinal Endoscopy (ASGE) in collaboration with other medical and surgical societies such as the European Society for Gastrointestinal Endoscopy (ESGE), American College of Radiology, College of American Pathologists, Amer-

ican Academy of Ophthalmology, and American Dental Association have defined a new supplement to the DICOM Standard [2]. This Supplement to the DICOM Standard specifies a DICOM Image IOD for Visible Light Images. This standard enables specialists working with color images to exchange images between different imaging systems using direct network connections, telecommunications, and portable media such as CD-ROM/DVD and magneto-optical disk. The DICOM Standard for endoscopy is part of a larger standard for color images in medicine that has been provisionally approved by the DICOM committee. The current version will go through a process of public comment and testing. This ensures that any interested party can review the document and suggest changes to a committee responsible for creating the final version. This process is time-consuming but ensures that the standard is comprehensive and meets the needs of a broad group of users.

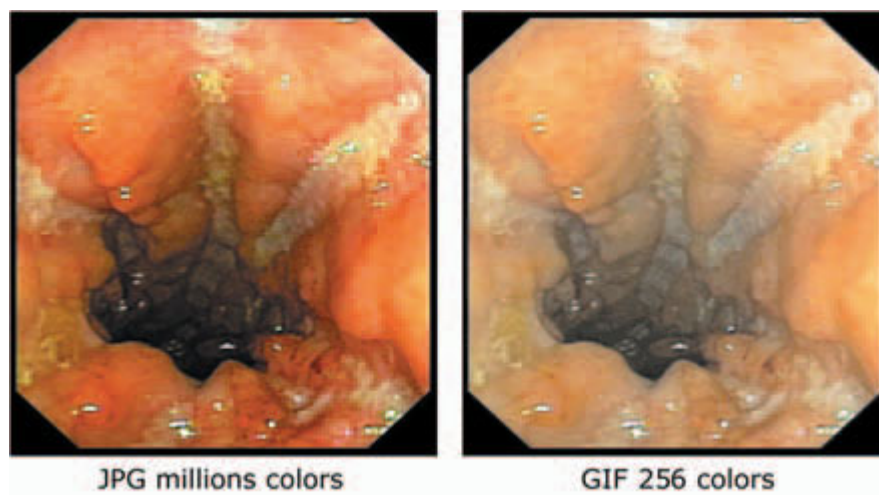
Through the ASGE and ESGE, the endoscopy community has also suggested that the DICOM Standard be expanded to incorporate other information associated with the imaging study. These expanded standards would include image labels and overlays, sound, and waveform. The goal of a true multimedia report will only be achieved when these standards have been thoroughly tested and implemented as part of the daily clinical activities of gastrointestinal endoscopists throughout the world. The cooperation of endoscopists, professional societies, and industry is absolutely necessary for improved endoscopic information systems and will result in improved patient care.

Clinically acceptable compression

Because of the specific nature of endoscopic images, the amount of compression that can be employed without compromising important information contained within the image must be determined by the endoscopist. Moreover, the acceptable compression rate would likely differ substantially depending on whether we are looking at a polyp or a case of mild gastritis. These issues have major impact on the utility of digital images in endoscopy but can only be resolved by endoscopists themselves. We have to be involved in deciding what imaging is required to be useful for clinical purposes.

Although the topic has been reviewed by Kim [1], very few studies have been published on the topic. Vakil and Bourgeois [3] conducted a trial to determine the amount of color information required for a diagnosis using an endoscopy image. The least amount of color information in an endoscope image that carries sufficient diagnostic information was unknown. Ten upper gastrointestinal lesions were presented in an 8-bit, 16-bit, and 24-bit format blindly side by side on a Macintosh II system with a 19-inch monitor that could display 24-bit color.

Fig. 17.3 Intelligent reduction of the number of colors in an endoscopic image does not ruin the image, because the color range is limited to the gray–yellow–red hues.



Eleven observers (six nurses and five endoscopists) were asked to rank each format for each lesion. There were a total of 330 observations and for each format and total the results were similar: the observers identified correctly in 22% of the images; identified incorrectly in 37% of the images; and could not see a difference in 41% of the images. In addition, all the lesions were correctly identified. From this study of endoscopic images, color resolution does not appear to affect an endoscopist's ability to make a diagnosis (Fig. 17.3).

Kim (personal communication) presented a set of six images to 10 expert gastroenterologists using software that allowed them to determine their personal cut-off level of acceptable compression for each of the images. Different types of lesions were studied and the acceptable compression ratio was predictably variable as well, but in general a compression ratio of between 1 : 40 and 1 : 80 was deemed acceptable (Table 17.1). This type of study provides important information about the order of magnitude that can be expected from compression. However, the clinical context is of interest as well: the arterial bleed was probably easily identified as such even at a high rate of compression, but for the endoscopist who might need to intervene at a rebleed would likely favor additional details about the exact location, structures next to the vessel, and so on. Thus, additional studies like this with a broader range of cases is needed to ascertain an ideal compression scheme.

Table 17.1 Clinical acceptability of compressed gastrointestinal images. (Adapted from Kim [1].)

Lesion	Original file size (kb)	Mean compressed file size (kb)
Arteriovenous malformation	903.3	14.1
Barrett's esophagus	903.6	10.6
Chromoscopy polyp	904.7	18.4
Arterial bleed	182.2	2.4
Pseudomembranous colitis	185.7	6.6
Duodenal ulcers	183.6	5.6

The area of image compression is a moving target. Compression schemes are evolving quickly and, at the same time, the requirements for minute files are becoming less crucial. Storage space is rapidly becoming cheaper and networks faster. The 28.8-kb modem is no longer a reasonable yardstick for download time. The virtue of compressing images remains but there is no reason to compromise image quality in order to achieve the tiny file sizes that yesterday's technology recommended. The endoscope manufacturers have been struggling hard to offer high-resolution endoscopes, structure enhancement, and magnification; it would be counterproductive to lose these advantages for a few kilobytes of file-size reduction.

As for clinical utility, we need to establish a general standard for compression and formats that will work across diagnoses. This will have to aim at a quality sufficient for our most difficult diagnoses: subtle diffuse lesions like mild gastritis or tiny erosions, or delineation of the vascular pattern of a colitis.

Pictures or live video?

Increasingly, digital video is becoming an option for endoscopic documentation. Many capture boards have the capability of storing video as well as still images, and in certain situations video may definitely offer an advantage. This is particularly true for teaching purposes,

although even clinical documentation can be enhanced by live footage in certain situations. Obvious examples are documentation of distensibility or propagating waves of the stomach, spasticity of the colon, or imaging in difficult areas (the cardia).

However, video clips come at a cost in terms of processing, storing, and even presentation. While still images can be vividly reproduced in the printed endoscopy report together with the recommendations, a video clip is forever tied to the computer or network. In the future, when electronic medical records become mainstream and wide area networks (WANs) a tool for medical purposes, these concerns may vanish, but for now a paper-based report is a prerequisite in most endoscopy laboratories. Then there is the issue of storage and transfer. Studio-quality video displays at 25 or 30 frames per second (fps). Although reasonable-quality video can be obtained with 10–15 fps, this still produces enormous files quickly and we need to determine if this cost of digital video can be justified by added value.

Again, fortunately, things are moving rapidly in the right direction. Compression algorithms allow significant compression of digital video file size with acceptable results. The most well known are probably the Quicktime and MPEG-1 formats, but this is a field of continuous development, MPEG-4 being the most promising option at the moment. Most of the compression algorithms use similar techniques, as discussed above for still images. For example, if a segment of the movie image is unchanged for a period of time (the sky, or the black portion to the left of the endoscopic image), the only information that needs to be stored is the boundaries of the area, the color value, and the start and stop timecodes. With this type of compression, a video of a newsreader for example can be reduced to a still picture with a small moving segment representing the mouth. This technique, in addition to a multitude of others, allow for increasingly efficient compression of video clips, offering efficient storage, as well as network-based distribution, with none or minimal depreciation of the diagnostic value.

What images are needed?

In parallel with the technologic developments in digital imaging and video, there are important decisions that need to be made by the endoscopic community. A crucial one is: What pictures are needed? If we want to report a polyp in the sigmoid colon, a single picture might be sufficient if it is a good one, showing the size and shape, stalk, amount of luminal obstruction, surface texture, and so on. But what about a distal rectal lesion? An extra picture of its relation to the anal verge might be important, not least if a surgeon was to remove it. A retroflexed view as well as a standard forward view would be rea-

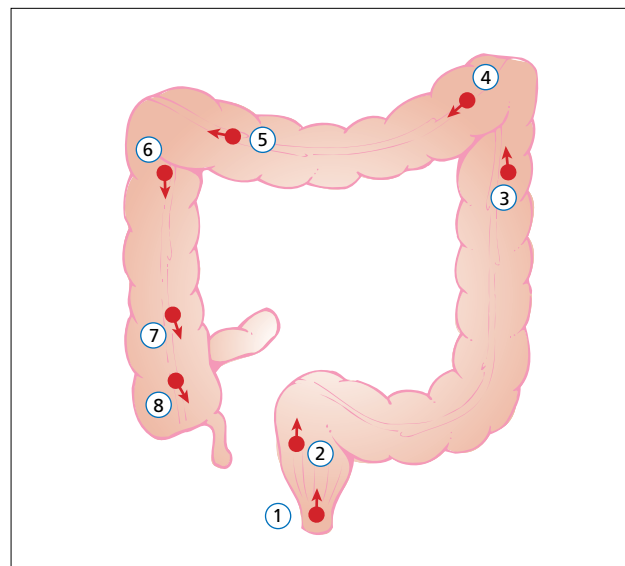


Fig. 17.4 Standard positions for default endoscopic imaging of the colon.

sonable in this situation. For diffuse pathology, typically more than one image might be preferable, and maybe high resolution becomes an issue for minimal changes.

More complex still is the issue of nonpathology. Which images are needed to *exclude* a lesion in order to document a normal colonoscopy? We obviously cannot picture every single fold, let alone behind them, but there may still be reasons to document normality, e.g. to show what kind of view, cleansing, and distension was available to the endoscopist. The virtue of this becomes even more obvious in the context of referrals and second opinions. When we are asked to evaluate a polyp for possible removal and pictures are sent from a referral source, too often we discard that study because the images that we receive are not the ones we expect. This expectation needs to be incorporated into a standard that will allow more efficient collaboration on patients based on images alone. Too many repeat endoscopies are performed because images are inadequate, although the study may have been excellent.

The ESGE [4] has made an attempt to establish guidelines for standard endophotographs at specific sites in the colon (Fig. 17.4) and has proposed a set of images at various areas of the colon to aid in the visual identification of each area (Fig. 17.5).

Image enhancement

The impact of video endoscopes has been substantial yet what they provide are still just natural-light images showing the gastrointestinal mucosa in a lifelike manner. Novel technologies are now emerging that offer modification of the original images, which may increase the diagnostic

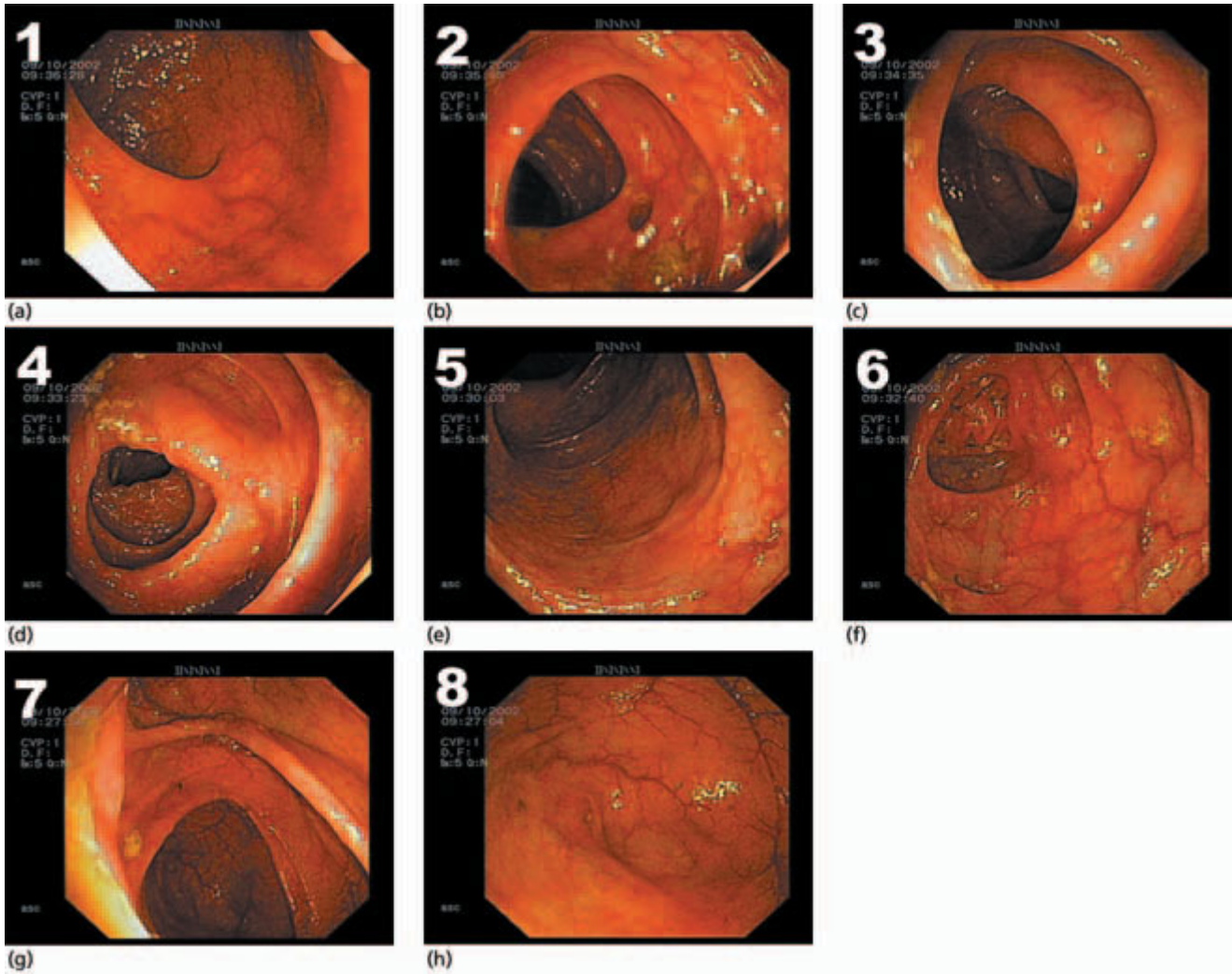


Fig. 17.5 Sample image set showing a colonoscopy of a normal colon.

output of the endoscopic procedure. These technologies do not relate to digital imaging itself, but they all rely on such imaging as the core technology for endoscopy.

Color manipulation methods deal primarily with the color characteristics of the pixels representing the image. This is a simple way of enhancing the contrast features of the image, but sometimes at the cost of resolution. These methods are so far only available for manipulation of still images and a live version of the technology would be needed to make this clinically applicable.

Narrow-band imaging and spectroscopy are just two examples of a host of other technologies that will enhance the diagnostic yield. In these technologies, parallel “imaging” is used to extract information about the imaged tissue, and the regular digital images are primarily used to guide the process of advanced tissue characterization.

Standardized terminology (see Chapter 16)

Endoscopic findings are conveyed with words, although the findings themselves are images. Thus the coupling between what we see and how it is described becomes crucial, and standardization of our endoscopic *language* is an integral part of this concept.

Endoscopic teaching includes descriptions of what is found, but the definitions of terms used have been weak or nonexistent. If the conclusion of the endoscopy report is the only item of value, then the specifics of the findings are of less importance. However, if the findings themselves are important, then the descriptive language becomes interesting too. For research purposes, particularly collaborative research, the utility of this is obvious, but even for general clinical purposes the objective description of lesions may be of interest, e.g. in a second-opinion referral of a case where the referral center needs to decide whether a repeat endoscopy is needed. Likewise, follow-up endoscopy in a patient with

a known lesion will profit from an unequivocal initial description of what was seen, at least when no image documentation is available.

OMED standardized terminology

OMED initiated the drive to standardize endoscopic language through the pioneering work of Professor Zdenek Maratka, who developed the first "Terminology, definitions and diagnostic criteria in digestive endoscopy" [1], later revised and translated into numerous languages. This terminology is a codified list of terms with explicit definitions that allows endoscopic findings to be matched to a hierarchical nomenclature and assigned a code, thus enabling international collaboration. This terminology has since been supplemented with images to exemplify the various terms. Despite deficiencies, this remains the de facto standard for describing the various findings of digestive endoscopy.

Minimal standard terminology

The OMED terminology, while defining the framework for the terminology efforts within digestive endoscopy, proved too complex for practical use in everyday endoscopy. A simplification was needed and the ESGE teamed up with its US counterpart the ASGE to develop minimal standard terminology (MST) for endoscopy [5]. This terminology is completely based on the OMED terminology but the lists of terms are limited, aiming to cover 95% of the terms needed for typical endoscopic practice and omitting the definitions, which are available when needed in the OMED terminology book. MST is meant to be a standardizing prerequisite for software companies developing reporting programs for digestive endoscopy, assuring that a joint language is used in the various available software solutions. The MST work has been endorsed and supported by all the major vendors of such systems (Fig. 17.6).

CORI		CLINICAL OUTCOMES RESEARCH INSTITUTE SARFIS ENDOSCOPIC REPORT CONTACT 1-800-878-CORI		COLONOSCOPY REPORT	
Patient Name:		Smith, Frederick	Exam Date:		10/16/2002
MRN:		1234567890	DOB:		10/10/1910
Page:		1 of 1			
Procedure:	Procedures: Colonoscopy 45378 with biopsy 45380				
Personnel:	The attending physician was present during the entire procedure. Endoscopist: Benjamin J. Dover, MD. Fellow: Elizabeth Winston. John Benson, MD. Nurse: Wendy Gunn.				
Exam Location:	Exam performed in Endoscopy Suite, Inpatient Ward Hosp. Rm. # 53 Visit #: 1.				
Patient Consent:	Consent obtained, Consent to be contacted was given.				
Indications:	Symptoms: Hematochezia, Weight Loss, Abdominal pain / bloating.				
History:	Current Medications: Patient is taking a non-steroidal medication, Antacids: Maalox 10, ac, started OCT 1, 2002. End date Oct 24, 2002. Anticonstipation: Enemas 1 enema, ac, started Oct 16, 2002. End date Oct 16, 2002. Non-Steroidals: Advil 200 mg, ac, started Feb 1, 2001.				
Medical/Surgical History:	Hypertension.				
Allergies:	No known allergies.				
Patient Habits:	Patient does not smoke. Drinking Status: social 2 drinks per day.				
Pre-Exam Physical:	Performed Oct 16, 2002. Height 70 inches. Weight 95 kg. P 85. BP 140/90. Entire physical exam was normal.				
Exam:	Extent of exam reached: Cecum, extent intubated: Cecum. The cecum was identified by appendiceal orifice and IC valve. Patient position: on left side. Colon retroflexion performed. Images taken.				
Monitoring:	Pulse and BP monitoring, Oximetry used. Supplemental O2 given.				
Colon Prep:	Used Oxytetyl for colon prep. Prep results: good.				
Sedation Meds:	Patient assessed and found to be appropriate for deep sedation. Sedation was managed by the Anesthesiologist. General anesthesia administered by Anesthesiology: Fentanyl 100 mcg, Midazolam 3 mg.				
Instrument(s):	CFQ160al variable stiffness. Serial #2010518.				
POCYP:	Sigmoid Colon, Maximum size: 15 mm, pedunculated polyp. Procedure: hot biopsy, removed, retrieved, Polyp sent to pathology.				
Assessment:	Abnormal examination, see findings above.				
Diagnoses:	211.3: Colon Polyps.				
Events:	Unplanned Interventions: No intervention was required.				
Unplanned Events:	There were no complications.				
Plans:	Medication Plans: Continue current medications.				
Patient Education:	Patient given standard instructions for: Polyps.				
Disposition:	After procedure patient sent to short stay unit. After recovery patient sent home.				
Path Results:	Pathology: Polyp: Sigmoid Colon - negative.				
Endoscopist:	Benjamin J. Dover, MD		Fellow:	Elizabeth Winston	
CC:	John Benson, MD				
Smith, Frederick	MRN: 1234567890	COL	Visit #: 1	10/16/2002	

Fig. 17.6 Sample endoscopy report including indexed color images.

The initial version of MST was thoroughly tested within the GASTER project [6] and this experience led to a number of adjustments as to the selection and definition of terms. Version 2.0 of the MST has been released and is presently undergoing a similar clinical benchmarking. In addition, term definitions are now being included and an image library is being developed through a joint European effort, to help illustrate the various terms of the MST by high-quality sample pictures.

Issues and shortcomings

The principles of MST have been endorsed almost universally and the utility of a joint standardized language of endoscopy is readily acknowledged. However, the knowledge, dissemination, and implementation of MST is at present insufficient, even disappointing. Why is this?

One issue is the MST term lists, which are still not perfect. They are designed to be “minimal lists,” meaning that in a substantial number of cases the term that is required is not included. This is partly a software issue, because the lists were never meant to be all-inclusive, and individual additions will be needed in most centers. Still, incomplete choice lists are difficult to accept.

More fundamental, though, is the whole concept of structuring the language of the endoscopist. We are used to formulating our findings and recommendations in natural language, and any superimposed structure will take extra time, be felt as cumbersome and limiting, and clearly as something that yields less informative reports.

The solution to this has not yet been found, and MST is at present primarily an excellent initiative. The utility of standardized terms is indisputable; the challenge is to embed this into software that allows them to be sufficiently transparent. Also, it is unlikely and probably unnecessary that the endoscopy report be produced exclusively by “point-and-click.” Segments of the endoscopy report will probably remain free text blocks with natural language.

Summary

Gastrointestinal endoscopy is a visual clinical discipline. The traditional mode of reporting these images has been through a written report. The endoscopy report is the core means of communication for the endoscopist and it should be meaningful to endoscopists, general gastroenterologists, and referring practitioners alike. The report should contain certain fixed elements in order to convey fully the results of the examination, the diagnosis, and recommendations. Modern communication methods now permit the transfer of pictures of endoscopy along with the written report. Elements of interest are detailed in this chapter.

Acknowledgments

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Chapter 18

Preparation for Colonoscopy

Jack A. DiPalma

Impact of proper colon preparation

Adequate cleansing is required for safe and reliable colonoscopy. Poorly visualized mucosa leads to missed diagnoses and increases colonoscopic risk [1–3]. The extent of the examination may be compromised and poor preparation may lead to the inability to reach the cecum. Even a minimal amount of residual stool can obscure small lesions and angiodysplasia [3]. Washing and aspirating the dirty colon during colonoscopy is time-consuming and frustrating, and a clean colon reduces procedure time and sedation requirements [3,4]. Colonoscopy perforation occurs with an incidence of 0.1–0.8% for diagnostic and 0.5–3% for therapeutic procedures [5]. The amount of peritoneal soilage by intestinal contents is an important determinant of subsequent septic complications and death after surgical repair [6]. Adequate colon preparation decreases risk if the complication of perforation occurs [1,3]. A recent work underscores the impact of bowel preparation on efficiency and cost of colonoscopy. Rex and colleagues [7] studied 400 colonoscopies, noting that suctioning fluid and washing occupied a measurable percentage of total examining time and that imperfect bowel preparation led to aborted examinations and earlier repeat surveillance. These problems resulted in an increase in average costs of 12% at the university hospital and 22% at the public hospital studied. Residual fecal matter also poses a risk from ignition of combustible gases during electrocautery [1]. Hydrogen and methane are the two major combustible gases found in the colon and explosions have been reported during colonoscopy and other related procedures [1,3,8–11]. Colon cleansing reduces the concentration of explosive gases [3,5,8,12,13].

Goals of preparation

A colon preparation regimen should provide safe and rapid cleansing acceptable to patients with minimal discomfort [1]. The ideal method would:

- 1 reliably empty the colon of fecal material;
- 2 have no effect on gross or microscopic appearance of the colon;
- 3 require a short period for ingestion and evacuation;

4 cause no discomfort;

5 produce no significant shifts of fluids or electrolytes [2].

The regimen should be simple and appropriate for use in inpatients and outpatients [14]. The presently available methods do not meet most of these criteria and few have been carefully studied [1]. Problems with patient compliance, safety, and adequacy of cleansing prompt continued investigation into alternative forms of cleansing [15].

Colon cleansing methods

Traditional cleansing methods evolved from barium enema preparations and local experience and were modified for colonoscopy and colon surgery. There are a wide variety of methods using diet restrictions with various purgatives and laxatives [16]. Three popular options for colon preparation are diet and cathartic regimens, gut lavage, and phosphate preparations.

Diet and cathartics

Early cleansing methods used 48–72 h of clear liquids with laxatives and enemas. Clear liquids (Table 18.1) include clear broth or bouillon, coffee without creamer, tea, fruit juices without pulp, gelatin, carbonated and noncarbonated beverages, popsicles, and water [3]. Milk and milk products should be avoided as should red

Table 18.1 Clear liquids.

Clear broth or bouillon
Coffee without creamer
Tea
Fruit juices without pulp
Gelatin
Carbonated and noncarbonated beverages
Popsicles
Water
Avoid
Milk
Milk products
Red juices, jello and gelatins

Table 18.2 Diet and cathartic regimens. (Modified from Toledo and DiPalma [1].)

Diet	Clear liquids for 72 h, or 1–3 days of a diet designed to result in a minimal colonic fecal residue
Cathartic	Magnesium citrate 240 mL chilled, X-prep liquid 240 mg (extract of senna fruit, Purdue Frederick Co., Norwalk, CT)
Additional cathartic	Bisacodyl 20 mg orally and/or two bisacodyl suppositories
Enemas	Tap-water enemas until clear the evening before or morning of the procedure

juices, jelly, and gelatins, which could mimic blood during colonoscopy. Beans, watermelon, and foods with similar appearance could be confused with polyps.

The effect of diet was demonstrated in a prospective study [12]. Three study groups had cleansing enemas and similar regimens of laxatives and cathartics. Subjects were fed either a clear liquid diet or a diet designed to leave a minimal colonic fecal residue for 1 or 3 days. The minimum-residue diet suggested foods for breakfast, including scrambled egg, white toast with jelly, apple, grape or cranberry juice, and water, tea or coffee. Sugar could be added but no milk or cream. For lunch, the diet allowed bouillon soup with crackers, and chicken or turkey white meat sandwich. No butter, mayonnaise, lettuce, or additive were allowed. Noncitrus juice, plain jello with no cream or fruit, and water, tea or coffee were advised. For dinner, suggestions included bouillon soup, noncitrus juice, jello, and water, coffee or tea. Fluids, water, or noncitrus juice were encouraged between meals. This study showed superior cleansing efficacy in patients randomized to receive 1 or 3 days of the minimum-residue diet compared with those who were randomized to receive 72 h of clear liquids [12]. No difference in cleansing efficacy was observed between the 1- and 3-day minimum-residue diet, although patients who received the 1-day minimum-residue diet reported less distress from dietary restrictions ($P < 0.01$).

Various laxatives and cathartics are acceptable for use in cleansing regimens [16,17]. Other studies that examined diet modifications and laxatives showed cleansing efficacy and favorable patient acceptance [18–20]. Dahshan and colleagues [18] reported that bisacodyl without dietary restriction provided unsatisfactory colon cleansing and that magnesium citrate combined with senna X-prep was acceptable with good cleansing. Chen and colleagues [19] showed magnesium citrate and bisacodyl to be effective and superior to castor oil for colonoscopy preparation.

A low-residue meal kit is available (Nutra Prep, EZ Em, Inc., Westbury, NY). A companion laxative kit completes the preparation using magnesium citrate and bisacodyl (LoSol, EZ Em, Inc.) [20]. Table 18.2 lists the components of diet and cathartic regimens.

Gut lavage

Orthograde, peroral gut lavage using saline or balanced

electrolyte solutions was found to provide rapid and effective colon cleansing [21–26] but the 7–12 L required volume necessitated nasogastric administration and was not well tolerated [22]. These saline and electrolyte solutions led to weight gain, sodium retention, and fluid shifts [14], prompting studies that incorporated mannitol or polyethylene glycol (PEG) for osmotic balance [27] so that there is no net loss or change in the body's electrolyte composition. In search of a more acceptable solution, Davis and colleagues [28] formulated an osmotically balanced electrolyte lavage solution, namely polyethylene glycol electrolyte lavage solution (PEG-ELS). In their initial description, these authors presented data showing their solution to have minimal water and electrolyte absorption or secretion [28]. These results, confirmed by others, showed that the osmotic balance in PEG-ELS had significant advantage to saline or electrolyte solutions when compared for water and electrolyte shifts [14]. Intestinal perfusion of PEG-ELS resulted in mean water absorption of 64 mL/h, whereas infusion of a basic electrolyte solution without osmotic balance resulted in water absorption of 799 mL/h [28]. Routine clinical cleansing using 3–4 L over 3–4 h would result in absorption of 190–250 mL fluid with PEG-ELS and 3400–3200 mL of electrolyte solution without osmotic balance [14]. Furthermore, since saline lavage frequently requires 7–12 L over 6–12 h, these patients have the potential for over 8 L of water absorption. In their report, Davis and colleagues [28] claimed that “any solution worth its salt should have a name” and they chose to call theirs Golytely, which subsequently became the brand name of a commercial product (GoLYTELY, Braintree Laboratories, Inc., Braintree, MA). PEG-ELS is also available as CoLyte (Swartz Pharma, Milwaukee, WI). Table 18.3 lists the commercially available gut lavage products.

PEG-ELS

Clinical trials established the safety of PEG-ELS for colon cleansing preparation for colonoscopy, barium enema X-ray examination, intravenous pyelograms, and colon surgery [4,12,29–34]. Compared with diet and cathartic methods with enema administration, PEG-ELS had better patient acceptance [4,12,29–31]. When compared with clear liquid and minimum-residue diet methods, PEG-ELS [12] was superior, with cleansing efficacy rated

Table 18.3 Cost of colon cleansing. (Modified from Toledo and DiPalma [1].)

	Price range* (\$)	Average price (\$)
<i>Diet and cathartic methods</i>		
Magnesium citrate 300 mL	1.16–4.99	1.31
Bisacodyl 5 mg		
Generic (four tablets)	1.44–1.96	1.64
Dulcolax (four tablets)	2.89–4.99	3.95
Dulcolax suppositories (two)	3.99–6.49	4.96
Phosphosoda enemas (Fleet) (two)	0.89–1.44	1.10
Total diet and cathartic	8.93–17.91	11.32
LiquiPrep (EZ EM, Inc., Westbury, NY)		6.25
NutraPrep diet (EZ EM, Inc.)		25.00
LoSo Prep System (EZ EM, Inc.)		4.99
<i>Polyethylene glycol electrolyte lavage solution (PEG-ELS)</i>		
GoLYTELY (Braintree Laboratories, Inc.)	23.72–32.69	27.07
Flavored GoLYTELY (pineapple)	24.79–27.09	25.94
CoLyte (Schwarz Pharma, Inc., Milwaukee, WI)	21.54–22.89	23.70
Flavored CoLyte (pineapple)	16.70–21.69	20.43
CoLyte with flavor packs (citrus, berry, lemon-lime, cherry, pineapple)	21.69–28.69	24.42
PEG-ELS (generic)	12.54–24.69	18.03
<i>Sulfate-free electrolyte lavage solution (SF-ELS)</i>		
NuLYTELY (Braintree Laboratories, Inc.)	25.72–33.69	28.02
Flavored NuLYTELY (cherry, lemon-lime, orange)	25.72–33.69	28.02
<i>Phosphates</i>		
Oral phosphosoda (Fleet's Phospho-soda, C.B. Fleet, Lynchburg, VA)	6.78–7.18	6.98
Phosphate tablets (Visicol, Incline Pharmaceuticals Co., Bluebell, PA)	44.94–55.99	50.98

* Average retail pharmacy price, Mobile, AL.

good or excellent in 92% PEG-ELS, 69% clear liquid diet, 80% 3-day minimum-residue diet and 80% 1-day minimum-residue diet groups ($P < 0.001$). Interestingly, it was noted that the 72-h clear liquid diet, enemas and cathartic group had the least optimal cleansing [12]. No clinically significant hematologic, biochemical, electrolyte, or metabolic abnormalities have been found with PEG-ELS colon cleansing [1–3,14,15,35].

Sulfate-free ELS

A sulfate-free electrolyte lavage solution (SF-ELS, NuLYTELY, Braintree Laboratories, Inc.) was developed in an attempt to improve patient compliance by decreasing the salty taste and “rotten egg” smell noted with PEG-ELS [36]. Whereas the mechanism of action of PEG-ELS cleansing was affected by the osmotic properties of PEG and by an electrochemical gradient for ion transport created by sodium sulfate, SF-ELS action is primarily based on the osmotic effects of PEG as sulfate was eliminated from the formulation. The PEG polymer isolates water from the solution [27] and when PEG molecular weight is greater than 1500 (as seen with PEG 3350 in PEG-ELS and SF-ELS), it is poorly absorbed in the gastrointestinal tract. PEG is inert and not fermented by colonic bacteria to combustible gases. Brady and col-

leagues [37] showed that the mean percent urinary PEG recovery of orally administered PEG-ELS was minimal and similar for normal (0.06%) and inflammatory bowel disease (0.09%) study subjects.

Clinical trials for colonoscopy, barium enema X-ray, and elective colonic surgery showed SF-ELS to be safe and effective [38–42]. In those who expressed a taste preference, DiPalma and Marshall [39] showed SF-ELS to be preferred to PEG-ELS (76.6% vs. 23.4%, respectively; $P < 0.001$). In a conflicting report, Froehlich and colleagues compared PEG-ELS and SF-ELS and found no taste preference [40,42]. In a clever attempt to reconcile the conflicting data concerning taste preferences, Raymond and colleagues [43] assigned patients to drink 1 L each of PEG-ELS or SF-ELS in a randomized fashion. Subjects were then asked to choose which solution they wished for the last 2 L of preparation. More study subjects preferred SF-ELS and more were willing to repeat SF-ELS rather than the traditional PEG-ELS if colon cleansing was needed in the future.

Flavoring and palatability

In further attempts to improve taste and compliance, gut lavage solutions have been flavored. PEG-ELS commercial solutions were flavored with pineapple and

one brand with flavor packs of pineapple, citrus berry, lemon-lime, or cherry. SF-ELS was flavored with cherry, lemon-lime, or orange. Since flavorings are carbohydrate-based, the SF-ELS solutions were studied and showed no production of combustible gases in either flavored or unflavored preparations [44]. A small study by Matter and colleagues [45] showed a preference by patients for flavored vs. unflavored solutions. These authors used lemon flavoring (Crystal Light Sugar Free Drink Mix, White Plains, NY).

It is advised to chill gut lavage solutions to improve palatability. Bottled water is used to reconstitute powdered solutions. Bottled water has less chlorine and minerals than tap water, and less additional tastes.

Adjuncts

In the original studies of PEG-ELS, metoclopramide was used as a premedication in an attempt to reduce distress associated with lavage [12,29,30,46]. Brady and colleagues [47] examined its efficacy in placebo comparison studies of 10 or 20 mg metoclopramide pretreatment. There were no differences between study medication groups or placebo for adequacy of feces removal as assessed by colonoscopy. Symptoms of nausea, bloating, fullness, or cramps associated with lavage were not different. In this study, plasma metoclopramide levels after metoclopramide and lavage were compared with metoclopramide controls, showing that absorption of the pretreatment medication was not influenced by lavage.

Cisapride has been studied as a pretreatment for lavage [48–51]. These studies have shown no benefit for effectiveness or patient tolerance of the electrolyte solution.

Although bisacodyl is required for barium enema X-ray to enhance mucosal coating [38,52], it and senna showed no significant differences compared with placebo for quality of preparation or residual colonic fluid aspirated during colonoscopy [53,54]. Both bisacodyl and magnesium citrate may reduce the volume of lavage required for adequate cleansing [55,56].

Simethicone may decrease residual bubbles or foam seen during colonoscopy [57], but cleansing enemas seem not to improve preparation [58]. Tap-water enemas after 4-L lavage did not improve visibility or decrease colon fluid and may cause anorectal trauma [58]. Therefore, enema administration is not necessary when using a balanced electrolyte gut lavage.

Reduced-volume lavage

Sharma and colleagues [56] compared 4-L PEG-ELS lavage with 2-L lavage with magnesium citrate pretreatment. A second trial by this group evaluated PEG-ELS

with magnesium citrate pretreatment [59]. Both studies showed similar efficacy for full lavage and for reduced-volume lavage and pretreatment. Adams and colleagues [55] found similar success with bisacodyl pretreatment before PEG-ELS.

Standard 4-L SF-ELS cleansing lavage has been compared with a reduced-volume preparation using 2 L SF-ELS and bisacodyl 20 mg (Half Lytely, Braintree Laboratories, Inc.). All study subjects were allowed normal breakfast and lunch, and clear liquids for dinner. Subjects taking the reduced-volume preparation received bisacodyl 20 mg as four 5-mg tablets taken orally at 12 noon; 6 h later, subjects were given 2 L SF-ELS. Patients randomized to receive the 4-L preparation also drank the solution at 6 p.m. Both groups were instructed to drink the solution at a rate of 1.5 L/h or 280 g (10 ounces) every 10 min. Two hundred patients were randomized at two centers (University of South Alabama, Mobile, AL and Mayo Clinic, Rochester, MN). The results (J.A. DiPalma, unpublished data) showed equivalent good to excellent cleansing in 92.5% of the group taking 4 L SF-ELS and 87.1% of the group taking 2 L SF-ELS plus bisacodyl. Subjects receiving the reduced-volume preparation reported significantly less fullness, nausea, vomiting, and overall discomfort. The reduced-volume preparation requires ingestion of seven 280-g (10-ounce) glasses over 1 h.

Gut lavage in the elderly

To assess tolerance of colonoscopy preparation in older patients, symptoms of nausea, cramps, abdominal fullness, vomiting, and overall discomfort were assessed by self-administered questionnaires in over 550 study subjects who received diet, cathartic and enema preparations, or gut lavage [60]. In general, patients over age 60 years tolerated preparations better than those under 60 regardless of the type of preparation. Most rated discomfort as “minimal”. The PEG-ELS method was preferred by 81% of the older group. Age did not influence adequacy of cleansing with either method.

Lashner and colleagues [61] randomized 124 consecutive patients over age 75 years to enema lavage or PEG-ELS. Patients 75 or older seemed to tolerate enemas better than PEG-ELS without a difference in cleansing adequacy.

Pediatric use of gut lavage

Gut lavage has been used in children and infants [18,62–65]. Compliance is limited by the volume required for cleansing but lavage is preferred because of its superior cleansing and limited adverse effects [18,63]. Dahshan and colleagues [18] advise that PEG-ELS be taken 20 mL/kg per h up to 1 L/h for 4 h.

Table 18.4 Reported and potential adverse experiences related to colon preparation.

<i>Gut lavage cleansing*</i>
Disagreeable taste
Hypothermia
Volume-related symptoms: fullness, nausea, bloating
Aspiration
Reactivation of bleeding
Esophageal tear
Perforation
Lavage-induced pill malabsorption
Allergic reaction: angioedema, urticaria or anaphylaxis
<i>Phosphate cleansing</i>
Electrolyte disturbances
Hyperphosphatemia
Hypocalcemia
Vomiting
Dehydration
Colonic aphthous ulcerations
Seizures

* Modified from DiPalma and Brady [12].

Safety of gut lavage

Several adverse experiences have been reported from gut lavage. Table 18.4 lists reported and potential adverse events [7]. Lavage patients may find taste disagreeable. If the administered solution is chilled excessively, hypothermia may result. Bloating, nausea, and vomiting can result from the volume of lavage and esophageal tears have been reported. Pill malabsorption with slow-release drug delivery preparations could occur, but most tested capsules recovered in the colon show them to be a “ghost” of the wax tablet matrix without active medication. Negligible hematologic and biochemical changes have been seen in cleansing investigations but anecdotes of pulmonary edema and anasarca exist. Metabolic and acid–base abnormalities are unlikely and several studies have evaluated pH and bicarbonate changes from PEG-ELS in a large number of patients [7]. Overall, PEG-ELS and SF-ELS are preferred over phosphates and cathartics for safety in renal, cardiac, and hepatic insufficiency where fluid balance is tenuous [1].

PEG appears nontoxic from animal and human studies [1]. Caution has been raised about PEG toxicity [66–69] but studies show negligible absorption even in patients with disrupted mucosa due to inflammatory bowel disease [37]. The issue of carcinogenesis and mutagenesis with low molecular weight polyethylene glycols is not relevant because high molecular weight PEG is used in cleansing solutions [37,68,69].

Concern is also raised for those who need nasogastric administration of PEG. These patients are at risk of aspiration and the head of the bed should be elevated during and after administration. If a nasogastric tube is

placed, careful attention should be given to insure that the tube is properly positioned. The patient should be carefully observed. Gut lavage by nasogastric tube is contraindicated in the presence of obstructive symptoms.

There are also reports of systemic allergic reaction to PEG, although serious adverse effects have been rare [70–72].

Administration options

Vilien and Rytönen [73] used 1.5 or 3 L PEG-ELS in combination with diet and cathartics. Rosch and Classen [74] described a two-stage method, administering 3 L the evening before colonoscopy and 1 L the following morning. Early studies administered 4 L PEG-ELS the day of the procedure [12], while subsequent studies gave SF-ELS the evening before the procedure [39]. Church [75] found lavage administration the morning of the procedure to have advantage when compared with afternoon lavage the day before the procedure.

Instructions for use

Patients should chill the gut lavage solution to improve palatability. The chlorine taste of tap water can be avoided by using bottled water. Patients can be allowed normal breakfast and a low-residue lunch before the procedure with a clear liquid supper. A lavage rate of 1.5 L/h is advised and can be accomplished by drinking 280 g (10 ounces) every 10 min. A timer should be used. No ice, additives, or flavoring should be added to the lavage solution because osmolarity could be altered and salt and water absorption could occur if sugars are added.

Phosphates

Phosphate preparations offer another alternative. They are available as solutions or tablets and are particularly attractive because less volume needs to be ingested.

Oral sodium phosphate (Phosphosoda, Fleet Pharmaceuticals, Lynchburg, VA) is administered as 45 mL solution diluted with water to 90 mL given the evening before the procedure and repeated 12 h later or 4 h prior to colonoscopy. Oral sodium phosphate has been shown to be at least as effective as, or better than, PEG-ELS [50,76–85]. It is generally well tolerated. Vanner and colleagues [76] randomized 102 patients to oral sodium phosphate or PEG-ELS. Overall, patients found sodium phosphate much easier to complete and colonoscopists rated cleansing better from sodium phosphate than from PEG-ELS. Hyperphosphatemia was noted but it was transient and the preparation was considered safe.

Sodium phosphate monobasic, monohydrate and sodium phosphate dibasic, anhydrous (Visicol, InKine

Pharmaceutical Co., Inc., Blue Bell, PA) uses a tablet formulation. Clinical trials support efficacy and patient acceptance [86–88]. Forty tablets are taken with 10 glasses of water (about 2.5 L). Rex and colleagues [89] showed efficacy of 28 or 32 tablets, and a new smaller tablet with less microcrystalline cellulose (reducing colonic residue) was approved by the Food and Drug Administration (FDA) in March 2002.

Safety

Oral sodium phosphate contains 48 g of monobasic sodium phosphate and 18 g of dibasic sodium phosphate per 100 mL, making it very hypertonic. The phosphate salt must be diluted to prevent vomiting and administration should be followed by adequate oral fluids.

Although some studies suggested no significant (or clinically insignificant) metabolic changes from oral sodium phosphate [76,79], these data were limited and adverse events attributed to phosphate have been recognized [1,14]. The biochemical effects of oral sodium phosphate were studied in seven healthy asymptomatic adult volunteers [90]. Calcium, ionized calcium, phosphorus, sodium, potassium, creatinine, and parathyroid hormone were analyzed 2, 4, 6, 9, 12, 14, 16, 18, 21 and 24 h after the first of two diluted 45-mL oral sodium phosphate challenges. Urinary studies and clinical data were also obtained. Significant hypocalcemia and hyperphosphatemia were observed. The peak range in phosphorus was 3.6–12.4 mg/dL. The nadir calcium fall was 8.0–9.8 mg/dL, with a corresponding fall in ionized calcium. Concern was raised for patients with cardiopulmonary, hepatic, or renal disease. An FDA safety review concurs and raises awareness of increased risk in patients with congestive heart failure, ascites, renal insufficiency, dehydration, debility, gastrointestinal obstruction, gastric retention, bowel perforation, colitis, megacolon, ileus, inability to take oral fluid, or patients taking diuretics or medications that may affect electrolytes, who may experience serious adverse events [91]. The review suggests that baseline and posttreatment laboratory evaluations of serum sodium, potassium, chloride, bicarbonate, calcium, phosphate, blood urea nitrogen, and creatinine be obtained, especially in those at risk who take more than 45 mL oral sodium phosphate in a 24-h period. Chan and colleagues [92] noted in a utilization survey of Canadian gastroenterologists that colonoscopists appeared unaware of the potential for complications from phosphates, even in these special circumstances.

Another FDA report raises concern about phosphate tablets after seizures were seen associated with electrolyte disturbances after Visicol [93].

Phosphate preparation has been noted to induce rectosigmoid aphthous ulcerations and in one study,

aphthous ulcers occurred in 5.5% of study subjects receiving sodium phosphate preparation [94].

Other options

There are various other ways to prepare for colonoscopy, including intraoperative colonic irrigation [95] and pulsed irrigation [2].

Special considerations

Colostomy

Colon cleansing in patients with colostomies can be performed using any of the routine preparations [3].

Histology

PEG-ELS does not alter the appearance of colonic mucosa [96]. Bisacodyl causes histologic and macroscopic changes in the colonic mucosa [97]. Phosphate preparations may be associated with colonic aphthous ulceration [94].

Lower gastrointestinal hemorrhage

PEG-ELS has been safely used in patients requiring urgent colonoscopy [98–100]. Some require as little as 500 mL for cleansing. In a study of 35 patients, effective cleansing was seen with good tolerance and no complications [99].

Inflammatory bowel disease

In general, patients with quiescent inflammatory bowel disease can be prepared in the usual manner with any preparation [3]. Those with moderate or severe disease could be prepared with less purgatives or no preparation. The PEG-ELS study showed no significant PEG absorption in patients with inflammatory bowel disease even when mucosal inflammation is present [37].

Contraindications for colonoscopy preparation

Preparation should not be performed if there is a contraindication to colonoscopy [3]. Examples include hemodynamic instability, perforation, diverticulitis, or obstruction. If gastric or bowel obstruction is suspected, peroral preparations should not be given, and gut lavage should be avoided in gastroparesis. Incomplete obstruction or gastroparesis could be tested with a 1-L trial of gut lavage solution with careful observation [3]. Peroral preparation may not be effective with ileus.

Cleansing instructions

The importance of proper cleansing cannot be overemphasized to the patient. Patients scheduled for colonoscopy must have adequate instruction about the cleansing procedure. They should understand the need for their collaboration and compliance in order to optimize safety, prevent missed lesions, and to avoid having to reprepare and reschedule the procedure. The colonoscopist should take an active role in this process. The cleansing methods should be reviewed by the nurse or gastrointestinal nurse assistant and all instructions provided clearly in writing. Videotape- or computer-based educational programs may help to instruct about preparation. The reasons for doing the procedure and what to expect with preparation before, during, and after the procedure will be helpful, particularly when the effectiveness of pain medications and sedation are explained [3]. A phone call before the colonoscopy is often appreciated and enhances compliance.

Summary

Adequate cleansing is required for safe and reliable colonoscopy. Poorly visualized mucosa leads to missed diagnoses and increased colonoscopic risk. Traditional cleansing methods have evolved from barium enema preparations and local experience, modified for colonoscopy and colon surgery. There are a wide variety of methods using diet restrictions with various purgatives and laxatives. Three popular colon preparation options are diet and cathartic regimens, gut lavage, and phosphate preparations. Early cleansing methods used 48–72 h of clear liquids with laxatives and enemas. When compared with clear liquid and minimum-residue diet methods, PEG-ELS was superior, with cleansing efficacy rated good or excellent. Phosphate preparations offer another alternative. The phosphate salt must be diluted to prevent vomiting and administration should be followed by adequate oral fluids. The phosphate preparation has been rated as a better cleansing agent than the electrolyte solution but has a number of contraindications that must be considered. The diet has undergone many modifications over the years, and enemas are no longer considered necessary, even with the electrolyte or phosphate preparation. The importance of proper cleansing cannot be overemphasized to patients, who must have adequate instruction about the cleansing procedure. They should understand the need for their collaboration and compliance to optimize safety, prevent missed lesions, and to avoid having to reprepare and reschedule the procedure. The colonoscopist should take an active role in this process. The endoscopist must be familiar with the various dietary requirements and the potential problems associated with the prepara-

tion regimen in order to ensure a safe and complete examination.

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Chapter 19

Antibiotic Prophylaxis for Colonoscopy

David J. Bjorkman

Introduction

The rational and appropriate use of antibiotic prophylaxis for colonoscopy is highly controversial. The current recommendations are complex and supported by few data. The potential indications for prophylactic antibiotic therapy for colonoscopy can be divided into two groups: the prevention of bacterial endocarditis and the prevention of other infectious complications. Inasmuch as the transmission of infection between patients by endoscopes is exceedingly rare in the setting of appropriate high-level disinfection of endoscopes [1], potential complications of endoscopy arise from procedure-induced bacteremia with endogenous (usually enteric) bacteria.

Incidence of bacteremia

Prospective studies of bacteremia following endoscopy have produced varying results [2–4]. This is not surprising when considering the different methodology of the studies. Because bacteremia during or following colonoscopy is transient, the ability to detect it depends upon the timing, frequency, and laboratory techniques used in sampling blood. The best estimate of the incidence of bacteremia following colonoscopy is 2.2%, based on the systematic review of Botoman and Surawicz [2]. This compares with an incidence of bacteremia of 4.2% for upper endoscopy, 4.9% for sigmoidoscopy, 45% for esophageal dilation, and 31% for esophageal sclerotherapy. As would be expected, the most common bacteria identified from blood cultures are enteric organisms (Gram negative, anaerobes, *Enterococcus* species) [2].

While studies show that colonoscopy can occasionally induce transient bacteremia, it is not clear that this is a significant risk for metastatic infections. The risk of bacteremia with colonoscopy should be considered in light of the many daily activities, including bowel movements and tooth-brushing, that also induce bacteremia but almost never have adverse clinical consequences [5]. There are no data to suggest that bacteremia from colonoscopy is more likely to result in a complication than bacteremia produced by any of these daily activities.

The risk of an infectious complication of colonoscopy is exceedingly small. Only occasional case reports suggest the occurrence of any infectious complications following colonoscopy. An extensive review of the medical literature, including MEDLINE searches from 1985 to 2002 using the key words “colonoscopy,” “endoscopy,” “bacteremia,” “infection” and “complications,” produced no controlled (prospective or retrospective) studies addressing this issue. Additionally, manual searches of review articles and the recommendations of various medical societies produced no studies that could quantify any risk of infectious complications of endoscopy or any evidence of benefit of prophylactic antibiotics. The rare case reports attributing infectious complications to colonoscopy or sigmoidoscopy do not provide compelling evidence that the infection was a result of the procedure. In summary, there are no reliable data to suggest that there is a significant clinical risk of infection resulting from colonoscopy with or without polypectomy.

Bacterial endocarditis

Despite the absence of any data suggesting that colonoscopy can result in bacterial endocarditis, guidelines from the American Heart Association (AHA) have recommended antibiotic prophylaxis for patients undergoing various procedures ranging from dental work to gastrointestinal endoscopy [6–8]. The rationale for these guidelines has been that bacterial endocarditis is a devastating complication that can result from the bacteremia produced by the procedures. However, there have been no data in humans to suggest that there is a clinically significant risk in the setting of endoscopy. Furthermore, there are reports of endocarditis occurring even in the setting of what has been termed “appropriate” antibiotic prophylaxis [9].

The recommendations of the AHA have driven the use of periprocedure prophylactic antibiotic therapy for gastrointestinal endoscopy. The AHA has modified its recommendations over the years, decreasing the indications for antibiotic prophylaxis and simplifying the suggested regimens. The current recommendations [8] recognize that most cases of endocarditis are spontaneous and not associated with invasive procedures. They also

recognize that there are cardiac lesions that have a higher risk of endocarditis and others that have no increased risk compared with the general population. High-risk lesions include prosthetic heart valves, a history of prior bacterial endocarditis, surgically constructed systemic pulmonary shunts, and complex cyanotic congenital heart disease. Importantly, the AHA statement identifies mitral valve prolapse without regurgitation, functional cardiac murmurs, and prior rheumatic heart disease without valvular dysfunction among the conditions that have no increased risk for endocarditis and do not warrant antibiotic prophylaxis. Further conditions, including other congenital cardiac malformations, rheumatic heart disease with valvular dysfunction, hypertrophic cardiomyopathy, and mitral valve prolapse with valvular dysfunction or thickened leaflets, have a moderate risk of endocarditis.

The most recent recommendations have also stratified procedures according to the risk of producing bacteremia, and thus different theoretical risks for causing endocarditis. Colonoscopy is included in the category “endoscopy with or without gastrointestinal biopsy” as a low-risk procedure. According to the AHA, routine antibiotic prophylaxis is not recommended but may be considered in patients with high-risk cardiac lesions. These recommendations have been modified slightly, with additional focus on gastrointestinal endoscopy, by the American Society of Gastrointestinal Endoscopy (ASGE) [1,10] (Table 19.1). Similar guidelines have been published by the American Society of Colon and Rectal Surgeons [11].

As noted above, both the AHA and the ASGE recognize colonoscopy, with or without biopsy or polypectomy, to be a low-risk procedure for bacterial endocarditis. The only setting in which antibiotic prophylaxis may be indicated is the use of laser therapy, which has a higher risk of bacteremia [10]. It should be noted that other procedures performed during colonoscopy have not been addressed by these guidelines, including the use of argon plasma coagulation and the endoscopic placement of colonic stents, both of which result in vigorous dilation of the colon, either with argon gas or mechanically. While no data are available for the rate of bacteremia following these procedures, the theoretical risk of bacteremia may be higher than colonoscopy with polypectomy and similar to that of laser therapy.

In the rare situation when antibiotic prophylaxis is contemplated for patients with high-risk cardiac lesions undergoing colonoscopy, the recommended regimen is ampicillin 2.0 g plus gentamicin 1.5 mg/kg up to a total of 120 mg i.m. or i.v. within 30 min of starting the procedure, followed 6 h later by either 1 g of ampicillin parenterally or 1 g of amoxicillin orally [8]. Vancomycin 1.0 g i.v. over 1–2 h can be substituted for ampicillin and

the postprocedure dose omitted in patients who are allergic to penicillin. Amoxicillin 2.0 g orally 1 h before the procedure is an acceptable regimen for patients who have a moderate cardiac risk.

Other infectious complications

Data on other potential infectious complications of colonoscopy are as sparse as those for the prevention of bacterial endocarditis. The rationale for potential prophylactic therapy is that certain medical conditions predispose a patient to a potential complication because of impaired immunity or a surgically implanted foreign body.

Impaired immunity

There have been several reported cases of spontaneous bacterial peritonitis (SBP) that have resulted from endoscopic sclerotherapy [12]. The hypothetical etiology of this association is intravascular injection using a nonsterile needle causing a predictable bacteremia and impaired immunity of a cirrhotic patient, particularly those with low ascitic fluid albumin. No cases of SBP have been reported following colonoscopy, but the theoretical risk of seeding the peritoneal fluid has prompted the ASGE to suggest individualizing prophylactic therapy based on the patient’s underlying condition. Inasmuch as most SBP results from infection with enteric organisms, the same antibiotics used to treat or prevent SBP in other settings are likely to be appropriate. There are no data to guide the timing or duration of therapy.

Similar concerns about infection have been raised for patients with impaired systemic immunity, specifically those who are neutropenic due to chemotherapy or bone marrow transplantation. The theoretical risk of any systemic infection from a transient bacteremia has suggested to some that antibiotic prophylaxis is appropriate in this setting. As with cirrhosis and ascites, there are no data to guide the specific drug regimen to be used. A retrospective study of bone marrow transplant patients who underwent 67 endoscopic procedures (both upper and lower) in 53 sessions found no evidence of procedure-induced infection in any patient [13]. In the study, 28 of the patients were on no antibiotic therapy and 25 were receiving broad-spectrum antibiotics.

It has been suggested that artificial joints are at risk for infection from transient bacteremia resulting from colonoscopy. Careful evaluation of the data, however, demonstrates that there is no significant risk of joint infection resulting from endoscopic procedures [10,14]. Antibiotic prophylaxis is not recommended for colonoscopy performed in the presence of artificial joints.

There are no data on the risk of infection of vascular grafts with colonoscopy. Because these grafts become endothelialized within a few months after placement,

Table 19.1 Antibiotic prophylaxis in endoscopy [1].

Patient condition	Procedure contemplated	Antibiotic prophylaxis	Comments
Prosthetic valve, history of endocarditis, systemic pulmonary vascular shunt, synthetic vascular graft (< 1 year old)	Stricture dilation, varix sclerosis ERCP/obstructed biliary tree	Recommended	High-risk conditions for development of infectious complication; procedures are associated with relatively high bacteremia rates While conditions are high risk, procedures are associated with low rates of bacteremia
Rheumatic valvular dysfunction, mitral valve prolapse with insufficiency, hypertrophic cardiomyopathy, most congenital cardiac malformations	Other endoscopic procedures, including EGD and colonoscopy (with or without biopsy/polypectomy), variceal ligation Stricture dilation, varix sclerosis ERCP/obstructed biliary tree	Insufficient data to make firm recommendation; endoscopists may choose on a case-by-case basis Insufficient data to make firm recommendation; endoscopists may choose on a case-by-case basis Not recommended	Conditions pose lesser risk for infectious complications than prosthetic valve, etc. Procedures are associated with relatively low bacteremia rates
Other cardiac conditions (including coronary bypass, pacemakers, implantable defibrillators)	Other endoscopic procedures, including EGD and colonoscopy (with or without biopsy/polypectomy), variceal ligation All endoscopic procedures	Not recommended	Conditions are low risk for infectious complications from endoscopic procedures
Obstructed bile duct, pancreatic pseudocyst	ERCP	Recommended	Prudent, but no substitute for definitive drainage
Cirrhosis and ascites, immunocompromised patient	Stricture dilation, varix sclerosis ERCP/obstructed biliary tree Other endoscopic procedures, including EGD and colonoscopy (with or without biopsy/polypectomy), variceal ligation Endoscopic feeding tube placement Any endoscopic procedure	Insufficient data to make firm recommendation; endoscopists may choose on a case-by-case basis Not recommended Prophylaxis recommended Not recommended	Risk for infectious complications related to endoscopic procedures not established Procedures are associated with relatively low bacteremia rates May decrease risk of soft-tissue infection No literature to support infectious risk from endoscopic procedures

EGD, esophagogastroduodenoscopy; ERCP, endoscopic retrograde cholangiopancreatography.

the theoretical period of risk is less than 6 months [8]. There is no need for antibiotic therapy for grafts older than 6 months. The indications and drug regimens for therapy of recently placed grafts is similar to that for endocarditis. There are no data regarding the risk of infection after cardiac transplantation, but the AHA recognizes that many transplant physicians recommend antibiotic prophylaxis similar to that for moderate-risk cardiac lesions because of the potential for valvular dysfunction and the chronic immunosuppression required in these patients.

Other prosthetic and implanted devices (including pacemakers, defibrillators) are felt to have a negligible risk for infection and are not indications for prophylactic therapy, although there are no data addressing the issue.

Appropriate antibiotic use

Despite numerous different recommendations for antibiotic prophylaxis in gastrointestinal endoscopy there remains considerable confusion around the subject. Both surveys and prospective studies have demonstrated that antibiotic prophylaxis is rarely appropriately used. Many patients receive antibiotics prior to endoscopy when there is no indication and the few patients who have a legitimate indication for periprocedure antibiotics often do not receive them. A retrospective analysis of antibiotic use in endoscopic procedures over a 1-year period demonstrated that only 10% of physicians used antibiotic prophylaxis appropriately (according to ASGE guidelines) [15]. Additionally, even when patients are instructed regarding appropriate antibiotic use, they often ignore the advice. A prospective and retrospective study evaluating a program to improve the appropriate use of antibiotics prior to endoscopy reduced the use by 50% [16]. This inappropriate use of antibiotics may have small marginal costs for each patient, but likely has a large aggregate cost for the health system. At the same time we can be reassured that the lack of appropriate antibiotic use has not resulted in any significant risk of infectious complications. It has been suggested that the risk of complications from antibiotic use (anaphylaxis, pseudomembranous colitis) is greater than the risk of the complications that the antibiotics are meant to prevent.

Summary

Colonoscopy, except in rare exceptions, has a very low risk for causing bacteremia. The risk has been estimated to be 1 in 5–10 million procedures [16]. There are no data to suggest that colonoscopy creates a greater risk for an infectious complication in high-risk patients than any one of a number of daily activities that also produce bacteremia. The current recommendations for antibiotic prophylaxis for colonoscopy are not data-driven. They

are based on theoretical risks and extrapolation from case reports in other clinical situations. The absolute risk of an infectious complication from colonoscopy is vanishingly small. The risk and costs of antibiotic use may outweigh the potential benefits. Antibiotic prophylaxis should be used rarely and in specific clinical situations where the benefits outweigh the costs and risks. ASGE guidelines can identify the unusual situations and guide specific therapy.

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Chapter 20

Management of Anticoagulation and Antiplatelet Agents

Glenn M. Eisen

Introduction

Performing colonoscopy can be complicated by patient use of anticoagulants and/or antiplatelet agents. These medications are widely used by the general population. The endoscopist is frequently faced with balancing the added bleeding risks associated with these agents with the potential thromboembolic complications that may ensue when these treatments are discontinued. If anticoagulants or antiplatelet agents are stopped, decisions are required as to when to safely restart them.

Scope of the problem

In the USA, more than 1 million patients chronically use anticoagulants on an annual basis for the prevention of thromboembolic complications [1]. The indications for anticoagulant use include a variety of conditions, such as mechanical heart valves, deep venous thrombosis (DVT), and cardiac arrhythmias [2]. Patients who are on warfarin therapy are at increased risk for gastrointestinal hemorrhage when the international normalized ratio (INR) is elevated [3]. Patients who are treated with conventional doses of either heparin or warfarin have a 2–4% annual of risk of bleeding requiring transfusion. The most common bleeding sites are gastrointestinal, genitourinary, and vaginal. Fatal hemorrhage risk is approximately 0.2% yearly [4].

Risk of discontinuing anticoagulants and antiplatelet agents

Many patients are continued on anticoagulation long after the suggested therapeutic intervals have been completed. In these situations, there is little risk to stopping these drugs. The majority of endoscopists stop warfarin use prior to performing colonoscopy. This may put the patient at increased risk for thromboembolic complications. There is little published information on this absolute short-term risk. A retrospective series by Kuwada and colleagues [5] found that of 27 patients who were anticoagulated and had warfarin held for a median of 4 days because of acute gastrointestinal hemorrhage, one

patient developed thrombosis 24 days after the bleeding episode. In a second series of 32 patients who had completed a course of therapy for DVT, 17 abruptly stopped warfarin therapy and two developed recurrence of thrombosis [6]. These reports suffer from being small and retrospective and are different from the scenario where anticoagulant therapy is withdrawn in an asymptomatic patient. Also, small series tend to overstate actual risk, as studies with few patients that show no adverse outcomes are less likely to be published. The absolute risk of stopping anticoagulation for the short term in patients undergoing colonoscopy remains unknown.

The uncertainty in managing these patients is reflected in the following survey published in 1996. Kadakia and colleagues [7] performed a survey of American Society for Gastrointestinal Endoscopy (ASGE) members regarding endoscopy in patients using anticoagulants and/or antiplatelet agents. Over 3000 ASGE members were queried, including all gastroenterology fellowship program directors; 1269 responses (38%) were analyzed. There was wide variation in practice regarding the discontinuation of anticoagulants as well as antiplatelet agents. Depending on the indication for anticoagulation, 71–82% of physicians stopped anticoagulation before colonoscopy, and 26–51% of physicians used a “heparin window” (see later). All physicians restarted warfarin immediately after diagnostic endoscopy, whereas 80% restarted it 7 days or less after therapeutic endoscopy. These findings demonstrate the wide variation in managing anticoagulants/antiplatelet agents in the pericolonoscopic period. An attractive alternative for high-risk patients who are anticoagulated and are to have screening colonoscopy or surveillance examinations, in the absence of symptoms suggesting the presence of colorectal neoplasia, is to perform the procedure while on warfarin. If only a small adenoma is found, the patient may be rescheduled at an appropriate interval. If a cancer is discovered, it can be biopsied, whereas another examination may need to be scheduled at a short interval if a significant polyp is discovered. This process should be explained to the patient in detail before embarking on the endoscopy sequence.

Table 20.1 Management of anticoagulation and antiplatelet agents in patients undergoing colonoscopy.

	High risk of thromboembolism	Low risk of thromboembolism
High procedure risk	Discontinue warfarin 3–5 days before procedure. Consider heparin while INR is below therapeutic level	Discontinue warfarin 3–5 days before procedure. Reinstigate warfarin after procedure
Low procedure risk	No change in anticoagulation. Elective procedures should be delayed while INR is in supratherapeutic range	

INR, international normalized ratio.

ASGE guideline

Until 1997, there were no published guidelines by any of the gastroenterology societies regarding the use of anticoagulants or antiplatelet agents. The first and still the only guideline regarding the periendoscopic management of patients taking anticoagulants or aspirin/nonsteroidal antiinflammatory drugs (NSAIDs) was published by the ASGE. This guideline was updated in 2002 [8]. The guideline categorizes endoscopic procedures into high and low risk and also classifies patient conditions in the same manner. The ASGE recommendations for the management of anticoagulation based on risk for thromboembolism are shown in Table 20.1.

Diagnostic colonoscopy with or without biopsy is considered a low-risk procedure, while colonoscopies that include polypectomy are deemed high risk (for periprocedure bleeding). Colonic polypectomy has been associated with an increased risk of bleeding compared with diagnostic colonoscopy [9]. Postpolypectomy bleeds can occur up to 14 days after the procedure [10] and large polyp size (> 2 cm), presence of bleeding disorder, and “poor” cautery technique are risk factors [11]. The short-term bleeding risk for polypectomy in patients not taking anticoagulants appears to be 1–2.5% [9]. The likelihood of a thromboembolic complication depends on the condition that necessitates the use of anticoagulants. Patients with mechanical heart valve prostheses have a risk of a major thromboembolic event (in the absence of anticoagulation) of 4 per 100 patient-years [12]. Using antiplatelet therapy, this risk is lowered to 2.2 per 100 patient-years and is further lowered with warfarin to 1 per 100 patient-years [3,13]. The short-term risk of complications in patients who have anticoagulation stopped for only a few days is not known. The absolute risk of thromboembolism also varies based on the location and type of valve. Mechanical valves in the mitral or mitral and aortic positions have the highest risk [3]. Patients with atrial fibrillation and a mechanical valve are also at high risk. The target INR in this population (patients with mechanical heart valves) is 3.0–4.0 [14].

Anticoagulation for DVT is generally continued for 1–6 months [15]. Ending anticoagulation early for short

intervals does not seem to significantly increase the risk of subsequent pulmonary embolus. There are no standardized anticoagulation parameters for patients with hypercoagulable states or endovascular grafts and these patients’ anticoagulation levels need to be individualized.

The ASGE has divided conditions prompting anticoagulation into low- and high-risk groups based on their thromboembolic risk. Low-risk conditions include chronic or paroxysmal atrial fibrillation not associated with valvular disease, DVT, mechanical valves in the aortic position, and bioprosthetic valves. High-risk conditions include mechanical valves in the mitral position, atrial fibrillation associated with valvular disease, and mechanical valves in patients who have had previous thromboembolic events.

Short-term heparin substitution for warfarin (heparin window)

The ASGE guideline recommends the following for high-risk procedures in high-risk patients.

- 1 Warfarin should be stopped 3–5 days prior to the planned procedure.
- 2 If heparin is used, it should be discontinued 4–6 h prior to the procedure and can usually be restarted 2–6 h after the procedure.
- 3 Warfarin can be restarted the night of the procedure.
- 4 Heparin administration with warfarin administration should overlap for a period of 4–5 days or until the target INR has been reached for 2–3 days [7].

One published protocol [16] for the management of patients on chronic warfarin therapy who are undergoing subsequent noncardiac surgical procedures is as follows.

- 1 Discontinue warfarin 5 days prior to surgery and begin intravenous heparin at 1000 units/h with adjustments to keep partial thromboplastin time (PTT) levels therapeutic.
- 2 Heparin is stopped early the morning of surgery and restarted at 200–400 units/h at 4–6 h after surgery.
- 3 Warfarin is restarted as soon as the patient can tolerate it.

It is relevant to note that this suggested protocol is based on a single center’s retrospective experience.

The absolute risk of an embolic event for patients with a low-risk condition who require the cessation of anticoagulant therapy for up to 1 week is estimated at 1–2 per 1000 patients [17]. It is recommended that elective procedures such as screening or surveillance colonoscopy should be delayed in patients on anticoagulation for DVT until this treatment is no longer indicated. In general, vitamin K should be avoided for elective procedures since, once used, it will significantly delay resumption of therapeutic anticoagulation.

Gerson and colleagues [18] subsequently performed a retrospective analysis of 104 patients who were on prescribed doses of warfarin at the Veterans Affairs Palo Alto Health Care System during the period 1996–99. No patient developed bleeding or had a thromboembolic event. All five of the patients who were deemed high risk by the ASGE guideline had heparin substituted for warfarin prior to undergoing high-risk procedures. However, heparin replacement therapy was also used in 44 of the 166 procedures (27%) performed in the other patients during this time period: 16 high-risk procedures in low-risk patients and 28 low-risk procedures. Overall, 90% of the cases where heparin replaced warfarin were not indicated by the ASGE recommendations. Practice patterns were not significantly different comparing pre-ASGE guidelines to post-ASGE guidelines ($P > 0.05$). There have been no further studies on practice management/variation in following the ASGE guidelines. Given that the ASGE now publishes the guideline on the Web, in the journal *Gastrointestinal Endoscopy*, and sends all members printed copies, it is possible that adherence has increased.

Low-molecular-weight heparin: is it acceptable to use yet?

The use of low-molecular-weight heparin (LMWH) may eventually alter the recommended protocol. However, there is a paucity of prospective studies on the use of LMWH in the periendoscopic period. It has been used as “bridging therapy” for patients on chronic anticoagulation undergoing invasive procedures [19–21]. The use of LMWH may result in significant cost savings as it could potentially avoid the need for inpatient monitoring, intravenous heparin therapy, and PTT assessment. LMWH has a predictable anticoagulant effect and does not require monitoring [22]. A cost modeling study recently assessed the economic outcomes of periprocedure anticoagulation approaches for elective colonoscopy [23]. This decision analysis assessed five different scenarios: outpatient LMWH, inpatient heparin infusion, continuous warfarin (with probability of repeat procedure using LMWH or heparin), and discontinuation of anticoagulation. Assumptions included drug therapy options being equally effective for high-risk patients in

preventing a thromboembolic event (0.1% risk) and a 0.4% risk for no anticoagulation. There was a 64.4% cost saving with LMWH vs. inpatient unfractionated heparin. The no anticoagulation option had the lowest costs per patient of all treatment scenarios despite the greatest risk of thromboembolic events and the associated costs for treating those complications. This is because the risk of thromboembolic complications even when anticoagulation is withdrawn remains low. Sensitivity analysis revealed that the use of LMWH would become more costly than heparin when the rate of thromboembolic complications was more than 32.9% of patients receiving LMWH. This is obviously much greater than any report of complications associated with this intervention. Most practitioners would not stop anticoagulation merely because it was the lowest cost option for a population of patients. Although the findings of this study strongly suggest benefits for the use of LMWH in the pericolonoscopy period, there are no prospective studies to confirm this as yet. Several small trials have reported nonendoscopic procedure outcomes when using LMWH [19–21]. These small studies are significantly under-powered for detecting differences in adverse thromboembolic outcomes. Despite this, the American College of Chest Physicians has recommended using LMWH bridge therapy as a possible alternative to unfractionated heparin in the perioperative period [24].

The aspirin controversy

Aspirin and most NSAIDs inhibit platelet cyclooxygenase, resulting in suppression of thromboxane A_2 -dependent platelet aggregation. It has been estimated that at least 25% of the adult population use aspirin and/or NSAIDs on a regular basis [25]. However, limited published data suggest that aspirin and other NSAIDs in standard doses do not increase the risk of significant bleeding after esophagogastroduodenoscopy with biopsy, colonoscopy with biopsy, polypectomy, or biliary sphincterotomy [26,27]. Despite this, some authors suggest discontinuing the use of aspirin/NSAIDs up to 14 days prior to a planned therapeutic colonoscopy [28].

The effect of aspirin on platelet aggregation may last as long as 1 week or longer [29]. This is due to irreversible binding and inactivation of the platelet by aspirin. The platelet lifespan is 9–12 days [30]. Nakajima and colleagues [31] used a novel method to assess colonic bleeding time. They developed a new endoscopic device to make a standard incision (7 mm long) on the colonic mucosa and measured the bleeding time of normal colonic mucosa in 47 cases. The colon bleeding time and skin bleeding time (Simplate method) were measured before and 1 h after aspirin ingestion (990 mg) in 10 healthy subjects. The bleeding time of

normal colonic mucosa was 156 ± 71 s. Significant prolongation was noted in both skin bleeding time (357 ± 192 vs. 477 ± 183 s; $P < 0.05$) and colon bleeding time (155 ± 47 vs. 244 ± 169 s; $P < 0.05$) after aspirin ingestion (990 mg). This suggests an increased risk of abnormal bleeding in patients on aspirin who undergo colonoscopy, but this does not contraindicate the procedure according to the authors. Outcomes data on concurrent aspirin use and colonoscopy are needed but for the most part lacking.

In the largest cohort study in the literature, Shiffman and colleagues [27] reported on a prospective cohort of patients undergoing upper endoscopy or colonoscopy. Of 694 patients, 46% had recently consumed NSAIDs (self-report within 1 week of the procedure). Postprocedure bleeding was assessed by both written questionnaire and telephone follow-up. Minor, self-limited, "clinically insignificant" bleeding occurred in 6.3% of patients taking NSAIDs and 2.1% of control patients ($P = 0.009$). Major postprocedure bleeding occurred in only 0.58% of patients (two on NSAIDs/aspirin and two in the control group), all of whom underwent snare polypectomy. No major events were seen in patients undergoing cold biopsy or biopsy with cautery (hot). The authors acknowledge that their study was likely underpowered and the lack of bleeding complications between those on aspirin/NSAIDs and those not may be attributed to type II errors. They estimate that more than 1200 patients would have had to be evaluated to detect a twofold difference between groups. Given the incidence of minor bleeding, even with cold biopsy, the authors recommend that patients discontinue aspirin/NSAIDs prior to colonoscopy.

The ASGE guideline states: "In the absence of a pre-existing bleeding disorder, endoscopic procedures may be performed on patients taking aspirin and other NSAIDs in standard doses" [8].

Novel antiplatelet agents

Two novel classes of antiplatelet agents are now available: (i) antagonists of the platelet cell-surface adenosine diphosphate receptor (P2T receptor); and (ii) antagonists of the glycoprotein IIb/IIIa receptor, which normally promotes adherence of platelets to fibrinogen and thrombus formation.

P2T receptor antagonists include ticlopidine and the newer agent clopidogrel, which appears to have fewer adverse effects than ticlopidine (neutropenia and thrombotic thrombocytopenic purpura). These agents are generally used in combination with aspirin to reduce the incidence of serious coronary events after stent placement, and are associated with an increased risk of bleeding complications, particularly the combination of ticlopidine and aspirin [32,33]. There are no published

reports on performing endoscopy while patients are using these agents.

Antiplatelet agents directed against the glycoprotein IIb/IIIa receptor include eptifibatid, abciximab, and tirofiban. These drugs are designed to reduce the risk of acute ischemic complications in high-risk patients after coronary angioplasty. In phase III trials, treated patients had an approximately twofold increased risk of major bleeding, but no increase in cerebral hemorrhage or lethal bleeding [34]. Again, there are no published data to guide the practicing endoscopist.

Data regarding gastrointestinal bleeding in patients treated with these newer antiplatelet agents are inadequate to make firm recommendations. Any decision regarding discontinuation of therapy before endoscopy has to be weighed against the patient's risk for an adverse coronary event related to cessation of medication (e.g. reocclusion of coronary stents). For elective high-risk procedures, temporary discontinuation of these medications, particularly if the patient is on concomitant aspirin, is desirable.

Summary

The management of anticoagulant and antiplatelet therapy in the pericolonoscopy period remains a difficult area. Until recently, there was little help for the practicing endoscopist. The ASGE has recently published guidelines on this management. The impact on practice patterns has not yet been demonstrated. For NSAIDs/aspirin, the guideline recommends that "in the absence of a pre-existing bleeding disorder, endoscopic procedures may be performed on patients taking aspirin and other NSAIDs in standard doses." However, most practitioners still prefer to temporarily discontinue these medications when feasible. Warfarin management depends on both the procedure risk and the patient's underlying thromboembolic risk (see Table 20.1). LMWH may become a significant advance in the management of high-risk patients. However, it cannot be recommended now due to the lack of published evidence regarding its safety. Newer antiplatelet agents have not been included in endoscopic studies yet. The use of these agents should be left to the discretion of the practitioner.

There are significant obstacles to developing an evidence-based algorithm for patient management: (i) lack of randomized controlled trials; (ii) lack of patient-centered outcome data; and (iii) inadequate prospective cohort studies with regard to size and follow-up duration. Randomized controlled trials are unlikely to occur due to logistic and ethical issues. Large prospective cohort studies with appropriate follow-up (i.e. 30-day complication rates) are perhaps our best chance to further assess the benefits and risks of the various management options.

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Chapter 21

Sedation for Colonoscopy

Gregory Zuccaro Jr

Introduction

Sedation and analgesia are commonly provided for the performance of colonoscopy. The goal of sedation and analgesia is to increase patient tolerance for the procedure, and to increase satisfaction for both patient and endoscopist. This chapter focuses on definitions of sedation and analgesia, the efficacy and safety of conventional means of delivery, the prospects of colonoscopy without sedation and analgesia, alternative techniques that may be employed, and finally newer medications that may increase efficiency while preserving efficacy.

Definitions of sedation and analgesia

The American Society of Anesthesiologists (ASA) has defined sedation and analgesia as a continuum of states ranging from minimal sedation through general anesthesia [1]. These states are listed in Table 21.1. Most frequently, the target of sedation and analgesia for the performance of colonoscopy is that of moderate sedation; this term is usually synonymous with the common but inaccurate phrase "conscious sedation." There are three key concepts that emerge from these definitions.

Table 21.1 American Society of Anesthesiologists scheme for levels of sedation and analgesia. (From American Society of Anesthesiologists [1].)

Minimal sedation

Normal response to verbal stimulation
Airway, ventilation, cardiovascular unaffected

Moderate sedation

Purposeful response to nonpainful stimulation
Airway, ventilation, cardiovascular adequate

Deep sedation

Response only after repeated or painful stimulation
May require airway/ventilatory intervention

General anesthesia

Unrousable
May require airway/ventilatory/cardiovascular support

1 Sedation is a continuum, i.e. patients receiving sedative/analgesic agents may move within one or more of these states during colonoscopy.

2 It is impossible to target only one state of sedation/analgesia, i.e. some patients in whom the intention is to provide moderate sedation may actually end up in greater or lesser states of sedation and analgesia.

3 Since the state of sedation and analgesia may be unpredictable, the training of the individuals providing this sedation must be such that they are able to successfully rescue patients from deeper levels of sedation and analgesia than intended. At a minimum, individuals providing sedation and analgesia toward a target state of moderate sedation must have the skills and equipment necessary to rescue patients from a state of deep sedation; those providing a target of deep sedation must have the skills necessary to rescue from general anesthesia.

Scenarios of sedation and analgesia for colonoscopy

There are two scenarios whereby sedation and analgesia are most commonly provided for colonoscopy. The first, and still the most common, is where the endoscopist/nursing team attend to both the sedation and analgesia, and also to the technical performance of the procedure. The use of an individual specifically trained in sedation and analgesia, such as an anesthesiologist, is reserved for the very ill or otherwise extremely challenging patient. The second scenario is where another professional with specific training in sedation and analgesia, e.g. an anesthesiologist or nurse anesthetist, provides the sedation and analgesia in all cases, and the endoscopist/nursing team attend only to the technical performance of colonoscopy. Each approach has its advocates and detractors. Those advocating the endoscopist/nursing team as provider of sedation note the cost savings over the use of another provider and the autonomy of not having to wait for another professional to perform their cases. Those advocating the regular use of another professional for sedation and analgesia note the efficiency for the endoscopist/nursing team: since the endoscopy team focuses only on the performance of the procedure, colonoscopy is performed more quickly and easily.

Further, since medications such as propofol, with its much shorter recovery time compared with narcotics and benzodiazepines, are frequently used by anesthesiologists and nurse anesthetists, patients leave the recovery suite more quickly, allowing more colonoscopies to be performed in the same amount of time. Which scenario is used depends primarily upon the practice structure of the individual endoscopist/nursing team. The first scenario, where the endoscopist/nursing team provides sedation and analgesia as well as performance of colonoscopy, is more common (presumably why a colonoscopist would read this chapter), and this model is the primary focus of this chapter. This is particularly appropriate now that gastroenterologist-administered propofol for colonoscopy, combining the best aspects of both scenarios, is under rigorous study and may well gain more widespread acceptance if issues of safety are adequately addressed.

Standard approach to sedation and analgesia

A combination of parenteral narcotic and benzodiazepine is the most common sedative/analgesic medication provided for colonoscopy. The narcotic is intended to provide pain relief, while the benzodiazepine may decrease anxiety and provide amnesia. Pain during colonoscopy is a major factor in patient dissatisfaction with the procedure. There are several factors that may account for pain during colonoscopy. These include looping of the colonoscope with resultant stretching of the colonic wall and mesentery, distension from air insufflation, force and torque on the insertion tube, and overall patient pain tolerance. Shah and colleagues [2] used a real-time magnetic imaging system to visualize the configuration of the colonoscope during episodes of pain in 102 patients. In all, 650 pain "episodes" occurred in these patients; 77% of pain episodes were associated with the tip of the colonoscope in the sigmoid colon. Most episodes of pain were associated with looping of the instrument, with a small minority attributed to overinsufflation or force/torque on the insertion tube. Sedation and analgesia are important for completing examinations in many cases. Rodney and Dabov [3] examined the effect of sedation on the rate of complete colonoscopic examinations performed by a group of family practitioners and trainees. For the patients receiving sedation, the cecum was reached in 85%; for those patients not receiving sedation, the cecum was reached in only 31%.

Goals of sedation and analgesia

The goals of sedation and analgesia may be different for colonoscopy than for upper endoscopy, and therefore

the endoscopist/nursing team may alter their regimens accordingly. For upper endoscopy, benzodiazepines form the basis for sedation and analgesia. In a survey, Daneshmend and colleagues [4] found that 90% of endoscopist/nursing teams used anxiolytic medication during upper endoscopy, with only 13% adding a narcotic. The data on whether benzodiazepines alone vs. benzodiazepines plus narcotics are superior for upper endoscopy are mixed. Schwartz and Fazio [5] found that the addition of atropine and meperidine to diazepam for upper endoscopy did not result in increased patient tolerance for the procedure compared with diazepam alone. However, Diab and colleagues [6] found that the combination of meperidine and midazolam was superior to midazolam alone with respect to degree of retching, ease of esophageal intubation, ability to complete the procedure, and endoscopist satisfaction. For colonoscopy, provision of analgesia, rather than anxiolysis, appears to be most important. DiPalma and colleagues [7] compared patients receiving alfentanil (a shorter-acting narcotic) alone with those receiving a combination of alfentanil and midazolam for colonoscopy. No clinically significant differences were observed between the two groups. Froehlich and colleagues [8] also found that single drug sedation and analgesia was comparable to the combination of a narcotic and benzodiazepine in provision of pain relief and achievement of patient satisfaction.

Novel approaches to standard sedation

Obviously, the approach to sedation and analgesia will vary based on the training and experience of the endoscopist/nursing team, local standards, and the individual patient. Use of parenteral narcotics and benzodiazepines may be modified in novel ways. At the Cleveland Clinic [9], we attempted to exploit the fact that most of the pain associated with colonoscopy occurred early in the procedure, when the colonoscope tip was maneuvered through the sigmoid colon. The rationale was that if a generous bolus of meperidine and midazolam were given initially, rather than a gradual titration of medications, then the patient would be more comfortable during the early phase of colonoscope insertion. Indeed, when we randomized patients to bolus medication (determined by nomogram) vs. gradual titration of the same medications, endoscopist time and recovery time were better with the bolus, less oxygen desaturation occurred with the bolus, and patient and endoscopist satisfaction were comparable. Stermer and colleagues [10] examined the concept of patient-controlled sedation and analgesia using standard narcotic/benzodiazepine combinations. They compared a group of patients receiving sedation prior to colonoscopy (plus further doses at the discretion of the

anesthesiologist) with another group receiving pre-procedure sedation augmented by further doses as requested by the patient. Patient tolerance and safety were comparable for the two groups. Terruzzi and colleagues [11] compared the use of meperidine and midazolam immediately before insertion of the colonoscope (i.e. traditional approach to sedation and analgesia for colonoscopy) with administration of the same dosage of medication during the procedure when requested by the patient. Overall, when examining parameters such as pain and willingness to undergo the procedure in the future, provision of medication in advance was superior to “on-demand” sedation. This is due in part to the time lag in onset of action of these medications when given during the procedure. However, among the patients over age 60 in the “on-demand” sedation group, only 23% required sedation. The concept of patient-controlled sedation is revisited later in this chapter with use of other agents.

Safety of standard sedation

Clearly there are benefits to the administration of sedative and analgesic medications prior to colonoscopy, including ability to complete the examination, increased patient and endoscopist/nursing team satisfaction, and willingness of patients to undergo the procedure in the future. However, with these benefits come risks, particularly in the form of potential compromise of ventilatory function. Ristikankare and colleagues [12] divided 180 patients undergoing colonoscopy into three groups: sedation with intravenous midazolam, placebo, and no intravenous catheter/no sedation. Midazolam lowered Sao_2 and blood pressure significantly compared with placebo or no-sedation groups. Thompson and colleagues [13] found that 72% of patients undergoing colonoscopy had some perturbation of hemodynamic or ventilatory parameters, including one patient with myocardial infarction during colonoscopy. Ginsberg and colleagues [14] found that the predicted appropriate dose of diazepam was excessive in 21% of patients provided with sedation and analgesia for colonoscopy, and that this overestimation was more common in senior patients.

Many experienced colonoscopists argue that there is a long track record of safety associated with sedation and analgesia as provided by gastroenterologists and other endoscopists, and that these transient decreases in Sao_2 or systolic blood pressure, while statistically significant in clinical studies, have little or no clinical significance. They further argue that when midazolam was first introduced, significant complications due to oversedation (including death) occurred but this problem has been corrected with greater experience with the medication. Examining the literature for all endoscopic procedures,

there are some data which unfortunately indicate that safety may still be an issue. Arrowsmith and colleagues [15] analyzed data from over 21 000 procedures and found serious cardiopulmonary complications in 0.5% and death in 0.03%. Midazolam could not be blamed for the complications; however, a combination of narcotic and benzodiazepine was more likely to be associated with a serious complication than the use of one agent. Daneshmend and colleagues [4] reported 156 severe cardiopulmonary complications and 52 deaths in the clinical experience of 665 endoscopists over a 2-year period.

Vasovagal response may affect hemodynamic parameters during colonoscopy. Herman and colleagues [16] examined this phenomenon in a group of 223 consecutive patients undergoing colonoscopy. They defined the vasovagal response as the occurrence of diaphoresis, sustained bradycardia, and/or hypotension. In all, 17% of patients experienced a vasovagal episode during colonoscopy. Patients experiencing vasovagal episodes received slightly more midazolam on average, and were more likely to have diverticular disease, compared with patients who did not experience vasovagal episodes. Other demographics, presence of preexisting cardiovascular disease, type of preparation, and perceived procedure difficulty did not predict a vasovagal episode. Interpretation of clinical studies describing cardiovascular changes during colonoscopy must include a consideration that changes may be due to multiple factors, including medication effects or vasovagal episodes.

One way to counteract the negative effects of sedative/analgesic medication during or after colonoscopy is to administer a reversal agent. Saletin and colleagues [17] gave 45 patients flumazenil and 46 placebo after midazolam for colonoscopy. Flumazenil was found to be an effective agent in restoring alertness and otherwise reversing the effects of midazolam. It must be noted that there are limitations to this approach, as the effects of the reversal agent may dissipate while the sedative is still active, leading to re-sedation. Routine administration of a reversal agent cannot therefore be used to decrease recovery times since most units will observe patients for a prolonged period to guard against re-sedation.

Approach to standard sedation: practice guidelines

It is acknowledged that the majority of sedation and analgesia provided for colonoscopy is administered by the endoscopist/nursing team. The ASA have developed a document entitled “Practice guidelines for sedation and analgesia by non-anesthesiologists.” This practice guideline was initially published in the mid-1990s, with a revision recently released [18]. The guideline was developed not only for the gastroenterology

suite but also for any service outside the operating room where sedation and analgesia are delivered, including cardiac catheterization, bronchoscopy, interventions in the emergency room, sedation for radiologic procedures. The practice guideline was developed under strict methodologic standards. The core committee (task force) consisted of seven anesthesiologists, one nonanesthesiologist (the author of this chapter), and two PhD methodologists. The process created a series of linkage statements that were in essence a series of directional statements about relationships between interventions and outcomes (e.g. whether patient monitoring, education in pharmacy of medications, availability of emergency equipment improves clinical efficacy and/or reduces adverse outcomes). Afterward, an extensive literature search was carried out for relevant articles published in the years 1958–2001. This yielded 1876 linkage statements. The strength of data present in the literature for each linkage statement was described as supportive, suggestive, equivocal, inconclusive, insufficient, or silent. In addition, a panel of consultants, who were experts in specialties affected by the guidelines including gastroenterology, were surveyed as to their opinions on each of these linkage statements. After a guideline draft was developed, a series of open forums were conducted, at which any interested parties could comment; these forums were held in various cities around the USA. From this extensive process emerged a practice guideline for all aspects of moderate or deep sedation provided by nonanesthesiologists.

Patient preparation and preprocedural evaluation

The task force reported that the literature was insufficient to evaluate the relationship between the performance of a preprocedural patient evaluation and outcomes of sedation and analgesia; data were also insufficient regarding the benefits of providing preprocedure information on sedation and analgesia. However, the consultants strongly agreed that a preprocedure assessment and provision of information increase the likelihood of satisfactory sedation and analgesia and improve patient satisfaction. According to the guideline, the historical points to consider include:

- abnormalities of major organ systems;
- previous experience with sedation and analgesia, whether moderate, deep or general;
- drug allergies;
- time and nature of last oral intake (the ASA recommends that for elective procedures the patient not ingest solid food for 6 h or more prior to the administration of sedation and analgesia, but may have clear liquids up to 2 h before the administration of sedation and analgesia [19]);
- history of tobacco, alcohol, or substance abuse.

Table 21.2 American Society of Anesthesiologists classification for risk stratification. (From [20].)

Patient profile	
Class I	Healthy patient
Class II	Mild systemic disease No functional limitations No acute problems, e.g. controlled hypertension, mild diabetes, chronic bronchitis, asthma
Class III	Severe systemic disease Definite functional limitation, e.g. brittle diabetes, frequent angina, myocardial infarction
Class IV	Severe systemic disease with acute unstable symptoms, e.g. recent (3 months) myocardial infarction, congestive heart failure, acute renal failure, ketoacidosis uncontrolled, active asthma
Class V	Severe systemic disease with imminent risk of death

Focused physical examination should include vital signs, auscultation of the heart and lungs, and airway evaluation.

Age and gender are parts of the demographic data collection that allows crude stratification of procedure risk. All patients should have an estimate of their risk classification as developed by the ASA [20] (Table 21.2). The ASA risk status, although unproven, provides a framework for the outcome of sedation and analgesia.

Intraprocedure personal monitoring of the patient

The literature is silent on whether or not monitoring consciousness during the procedure will improve outcomes. The consultants strongly agreed that monitoring consciousness decreases risks of sedation. The literature was judged insufficient to assess the benefit of monitoring ventilation by observation or auscultation. However, the consultants strongly agreed that monitoring ventilation would reduce the likelihood of adverse reaction to sedation/analgesia. The guideline recommends that ventilation be monitored (by personal observation in most cases). If the patient is in a state of moderate sedation, the endoscopist/nursing team may perform brief interruptible tasks related to the performance of colonoscopy (e.g. snaring a polyp, placing a specimen in a jar); however, if the patient is in a state of deep sedation, another individual must be present whose sole job is to monitor the patient.

Automated monitoring

The literature suggests that use of pulse oximetry effectively detects oxygen desaturation and hypoxemia in patients receiving sedation and analgesia. The consult-

ants strongly agreed that use of pulse oximetry decreases the likelihood of adverse outcomes. The literature is insufficient to make a conclusion regarding the regular assessment of vital signs, but again the consultants strongly agreed that regular assessment of vital signs reduces the risk of adverse events. The guideline recommends that pulse oximetry be continually monitored and that vital signs be recorded regularly throughout the procedure. It must be recognized that pulse oximetry is a measure of oxygenation not ventilation. Patients may have satisfactory oxygenation early in the course of prolonged apnea, particularly if they are receiving supplemental oxygen.

Training of personnel

The literature is silent regarding the impact of appropriate training on outcomes of sedation and analgesia. However, the consultants strongly agreed that such training improves the likelihood of satisfactory outcomes for sedation and analgesia. The guideline recommends that personnel involved in the provision of sedation and analgesia be trained in the pharmacology of sedative/analgesic medications, as well as their antagonists. These individuals must be trained to recognize the complications of sedation and analgesia. At least one individual capable of establishing a patent airway and positive-pressure ventilation should be present when sedation and analgesia are administered. An individual or team with advanced cardiac life support should be available within 5 min (preferably less) when moderate sedation is administered (and should be in the procedure room for those rare cases where deep sedation is delivered for colonoscopy).

Availability of equipment/access

The literature supports the use of supplemental oxygen to reduce the frequency of hypoxemia during moderate sedation, is silent concerning the availability of emergency equipment such as defibrillators, and is equivocal regarding the relative efficacy of sedative/analgesic agents administered intravenously compared with agents given by other routes to achieve moderate sedation. The consultants agreed that supplemental oxygen decreases patient risk during moderate sedation, that a defibrillator should be immediately available, and strongly agreed that the intravenous route for sedative/analgesics increases the likelihood of satisfactory moderate sedation. The guideline recommends that emergency equipment to establish a patent airway and provide positive-pressure ventilation with supplemental oxygen, suction, resuscitation medications, pharmacologic antagonists, and continuous intravenous access should be present whenever sedation and analgesia are administered. In

the routine course of moderate sedation, supplemental oxygen should be available, and administered if hypoxemia is anticipated or develops.

Anesthetic induction agents used for sedation and analgesia

As stated earlier, narcotics and benzodiazepines comprise the standard parenteral medication administered by colonoscopists for sedation and analgesia. The ASA recognizes the increasing prevalence of deep sedation outside the operating room, and interest by endoscopists in anesthetic induction agents such as propofol. Interestingly, the guideline, written primarily by anesthesiologists, does provide for the use of such agents by nonanesthesiologists. The literature suggests that propofol and ketamine can provide satisfactory moderate sedation but is insufficient to determine whether moderate sedation with propofol is associated with a different incidence of adverse outcomes than similar sedation with midazolam. The consultants agreed that avoiding these medications decreases the likelihood of adverse outcomes during moderate sedation.

Kentrup and colleagues [21] examined the use of one of these medications, ketamine, as a premedication for colonoscopy. Ketamine produces a cataleptic-like state in which the patient is dissociated from the surrounding environment by direct action on the cortex and limbic system. It also causes release of endogenous catecholamines (epinephrine, norepinephrine) which maintain blood pressure and heart rate. Ketamine is a potent agent that produces dose-related decreases in level of consciousness culminating in general anesthesia. The goal of the authors was to minimize the dose of midazolam in a group of patients undergoing colonoscopy. Patients received ketamine and differing doses of midazolam based primarily on weight. They found that with the use of ketamine at sufficient analgesic doses, midazolam 0.05 mg/kg (or 3.5 mg for a 70-kg patient) provided optimal cooperation and pain tolerance without relevant depression in respiratory parameters. The clinical experience with propofol in colonoscopy is discussed later.

Recovery care

The literature is insufficient to examine the effects of postprocedure monitoring on patient outcomes. The consultants strongly agreed that continued observation and monitoring and predetermined discharge criteria decrease the likelihood of adverse outcomes for moderate sedation. The guideline recommends that following sedation and analgesia, patients be observed until they are near baseline level of consciousness and are no longer at risk for respiratory depression. Monitoring

oxygenation should be done at least periodically until the patient is no longer at risk for hypoxemia. Discharge criteria should be designed to minimize the risk of central nervous system or cardiorespiratory depression following discharge.

Use of anesthesiologists

The literature suggests that certain patients are at risk for complications related to sedation and analgesia. The guideline separates these patients into two categories. The first category includes patients with significant underlying medical conditions, such as severe cardiac, pulmonary, hepatic, or renal disease; the consultants agreed and the guideline recommends that these patients undergo evaluation by an appropriate medical specialist prior to administration of sedation and analgesia. Even after this consultation, if the patient is severely compromised or unstable or if it is likely that sedation to the point of unresponsiveness will be necessary to perform the procedure, consultation and involvement with an anesthesiologist should be obtained. In the second category is the patient with significant *sedation-related* risk factors (e.g. the uncooperative patient, morbid obesity, potentially difficult airway, sleep apnea); the consultants agreed and the guideline recommends that preprocedural consultation and involvement by an anesthesiologist will increase the likelihood of a satisfactory outcome.

Effect on outcomes

Of the multiple recommendations in the ASA guideline, more are based on expert opinion than on evidence. The rigorous personal and automated monitoring currently performed with sedation and analgesia increases the space requirements in the endoscopy suite and raises the cost of endoscopy. Since many of the recommendations are based on opinion rather than evidence, the possibility exists that one or more of these recommendations does not positively impact the desired outcome. Froehlich and colleagues [22] reported a nationwide survey of Swiss gastroenterologists to address this specific question. Data from 115 120 endoscopic procedures performed by 123 gastroenterologists were analyzed. Automated monitoring was rarely performed. The overall sedation-related morbidity was 0.1%, with no deaths. The authors point out that these figures are similar to those from the USA, where automated monitoring is common. The authors assert that clinically significant complications are rare with moderate sedation and analgesia, and raise the possibility that the degree of automated monitoring recommended in current practice guidelines may not truly improve outcomes. Nevertheless, the practicing clinician is wise to follow the current guideline recommendations. Preprocedural evaluation,

intra-procedural and postprocedural personal and automated monitoring, recovery protocols, emergency equipment, continuous intravenous access, and other measures mentioned above have become a de facto standard of care for patients receiving moderate sedation.

Colonoscopy without parenteral sedation and analgesia

Screening flexible sigmoidoscopy is typically performed without parenteral sedation and analgesia. Since a significant portion of the cost and time required to perform colonoscopy is related to sedation and analgesia, colonoscopy without parenteral sedation and analgesia has been proposed. Several European studies advocate the feasibility of unsedated endoscopy. In the previously mentioned study by Ristikankare and colleagues [12], 180 patients were randomized into three groups: sedation with midazolam, infusion of intravenous saline only, or no intravenous access at all. Shortly after the procedure, patients receiving midazolam rated the examination less difficult but otherwise there were no differences in other parameters, such as examination time, patient satisfaction, or endoscopist satisfaction. Eckardt and colleagues [23] performed 2500 colonoscopic examinations all started without premedication, with the administration of a sedative/analgesic agent in the event of significant discomfort; 95% of patients required no medication. In a similar design, Ladas [24] found that 92% of patients starting colonoscopy without sedation were able to complete the procedure without administration of sedation/analgesia, with a cecal intubation rate of 88%. Male gender and previous colon resection were associated with ability to complete colonoscopy without sedation. Thiis-Evensen and colleagues [25] performed screening colonoscopy in 451 patients without sedation and analgesia. The cecal intubation rate was 82%. Half the patients rated the examination very uncomfortable or moderately uncomfortable; 90% of patients voiced willingness to return in 5 years for a repeat examination under the same circumstances. The authors caution that this approach may decrease the overall cecal intubation rate. Cacho and colleagues [26] randomized 50 patients to sedation/analgesia or no medication prior to colonoscopy. In the nonmedicated group, two patients required medication to complete the examination, while 80% stated willingness to undergo a future colonoscopy without sedation. Overall pain scores were similar between the two groups.

In clinical studies in the USA, the results of unsedated colonoscopy are less optimistic. Herman [27] performed office colonoscopy in 212 consecutive patients, with parenteral benzodiazepine administered during the examination only for significant discomfort. The cecal intubation rate was 95%, and 82% of patients required no

medication. However, Early and colleagues [28] found that only 20% of patients approached about the concept of unsedated colonoscopy were willing to consider it. Male gender, higher levels of education, and low anxiety scores were associated with willingness to consider unsedated colonoscopy. Rex and colleagues [29] invited 250 patients to be randomized to sedation/analgesia vs. sedation/analgesia as needed; 17 who preferred no sedation and 163 who preferred sedation refused to be randomized. Therefore, 70 patients were randomized. Male gender, absence of preprocedure abdominal pain, and increasing age were correlated with willingness to be randomized. Only 6% of the patients on sedation/analgesia as needed received medication. It appears that there is a subset of patients willing to accept colonoscopy without sedation and analgesia with acceptable outcomes; however, in the USA it should be assumed that sedation and analgesia will be the expectation of the majority of patients.

A 50% mixture of nitrous oxide and oxygen has been shown to be effective in diminishing the discomfort associated with colonoscopy. In several clinical trials comparing nitrous oxide to parenteral sedation and analgesia, pain relief was equivalent and recovery times decreased with the use of nitrous oxide [30–33]. There are major drawbacks to the use of this agent, including inadequacy of ventilation and air exchange in endoscopy units not specifically designed for its use, a risk of significant hypoxemia [34], and the possible risk of spontaneous abortion among staff exposed to this agent [35].

Use of remifentanil and propofol for colonoscopy

With current demands on colonoscopists to increase the number of procedures and the reality that unsedated colonoscopy will not be consistently accepted by patients in the USA, attention is being given to agents with rapid onset and rapid recovery times while providing excellent sedation and analgesia. These agents are labeled for administration by anesthesiologists or others with advanced training in providing deep sedation or general anesthesia. Remifentanil is a narcotic analgesic intended for use during general anesthesia for continued analgesia. It is a rapidly acting agent with a rapid transition between intense analgesia and minimal residual effect. Greilich and colleagues [36] compared remifentanil to meperidine in 100 patients undergoing colonoscopy. Sedation and analgesia were administered by an anesthesiologist. The patients receiving remifentanil had less incidence of tachycardia, hypotension, and nausea but higher verbal pain and anxiety scores. The mean length of time before the patient was ready to leave after the procedure was 48 min for meperidine and 40 min for

remifentanil. DiPalma and colleagues [7] similarly concluded that there was no clear advantage to the use of alfentanil (another fentanyl derivative with rapid onset of action and rapid recovery) over fentanyl for colonoscopy.

Propofol is an anesthetic induction agent that may provide excellent moderate to deep sedation and markedly decreased recovery times compared with narcotic/benzodiazepine combinations. It is labeled for use by anesthesiologists or those with similar training. However, the ASA guideline does allow for use of these agents by nonanesthesiologists, provided that patients are monitored for deep sedation and that the practitioner administering the medication should be qualified to rescue patients from any level of sedation, including general anesthesia. This is problematic, since such training and qualifications are not part of current fellowship programs in gastroenterology, and it is not clear that ACLS certification alone meets this recommendation.

Nevertheless, there are multiple studies that have examined the use of propofol with colonoscopy, some of which involve the administration of the drug by nonanesthesiologists. Propofol may be given in combination with narcotics or benzodiazepines. Paspatis and colleagues [37] reported that synergistic sedation with propofol and midazolam was superior to pethidine and midazolam in a prospective randomized study. Reimann and colleagues [38] demonstrated that propofol and low-dose midazolam provided better procedure tolerance and decreased recovery times compared with midazolam and the opioid nalbuphine. Propofol administered in patient-controlled fashion for colonoscopy has also been investigated. Propofol was judged to be an effective agent when administered in this fashion, but since it is not an analgesic, it was usually combined with a narcotic to provide adequate pain relief [39–42]. Propofol may also be administered as a sole agent in bolus fashion or continuous drip at the discretion of the colonoscopist. Rex and colleagues [43] reported 2222 such patients, 977 of whom underwent colonoscopy. The medication was administered by gastrointestinal nurses under the supervision of the gastroenterologist. The overall experience was quite satisfactory for the patients and endoscopist/nursing team. However, four episodes of prolonged apnea necessitating brief mask ventilation were noted. From the same institution, Sipe and colleagues [44] randomized 80 patients to propofol vs. meperidine/midazolam for colonoscopy and found that propofol provided excellent patient satisfaction, quicker recovery times, and comparable safety profiles. It should be anticipated that more research will be conducted into the use of propofol administered by gastroenterologists for colonoscopy; however, at present, gastroenterologist-administered propofol should be considered a topic for clinical research and not one for clinical practice.

Summary

Standard sedation for colonoscopy is safe and effective when administered by colonoscopists. The medication typically used in current practice is a combination of narcotic and benzodiazepine. Certain measures are expected when sedation and analgesia is provided for colonoscopy, which are clearly outlined in the guideline prepared by the ASA. Unsedated colonoscopy can be accomplished in selected patients but is unlikely to gain widespread acceptance in the USA. Propofol is an agent that can provide excellent patient and colonoscopist satisfaction, and can increase productivity by decreasing recovery times. However, it may cause profound apnea and is therefore labeled for administration by anesthesiologists or others with similar training. With more experience, and more sophisticated monitoring and administration techniques, it may prove to be an agent safe and effective for administration by the gastroenterologist.

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Chapter 22

The Video Colonoscope

David E. Barlow

Introduction

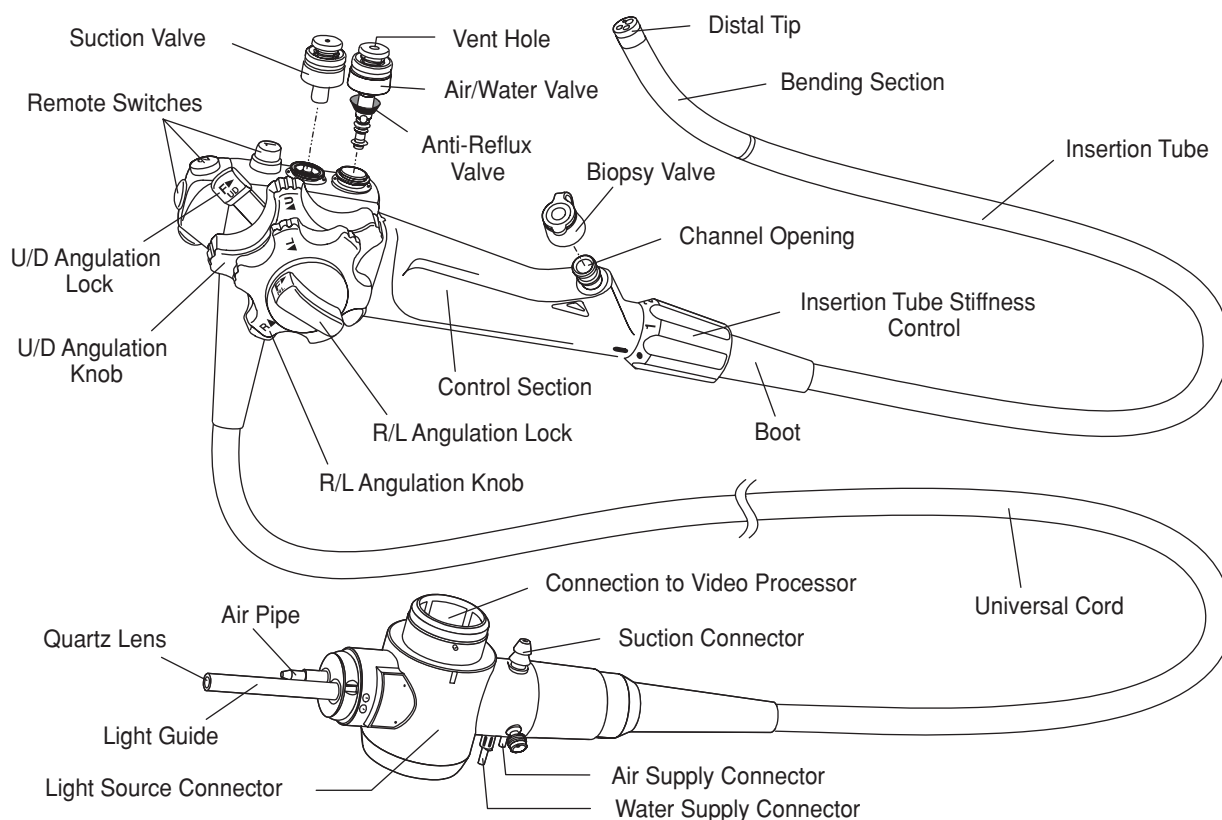
The modern video colonoscope embodies more than two decades of refinements in solid-state imaging technology and mechanical design. The basic components and controls of the colonoscope are illustrated in Fig. 22.1. The instrument is designed to be held and operated by the endoscopist's left hand. Some physicians use their index finger to alternately control the suction and air/water valves, while the rest of the left-hand fingers grip the instrument. Others use the index finger for the suction valve, the middle finger for the air/water valve, and the final two fingers to grip the instrument. The up/down angulation knob is manipulated by the left thumb. The left/right angulation knob is controlled

either by the left thumb and first two fingers of the left hand or, alternatively, by the right hand. The endoscopist's right hand is primarily used to control the insertion tube, pushing, torquing, and withdrawing as necessary.

Although alternative designs for the control section have been proposed (e.g. "pistol-grip"), the basic shape and layout of the instrument are relatively unchanged since the colonoscope was first introduced. Evolutionary changes made over the past 15 years include:

- elimination of the eyepiece found on fiberoptic instruments and using this space for three to four switches to control video processor functions (e.g. image freeze, image capture, etc.);
- substituting a watertight molded plastic shell for the simple thin aluminum shell found on earlier colonoscopes;

Fig. 22.1 Colonoscope: components and controls.



- and converting to valves that can be easily snapped on and off, in place of the former cumbersome screw-on valves.

Insertion tube

While endoscopists may prefer using a particular model of colonoscope for a variety of reasons, it is perhaps the instrument's insertion tube characteristics that more than anything else influence an endoscopist to select a particular colonoscope as the instrument of choice. Indeed, if any single specification of the instrument can determine the speed and ease with which the endoscopist can insert the instrument, it is the mechanical characteristics of the insertion tube.

Endoscope manufacturers have put significant effort into refining the construction of the insertion tube and selecting appropriate materials. Figure 22.2 illustrates the internal components of a typical colonoscope insertion tube. The insertion tube contains tubes for suction (biopsy), air and water feeding, and often an additional tube for a forward water-jet. Four angulation control wires run the length of the insertion tube. The very fine electrical wires that connect the charge-coupled device (CCD) image sensor at the distal tip of the endoscope to the video processor also travel through the insertion tube. These wires are in a protective sheath to prevent them from being damaged. The delicate glass fibers bringing light from the light source to the distal end also travel in a protective sheath. Colonoscopes with adjustable insertion tube flexibility have an additional component, a tensioning wire to control insertion tube stiffness.

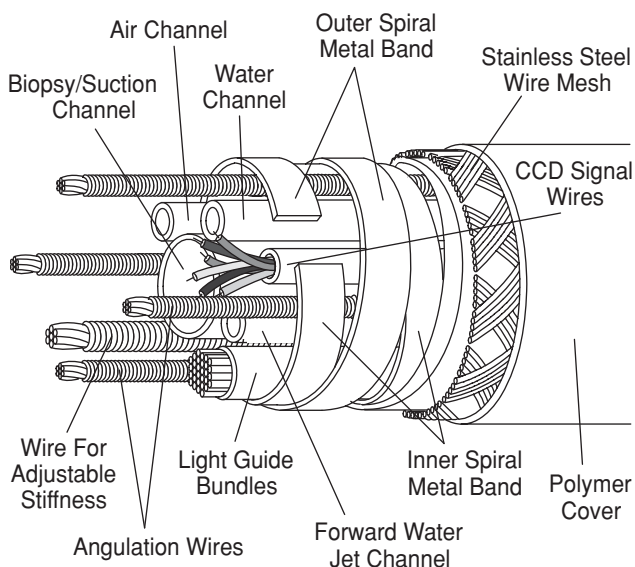


Fig. 22.2 Insertion tube: internal components and construction.

It is the job of the endoscope designer to pack all of these individual components into the smallest area possible in order to minimize the outer diameter of the insertion tube, but still provide enough free space to allow the components to move about without damaging the more fragile components (CCD wires, fiberoptic strands) as the instrument is torqued and flexed during use. A dry powdered lubricant is applied to all internal components to reduce the stress they place on each other during insertion tube manipulation.

Flexibility

As previously mentioned, the handling characteristics of the insertion tube are extremely important. For easy insertion, the instrument must be capable of accurately transmitting torque. Any rotation that the endoscopist applies to the proximal portion of the shaft must be transferred to the distal tip of the instrument in a one-to-one manner. The torqueability of the instrument is facilitated by flat spiral metal bands that run just under the skin of the insertion tube (see Fig. 22.2). Because these bands are wound in opposite directions, they lock against one another as the tube is torqued, accurately transmitting rotation of one end of the tube to the other. At the same time, gaps between these spiral bands allow the shaft to flex freely. The bands also give the insertion tube its round shape and prevent the internal components of the insertion tube from being crushed by external forces.

Fine strands of thin stainless steel wire, braided into a tubular mesh, cover the spiral metal bands. A plastic polymer layer, typically black or dark green, is then extruded over this wire mesh to create the smooth outer surface of the insertion tube. The polymer layer provides an atraumatic, biocompatible, watertight surface for the insertion tube. It is usually marked with numbers to gauge depth of insertion.

Colonoscopists ideally want a tube that is flexible yet highly elastic. They want the instrument to be sufficiently floppy (nonrigid) to conform easily to the tortuous anatomy of the colon and not to exert undue force on the colon or attached mesentery. On the other hand, they want the instrument to have sufficient column strength to prevent buckling when the proximal end of the instrument is pushed. (By comparison, a wet noodle, which is extremely flexible, has no column strength and easily buckles when pushed.) In addition to its flexibility, the colonoscope should have sufficient elasticity to pop back into a straightened condition whenever it is pulled back. This aids the endoscopist in removing colon loops. Therefore, the goal in designing the proximal portion of the insertion tube is to prevent the reformation of bowel loops. Obtaining the best combination of flexibility, elasticity, column strength, and torqueability is the art and science of insertion tube design.

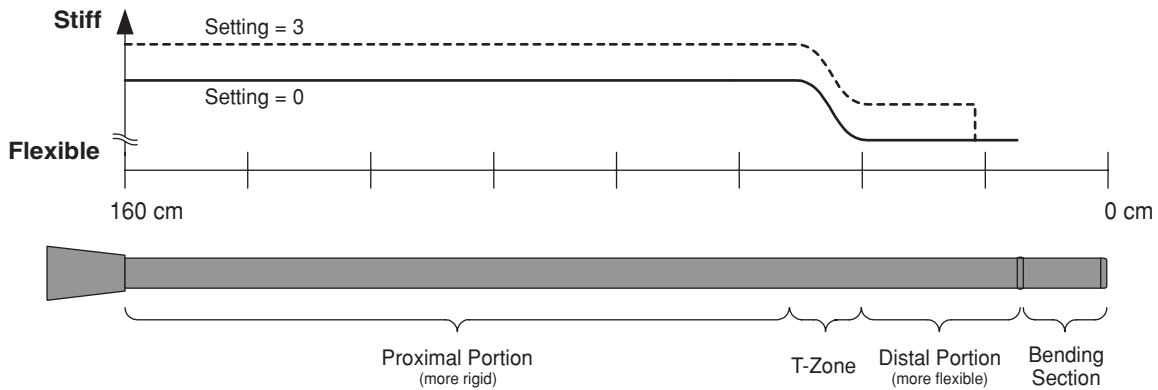


Fig. 22.3 The flexibility of the insertion tube varies over its length. It can be further stiffened by changing the setting on the adjustable stiffness control.

To further improve insertability, the flexibility of the insertion tube typically varies throughout its length. As Fig. 22.3 illustrates, the distal 40 cm of the insertion tube is significantly more flexible than the proximal portion of the tube. This variation in flexibility is achieved by changing the formulation of the tube’s outer polymer layer as it is extruded over the wire mesh during manufacturing. As Fig. 22.4 illustrates, the extruder typically contains two types of resin, one significantly harder than the other. Initially, as the distal end of the insertion tube passes through the machine, a layer of soft resin is applied to the distal 40 cm of the wire mesh. This soft resin is gradually replaced by the hard resin within a transition zone (T-Zone in Fig. 22.3) near the middle of the tube. The proximal portion of the insertion tube (50–160 cm) is then constructed totally from the hard resin [1]. The end result is an insertion tube that has a soft distal portion for atraumatically snaking through a tortuous colon, with a stiffer proximal portion that is effective at preventing loop reformation in those portions of the colon which have already been straightened by the colonoscope.

Fig. 22.5 Colonoscope insertion tube: adjustable stiffness tensioning system.

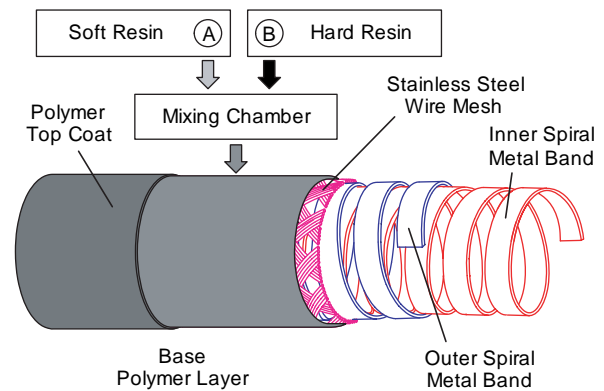
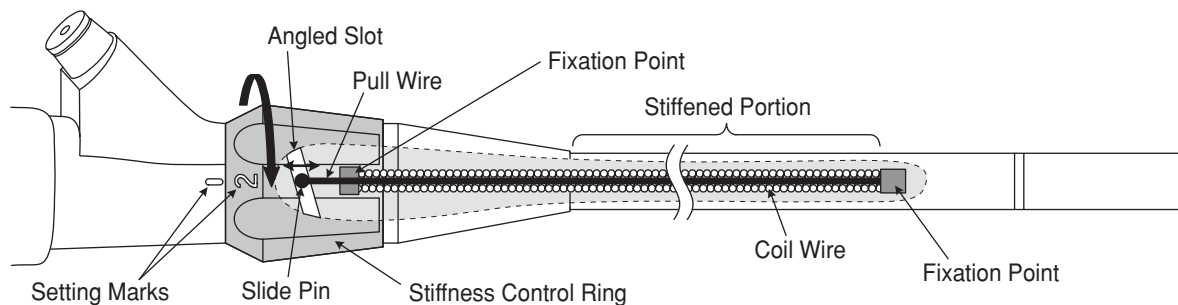


Fig. 22.4 Insertion tube manufacturing method.

Adjustable flexibility

Clinical experience has shown that endoscopists often disagree over what constitutes the “ideal” insertion tube. This may be due to differences in the endoscopist’s training, insertion technique, and past experience. In addition, some endoscopists have expressed a desire to change the characteristics of the insertion tube during the procedure itself, based on insertion depth or the patient’s anatomy. This has led to the development of an insertion tube with adjustable stiffness [2]. Colonoscopes with adjustable stiffness have a tensioning wire that runs the length of the insertion tube (see Fig. 22.2). The amount of tension in this wire is controlled by rotating a ring at the proximal end of the insertion tube, just below the control section (Fig. 22.5). When the inner wire in

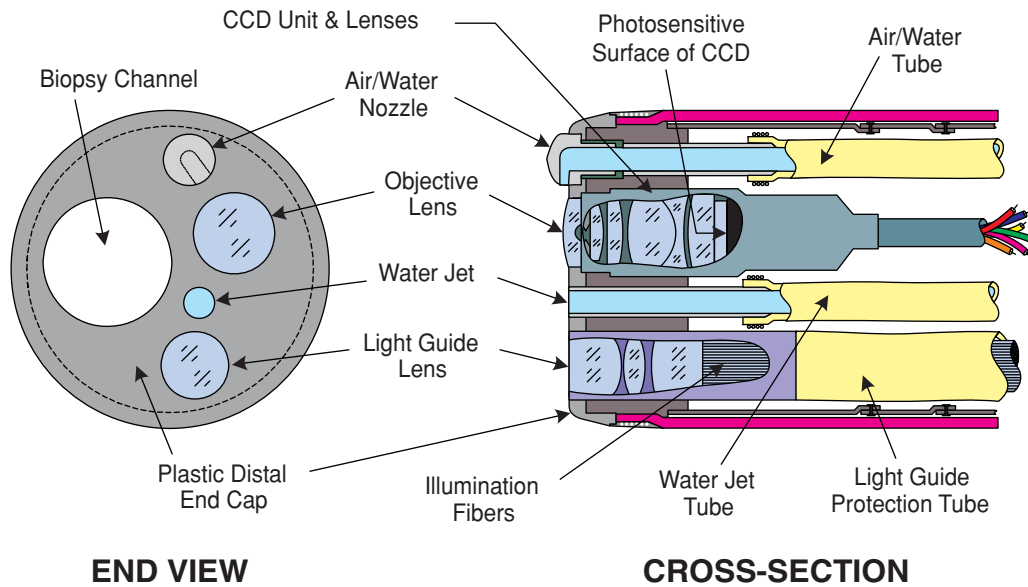


Fig. 22.6 Colonoscope distal tip.

the stiffening system is in the “soft” position, the stiffening system provides no additional stiffness to the insertion tube beyond that provided by the wire mesh and polymer coat. As Fig. 22.5 illustrates, when the control ring is rotated to one of the “hard” positions, the pin at the end of the pull wire is stretched via an angled slot and is put under heavy tension. This stiffens the coil wire surrounding the pull wire and adds significant rigidity to the insertion tube. As Fig. 22.3 illustrates, the base stiffness of the insertion tube (setting 0) is established by varying the mixture of hard and soft resins in the outer polymer coat of the insertion tube. However, this base stiffness can be further enhanced by increasing the tension in the variable-stiffness pull wire (setting 3).

Distal tip

An end view and a cross-section of the distal tip of a typical colonoscope are shown in Fig. 22.6. Light to illuminate the interior of the colon is carried through the instrument via fiberoptic illumination fibers. This light is then evenly dispersed across the colonoscope’s field of view via a light guide lens system. Some instruments have a single illumination system. Other instruments have two fiberoptic bundles and two light-guide lenses to improve illumination on both sides of the biopsy forceps (snare, etc.) and to facilitate the packing of components within the insertion tube.

The CCD unit, the solid-state image sensor that creates the endoscopic image, is placed behind the objective lens of the endoscope. This image sensor sends a continuous stream of images back to the video processor for display on a video monitor. It is very important that the objective

lens and CCD unit be well sealed to prevent condensation from fogging the image and to protect the imaging system from damage if fluid were to accidentally enter the instrument.

The channel used for biopsy and suction exits close to the objective lens on the distal tip. The position of the biopsy channel relative to the objective lens determines how accessories appear in the image as they enter the visual field. For example, on some instruments, the snare or biopsy forceps appears to emanate from the lower right corner of the image. On other instruments, these accessories enter the visual field from the lower left corner; and so forth.

The small tubes that carry air and water through the insertion tube (see Fig. 22.2) are typically merged into a single tube just above the bending section of the instrument (see Fig. 22.8). This combined air/water tube then connects to the air/water nozzle on the tip of the instrument. Under control of the endoscopist, water can be fed across the objective lens to clean it or air can be fed from the nozzle to insufflate the colon. Some colonoscope models have an additional water tube and a water-jet nozzle on the distal tip, used to wash the wall of the colon (see Fig. 22.6).

Bending section and angulation system

The most distal 9 cm of the insertion tube can be angulated under the control of the endoscopist. This deflectable portion is referred to as the bending section, and is constructed quite differently from the rest of the insertion tube. As Fig. 22.7 illustrates, the bending section is composed of a series of metal rings, each one connected to the ring immediately preceding it and the ring immediately following it via a freely moving joint. These

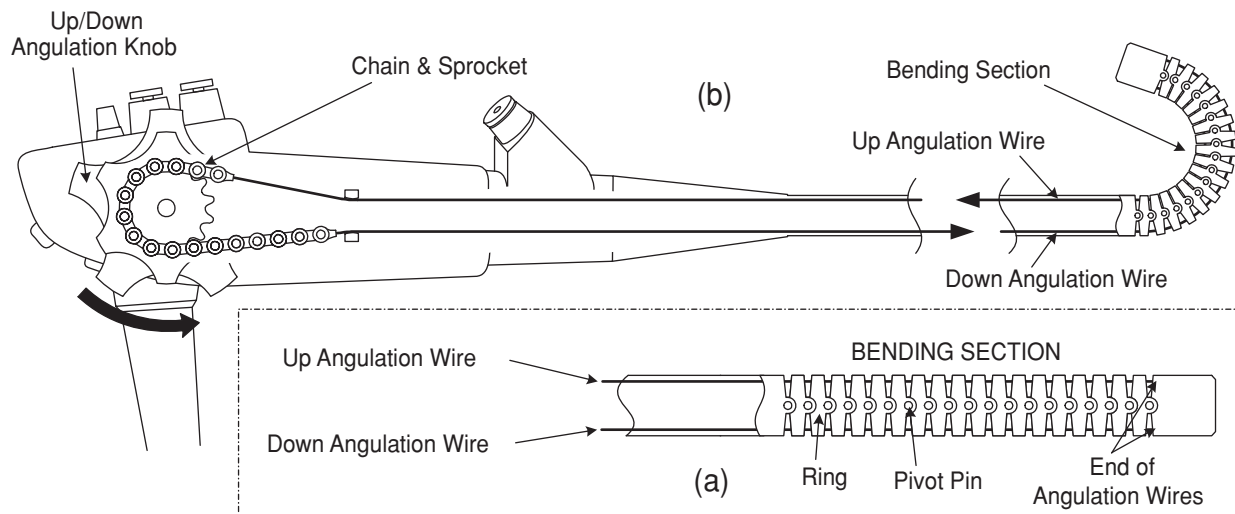


Fig. 22.7 Construction of bending section and angulation system.

joints are constructed using a series of pivot pins, each one displaced from its neighbors by 90° . This construction allows the bending section to curl in any direction. The direction of the curl is controlled by four angulation wires running the length of the insertion tube (see Fig. 22.2). These four wires are firmly attached to the tip of the bending section in the 3, 6, 9, and 12 o'clock positions, respectively. Pulling on the wire attached at the 12 o'clock position will cause the bending section to curl in the "up" direction and achieves what endoscopists refer to as "up tip deflection." Pulling on the wire attached at the 3 o'clock position will cause "right tip deflection." Pulling the other two wires will cause "down" and "left deflection" respectively.

The endoscopist is able to pull on each of these wires in turn by rotating either the up/down or right/left angulation knobs. (For simplicity, Fig. 22.7 illustrates only the up/down angulation system.) Rotating the two knobs together will produce a combined tip movement (e.g. upward and to the right). By using the two angulation knobs together, the endoscopist can sweep the tip of the endoscope in any direction. Colonoscopes typically have 180° of deflection in the up and down directions. Deflection in the right and left directions is typically limited to 160° to avoid overstressing the internal components of the instrument.

Air, water, and suction systems

A schematic of a typical colonoscope air, water, and suction system is shown in Fig. 22.8. An air pump in the light source provides air under mild pressure to a pipe protruding from the endoscope's light source connector.

This air is carried by an air channel (tube) to the air/water valve on the control section. If this valve is not covered, the air simply exits from a hole in the top of the valve (see Fig. 22.1). This vent hole allows the air pump to pump freely when air is not needed, thus reducing wear and tear on the pump. To insufflate the colon, the endoscopist covers the vent hole with the tip of the finger. This closes the vent and causes air pressure to build up inside the air feeding system. With the vent closed, the increasing air pressure forces air down the air channel, exiting the instrument through the nozzle on the distal tip. Colonoscopes typically have a maximum air flow rate of $30 \text{ cm}^3/\text{s}$.

A one-way valve is incorporated into the shaft of the air/water valve (see Fig. 22.1). This antireflux valve is necessary to hold air in the colon during patient examination. During examination, the colon is insufflated to a pressure considerably above atmospheric pressure. If it were not for this one-way valve in the system, air from the colon would flow back into the nozzle, up the air channel in the insertion tube, and out of the hole in the air/water valve whenever the operator removes a finger from the air/water valve. This antireflux valve is necessary to keep the colon insufflated.

Water is used to clean the objective lens of the instrument during the procedure and is stored in a water bottle attached to the light source or cart (see Fig. 22.8). In addition to feeding air for insufflation, the air pump also pressurizes this water container, forcing water out of the bottle and into the endoscope. Water from the water bottle is carried via a tube on the water bottle cap to the light source connector of the endoscope. It is then carried by the water channel up the universal cord to the air/water valve. When the endoscopist depresses the air/water valve, it allows water to continue down the water channel in the insertion tube and out of the nozzle on the

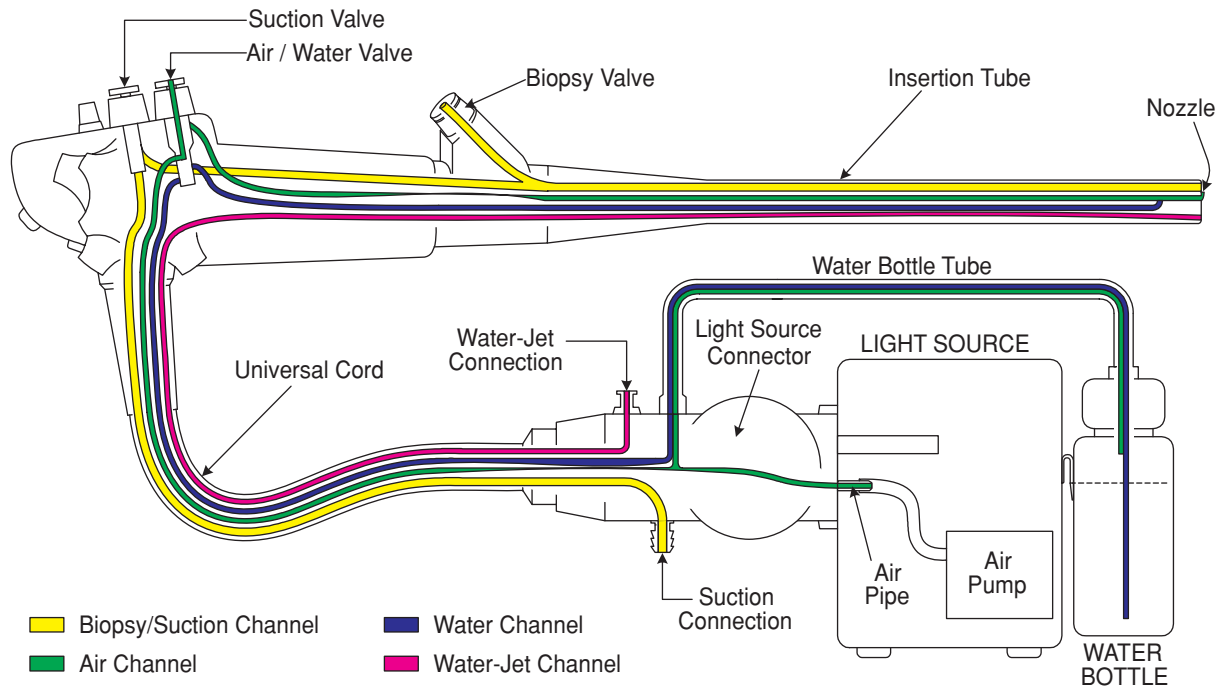


Fig. 22.8 Schematic representation of a typical colonoscope air, water, and suction system.

distal tip. The nozzle then directs this water across the surface of the objective lens, thereby cleaning it.

Suction is also controlled by a valve. A suction line, either from the hospital's wall suction system or from a portable suction pump, is connected to the light source connector of the endoscope. A slight vacuum is applied to the suction channel in the universal cord. When the endoscopist depresses the suction valve, suction is further applied to the suction-biopsy channel within the insertion tube. Any fluid (or air) present at the distal tip of the endoscope will be drawn into the suction collection system. A channel-opening valve (also called a biopsy valve) closes off the proximal opening of the biopsy channel and prevents room air from being drawn into the suction collection system.

There are several inherent safety features in the design of the air, water, and suction system shown in Fig. 22.8.

1 There is no air valve, which could stick in a continuously "on" position and result in accidental overinsufflation of the patient. Rather, the air simply exits the vent hole in the valve unless the physician covers this opening.

2 In the event that the suction system becomes obstructed and the endoscopist has difficulty with possible overinsufflation, all valves can quickly be removed from the endoscope. This will stop all feeding of air and water and will allow the patient's colon to depressurize through the open valve cylinders.

Illumination system

Colonoscopes use an incoherent fiberoptic bundle to carry light from the external light source to the distal tip of the endoscope. This fiber bundle is composed of thousands of hair-like glass fibers (30 μm in diameter) that are optically coated to trap light within the fiber and to transmit it from end to end via a phenomenon known as *total internal reflection*. Light rays entering one end of such a fiber reflect off the walls of the fiber many thousands of times before exiting the opposite end of the fiber. The types of glass used to make the core and cladding of the fiber and the dimensions of the core and cladding are all carefully chosen to enable the fiber bundle to carry as much light as possible (for a more complete discussion of fiber optics, see reference 3).

Endoscopic light sources typically employ 300-W xenon arc lamps to produce the bright white light needed for video endoscopy. These lamps also produce considerable heat. Heat sinks, infrared filters, and forced-air cooling systems within the light source prevent the light-guide fiber bundle from overheating and burning. A close inspection of the tip of a colonoscope's light guide will reveal a burn-resistant quartz lens that serves to collect light from the light source lamp and direct it into the endoscope (see Fig. 22.1). At the other end of the endoscope, the light-guide lens at the distal tip of the instrument spreads this light out uniformly over the visual field (see Fig. 22.6). An automatically controlled aperture (iris) in the light source controls the intensity of the light emitted from the endoscope (see Fig. 22.23). When the endoscope is looking down

the lumen of the colon and bright light is required, the aperture in the light source opens up, allowing the colonoscope to transmit maximum light. On the other hand, when the colonoscope tip is very close to the colon wall and the illumination is very bright, the aperture in the light source automatically closes down to reduce the amount of light exiting the light source. If illumination is too low, the image on the monitor will be dark and grainy. If the illumination is too strong, the image on the monitor will be washed out (i.e. "bloom"). The video processor automatically keeps the brightness of the illumination within a range that is acceptable for the CCD image sensor by carefully controlling the amount of light produced by the light source.

Solid-state image capture

The image sensors used in video colonoscopes are typically referred to as CCDs. These sensors are solid-state imaging devices made of silicon semiconductor material. The silicon on the surface of the sensor is responsive to light and exhibits the *photoelectric effect*. When a photon of light strikes the photosensitive surface of the CCD, it displaces an electron from a silicon atom on the surface. This produces a free, negatively charged electron in the silicon material and a corresponding positively

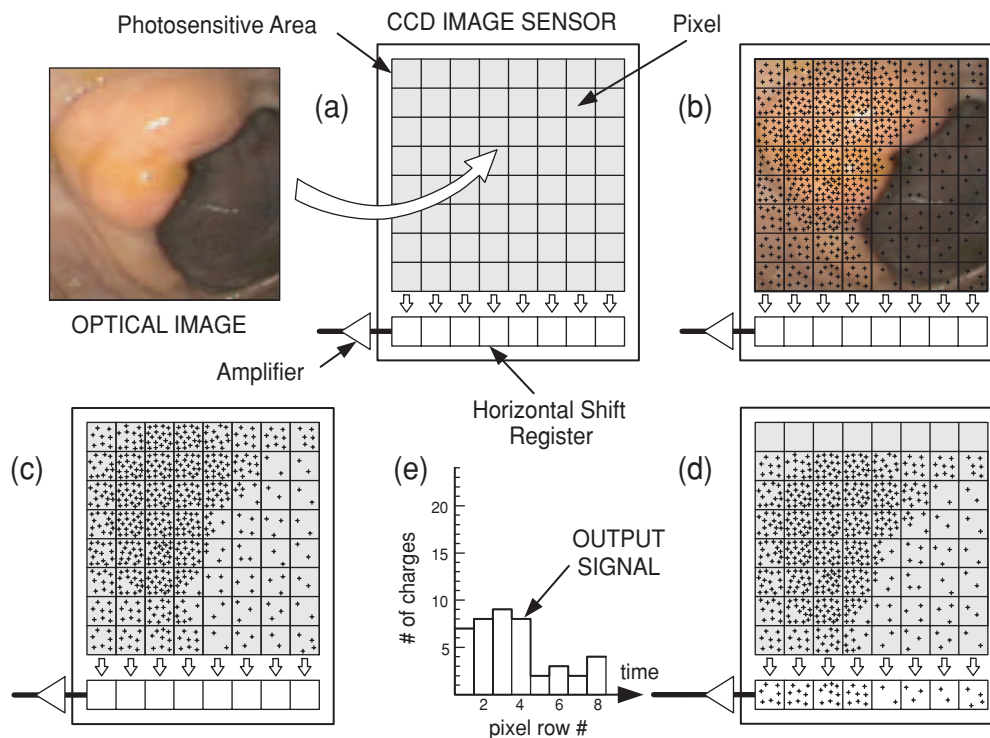
charged "hole" in the crystalline structure of the silicon where the electron was previously bound. As additional photons hit the surface of the sensor, more free electrons and more corresponding holes are created. The charges built up on the surface of the sensor are directly proportional to the amount of light falling on the CCD.

Although a single photosensitive element can be used to measure the brightness of the light falling on the device (as in a light meter), it cannot reproduce an image. In order to reproduce an image, the photosensitive surface must be divided up into a matrix of thousands of small independent photosites. When an image is focused on the surface of such a sensor, the brightness of the image is automatically measured at each individual photosite. Knowing the brightness of every point in the image allows the processing system to subsequently reproduce the image on a viewing monitor or to generate a printed copy of the image.

The surface of a CCD sensor is divided into a rectangular array of discrete photosites, individually referred to as picture elements ("pixels"). Figure 22.9 illustrates a sensor with such an array. For simplicity, the array illustrated in Fig. 22.9 contains only 64 pixels in an 8-row by 8-column matrix. An actual endoscopic CCD contains several hundred thousand pixels. The greater the number of pixels on a CCD, the higher the resolution of the reproduced image.

In a video-image colonoscope, the CCD is located in the distal tip of the instrument directly behind the objective lens (see Fig. 22.6). The objective lens focuses a

Fig. 22.9 Schematic representation of how a line-transfer CCD captures an optical image. The "electrical representation" of the image is then read off in an orderly manner.



miniature image of the observed mucosa directly on the surface of this sensor (see Fig. 22.16). The pattern of light falling on the CCD (i.e. the image) is instantly converted into an array of stored electrical charges, as a result of the photoelectric effect previously described (see Fig. 22.9). Because the charges stored in each of the individual pixels are isolated from neighboring pixels, the sensor faithfully transforms the optical image into an electrical replica of the image. This electrical representation is then processed and sent to a video monitor for reproduction.

Pixels in dark areas of the image develop a low voltage, due to the generation of fewer charges. Pixels in brighter areas of the image develop a proportionately higher voltage, due to the creation of more electron-hole pairs. Each pixel is able to develop any charge, from some minimum to some maximum, depending on the brightness of the incident light. This process is linear. Doubling the number of photons of light falling on a pixel doubles the number of charges generated at the pixel until they reach the maximum storage capacity of the photosite. This conversion of an optical image into an electrical replica of the image is illustrated in Fig. 22.9.

“Reading” the image created on the CCD

After the CCD is exposed to the image, the charges developed in the CCD must be “read” in an orderly manner and then processed to reproduce the original image. The manner in which the charges are moved about within the CCD as they are read depends on the configuration of the CCD. The three most common types of CCDs are the line-transfer CCD, the frame-transfer CCD, and the interline-transfer CCD [4]. Each of these CCD types has specific advantages in terms of the CCD’s sensitivity to light (i.e. the brightness required of the colonoscope illumination system), the type of light source required (strobed or nonstrobed), the size of the CCD (which in turn affects the size of the distal tip of the endoscope), and the speed at which the charges can be transferred out of the CCD. The method used to read an image from a line-transfer CCD is used here as an example.

The CCD schematically illustrated in Fig. 22.9 is a line-transfer CCD. Figure 22.9(a) illustrates the projection of an optical image onto the photosensitive surface of the CCD. Electrical charges are developed at each photosite in the array following brief exposure to the image (see Fig. 22.9b,c). (For simplicity, Fig. 22.9 illustrates an array with only a few pixels and only a few resulting charges. These charges are represented by small + signs within the photosites.)

The charges within each pixel are then controlled and shifted over the surface of the CCD via electrodes adjacent to each photosite (not shown in Fig. 22.9). By varying the voltages applied to these electrodes, the elec-

trons within individual pixels are transferred as “charge packets” from one pixel to another. Sequential voltage changes on these electrodes march the charges toward the bottom edge of the CCD and into a horizontal shift register (see Fig. 22.9d). The charges in the horizontal shift register are then passed through an output amplifier and converted into an output signal. The output signal fluctuates in direct proportion to the number of charges stored in each pixel. At the point in the process illustrated in Fig. 22.9(e), the bottom row of the original image is being read out and sent to the video processor for reconstruction. The electrical representation of the entire image has shifted down one row on the CCD.

Once the horizontal shift register has been read and cleared (emptied), the charges in each pixel of the array are then sequentially transferred down to the pixel below, resulting in a second shift of the image replica. This fills the horizontal shift register with the charges that were originally in the second-to-the-bottom row of the array. The charges in the horizontal shift register are again read out, resulting in an output signal that is representative of the brightness of the image falling on the second-to-the-bottom row of the original image. The processing of the image replica continues, in a step-by-step fashion, until the entire CCD has been read. Once the CCD is read and cleared, it is ready for another exposure.

The “charge-coupling” process (i.e. the transfer of charges from pixel to pixel as packets) gives the CCD its name. The charges in the furthest corners of the CCD are actually moved sequentially through several hundred photosites before they reach the horizontal shift register. In current video endoscopes, the CCD is exposed, read, and reexposed 60–90 times each second. To maintain image fidelity during these repetitive transfers, it is essential that these charge packets remain intact with no loss or gain in charge quantity as they undergo hundreds of thousands of transfers per second as the CCD is being read.

One characteristic of a line-transfer CCD is that the photosensitive area of the CCD (the photosite array) must be shielded from light during the entire time that the image is being transferred and read. This is necessary to prevent mixing information from the image being transferred through the photosite array with new charges being generated at the photosites due to the light still falling on them. To preserve the original image, the photosites must be completely dark while the image replica is being transferred. One method of doing this in an endoscopic application is to strobe, or momentarily interrupt, the light emitted by the endoscope as the CCD is being read. This creates a momentary burst of light to expose the image sensor, followed by momentary darkness, as the CCD is read and cleared. Endoscopists who have used a red, green, and blue sequential endoscopy system (typically called a “black and white” CCD

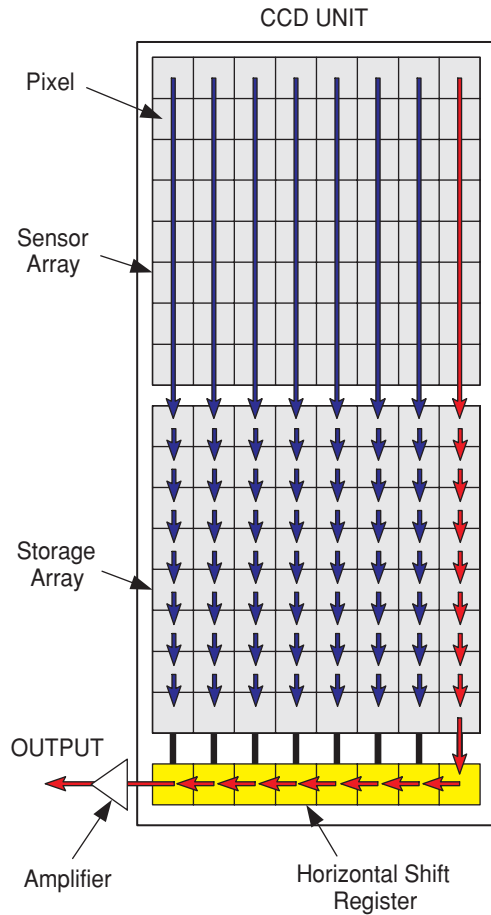


Fig. 22.10 Schematic representation of a frame-transfer CCD.

system) are quite familiar with the concept of strobed endoscopic light sources.

Types of CCD

As mentioned above, as an alternative to the line-transfer CCD, some video endoscopes use a frame-transfer CCD (Fig. 22.10). The frame-transfer CCD differs from the line-transfer CCD in that the frame-transfer CCD has a second array, used only for charge storage. The first array is a photosite (sensor) array, which generates an electrical replica of the image, similar to the line-transfer CCD. After creating the image replica, all of the charges in the sensor array are immediately transferred to the storage array (illustrated by the long arrows in Fig. 22.10). Here they are held until they can be read out, line by line, in a process similar to a line-transfer CCD (illustrated by the short arrows in Fig. 22.10). The red arrows illustrated in Fig. 22.10 define the path taken by the charges in the upper right corner pixel of the sensor. Charges in other pixels take a similar path.

The advantage of the frame-transfer CCD is that the device can be collecting light and generating charges

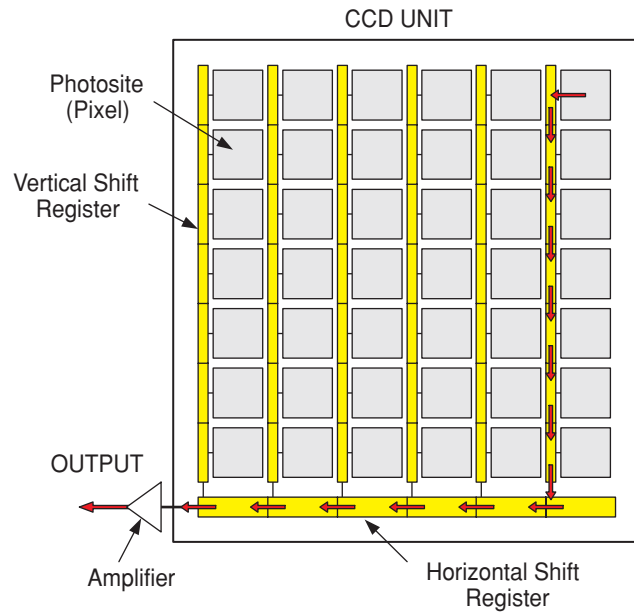


Fig. 22.11 Schematic representation of an interline-transfer CCD.

in the sensor array while the storage array is being read and processed. Since the frame-transfer CCD has more time to gather light, it does not require as much illumination as a line-transfer CCD. As a result, the number of light-guide fibers in the endoscope can be reduced. The disadvantage of frame-transfer CCDs is that they are physically larger than line-transfer CCDs because of the addition of a storage array. This additional size is a distinct drawback in many endoscopic applications. In addition, frame-transfer CCDs also require illumination strobing.

The interline-transfer CCD is a hybrid of the previous two types. This type of CCD has vertical shift registers placed adjacent to each column of photosites (Fig. 22.11). Immediately after exposure, the charges developed at the photosites are transferred in one quick step to the adjacent vertical shift registers. Owing to the rapid one-step transfer of charges, illumination of the CCD does not need to be interrupted and the CCD can continue to collect light. In the mean time, the charges in the vertical shift registers are transferred, step by step, down to the horizontal shift register, where they are then read in an orderly manner. (The red arrows in Fig. 22.11 illustrate the path of charges generated in the upper right corner pixel.) The vertical shift registers are shielded from light, allowing them to be emptied as the CCD is continuously exposed to light. The CCD thereby collects a second image as the first is being read. When the vertical shift registers are finally empty, the newly created image replica in the sensor array is instantly transferred from the photosites to the vertical shift registers, and the process repeats.

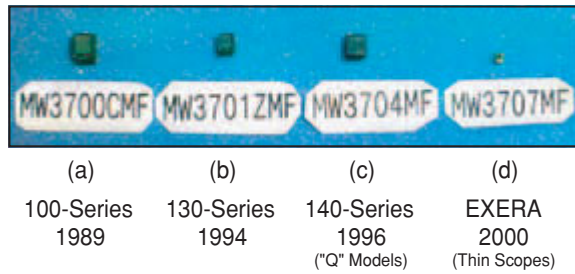


Fig. 22.12 History of CCDs used in Olympus EVIS color-chip endoscopes.

A big advantage of the interline-transfer CCD is that it does not require strobing of the illumination. Since the entire sensor array is cleared to the vertical shift registers in one step, the sensor array is immediately ready to capture the next image. So-called "color chip" endoscopes, which use continuous nonstrobed light sources, are examples of interline-transfer CCD systems.

All three types of CCD described above have been used in commercial video colonoscopes. Each type has its own advantages and disadvantages in terms of physical size, circuit complexity, light sensitivity, and illumination requirements. Because of the predominance of "color chip" systems, the interline-transfer CCD is currently the most commonly used CCD in the USA.

History of endoscope CCD development

The first video colonoscope was introduced in 1983 by Welch Allyn [5]. The market launch of this system was made possible when advancements in image sensor technology allowed the CCDs used in hand-held video cameras to be reduced to a size that would fit within the distal tip of an endoscope. Since then, technology has continued to advance, allowing further reductions in the physical size of the CCD, while at the same time increasing the number of pixels in the sensor array. This has allowed video colonoscopes to become progressively thinner, with larger channels and higher resolution, with each new generation. Figure 22.12 illustrates the progress made in reducing the size and increasing the resolution of sensors over the last 13 years. The CCD in Fig. 22.12(b) is smaller in size yet has the same resolution as the CCD in Fig. 22.12(a). The CCD in Fig. 22.12(c) is approximately the same size as the one shown in Fig. 22.12(a) but has much greater resolution. The CCD in Fig. 22.12(d) is the world's smallest endoscopic CCD and is used in the very thinnest video endoscopes.

Shape of displayed image

All endoscopes emit a conical beam of light from their distal tip (see Fig. 22.16). Likewise, the round objective lens at the tip of the instrument produces a circular-

shaped image of the tissue being viewed. Because of these geometric considerations, fiberoptic colonoscopes typically use round image fiber bundles and a round image is seen in the fiberscope's eyepiece.

In contrast, the photosensitive area of a CCD is always square or rectangular, since all CCDs use a sensor array composed of columns and rows to capture and transfer charges. The manner in which the video colonoscope designer attempts to make best use of the mismatch between the round endoscopic image and the square/rectangular image sensor determines the shape of the video endoscopic image as it appears on the monitor. If the magnification of the lens system is adjusted to fit the endoscopic image entirely within the borders of the photosensitive area, then a round endoscopic image will be reproduced on the observation monitor (Fig. 22.13a). The advantage of this design is that the entire wide-angle view of the colonoscope is captured. The disadvantages are that the image on the monitor is relatively small, and the image has low resolution because pixels in the corners of the CCD are not illuminated and therefore not used.

If the designer enlarges the image so that it covers the entire CCD, a square image will result (Fig. 22.13b). In this case the full CCD is used but large portions of the endoscopic image fall outside the photosensitive array and are not captured and not displayed. This wastes light produced by the endoscope and makes large portions of the peripheral endoscopic field of view unobservable.

A compromise between these two extremes is illustrated in Fig. 22.13(c). In this case the objective lens is designed to produce an intermediate-sized image. This allows the CCD to capture most but not all of the projected image, while minimizing the number of unused pixels at the corners of the CCD. This results in an eight-sided image on the observation monitor. All three imaging configurations have been used by video endoscope manufacturers.

Reproduction of color

All solid-state image sensors are inherently monochromatic devices. They can reproduce only black-and-white images. The silicon photosites employed on the surface of the CCD develop charges in proportion only to the intensity (brightness) of the light falling on the array. They cannot distinguish the color of the incident light. For an endoscope to reproduce the necessary attribute of color, the system must have an additional means to analyze the color (wavelength) of the light falling on the sensor.

To understand the process of color reproduction, it is helpful to first understand how humans perceive color. All photographic and electronic imaging systems attempt to mimic the way in which the human eye and

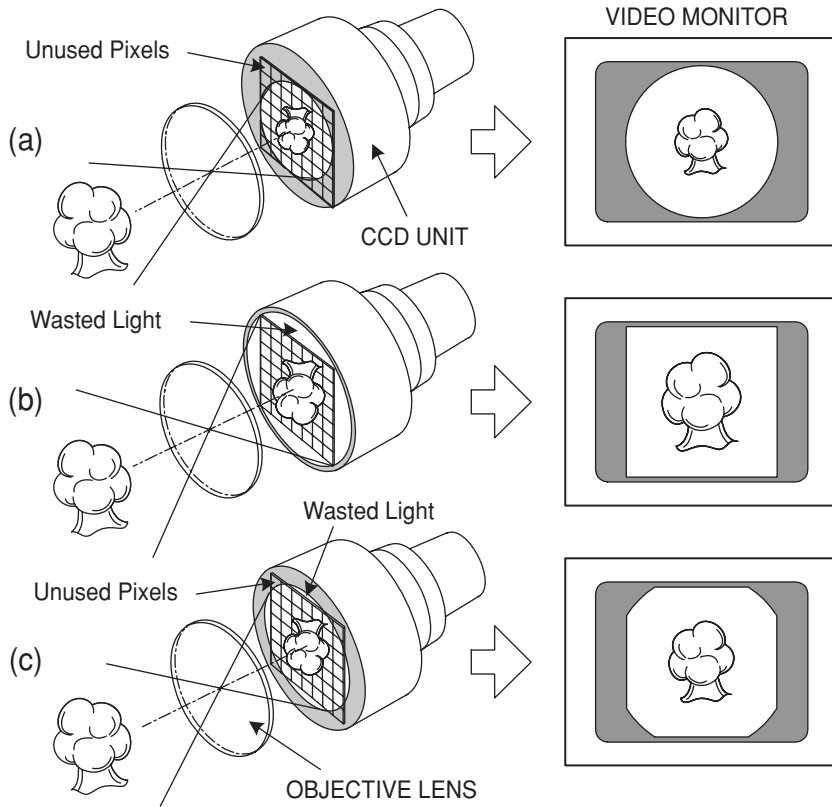


Fig. 22.13 Design and magnification of the objective lens affect the shape of the image displayed on the monitor.

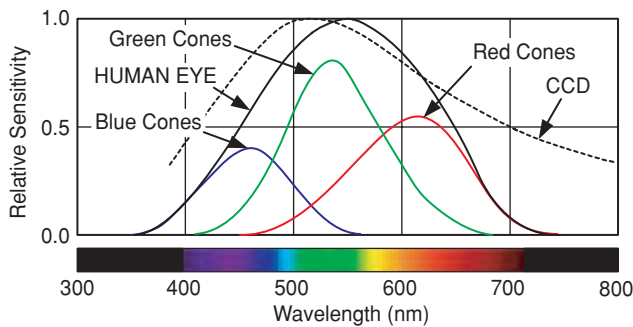


Fig. 22.14 Light sensitivity of CCDs compared with the human eye.

brain respond to color. The sensitivity of the human eye to light intensity varies with the wavelength or color of the light (Fig. 22.14). The human eye is most sensitive to green and less sensitive to reds, blues, and other colors. The CCD has a similar but broader sensitivity, ranging from infrared light (wavelengths > 780 nm), through the visible spectrum, to ultraviolet light (wavelengths < 380 nm).

Anybody who mixes paints or dyes of two or more colors will find that they are incapable of detecting the original colors but instead see a single, newly created color. When observing a mixture of colors, the human eye is nonanalytical and cannot distinguish the original component colors. The hue of this newly created color is

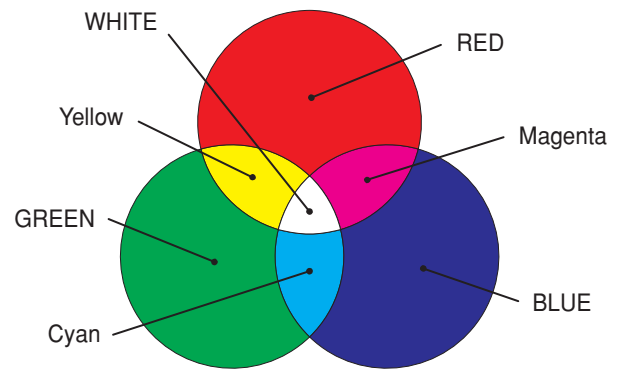


Fig. 22.15 Color theory: additive primary colors.

determined by what scientists refer to as *trichromatic vision*.

Trichromatic vision

Nearly any color to which the human eye is sensitive can be matched by mixing light of three colors: red, green, and blue. If three light projectors were fitted with red, green, and blue filters and the projected light were overlapped, the resulting image would appear similar to that shown in Fig. 22.15. The color resulting from the overlap of the red and green projectors would be indistinguishable from monochromatic yellow light. Likewise, light

from the overlapping green and blue projectors would produce the mental sensation of looking at pure cyan light. The overlap of red and blue produces magenta. It is somewhat amazing that where all three of the projectors overlap in the center, the observer will see an area of pure white, with no hint of the three component colors. If the intensities of each of the three projectors were accurately controlled and varied, it would be possible to reproduce essentially any spectral color in the central area of the overlap.

In the early 1800s, Thomas Young performed such experiments with projectors and was the first to propose the theory that humans possess trichromatic vision. His experiments, and those of his successors, have caused scientists to postulate that humans perceive color through the stimulation of three different types of neural cells (cones) located in the retina of the eye. These cells are presumed to have the approximate sensitivity curves depicted for the red, green, and blue cones in Fig. 22.14. Since our eyes perceive color based on a trichromatic system, we can trick the eye into seeing full color when looking at a brochure printed using inks of only three colors. A chemist can manufacture color film using only three color emulsions. An engineer can design a color video monitor using only red, green, and blue phosphors. In fact, the basis of all color video systems is tightly linked to the concept of trichromatic vision.

Theory of color video

All video images are reconstructed using the three component colors of red, green, and blue. Because these three colors can be additively combined to mimic all other spectral colors, they are commonly referred to as the *additive primary colors*. It is these three colors that are in fact the colors of the phosphors used to create full-color images on the face of a video monitor (see Fig. 22.16).

There are currently two very different types of color imaging systems used in commercial video endoscopes. The first commercial video-image endoscope system, the VideoEndoscope™ introduced by Welch Allyn in 1983, was based on a red, green, and blue (RGB) sequential imaging system. Many current instruments continue to use this system. The second system, the so-called “color-chip” endoscope, despite being developed later, has now become the predominant system worldwide. Each color reproduction system has its own advantages and disadvantages, as explained below.

RGB sequential imaging

The components of an RGB sequential videoscope system are schematically shown in Fig. 22.16. The endoscope has a monochromatic (black and white) CCD

mounted in its distal tip. The objective lens at the tip of the endoscope focuses a miniature image of the endoscope’s field of view on the photosensitive surface of this CCD. This image is illuminated via a fiberoptic bundle running through the endoscope (not shown), carrying light from a lamp within the light source to the distal tip of the endoscope. Unlike the light used for fiberoptic or color-chip endoscopes, this light is not continuous but is strobed or pulsed.

The high-intensity xenon lamp within the light source emits continuous white light with the approximate color temperature of sunlight. A rotating filter wheel with three colored segments (red, green, and blue) is placed between this lamp and the endoscope’s light-guide post. This filter wheel chops and colors the light falling on the endoscope’s light-guide bundle. When observed at the distal tip of the endoscope, this illumination appears to be a flickering white light rather than actual sequential bursts of red, green, and blue. Rotating at 20–30 revolutions per second (rps), these three primary colors appear to merge, creating white illumination when observed with the unaided eye.

The purpose of this unique illumination system is to produce three separate monochromatic images, each obtained when the field of view is sequentially illuminated by each of the three primary colors in turn. During the fraction of a second when the red filter is in the light path, the interior of the colon is illuminated only by red light. The CCD image sensor captures a monochromatic (black-and-white) image of the colon as it appears under this red illumination (Fig. 22.17). Areas of the colon that are naturally reddish in color reflect heavily under red light and appear to be bright. Areas of tissue with less red reflect red light weakly and appear dark under red illumination.

After a monochromatic image of the colon wall is obtained under red illumination, the filter wheel rotates to the adjacent opaque area of the wheel. At this point the endoscopic illumination goes momentarily dark and the image on the CCD is read, directed through a processing and switching circuit, and stored in the “red image” memory bank of the video processor (see Fig. 22.16).

After the red image is stored, the filter wheel rotates to place the green filter in the light path. A monochromatic image of the colon wall as it appears under green illumination is then obtained by the CCD (Fig. 22.17). This image is then read and sent to the video processor for storage in the “green image” memory bank. In a similar manner, a third monochromatic image is obtained when the filter wheel rotates to the blue segment; this image is correspondingly stored in the “blue image” memory bank. This sequence of capturing a set of images for each of the three primary colors is repeated 20–30 times each second, the precise speed being determined by the video processor. Synchronization circuitry

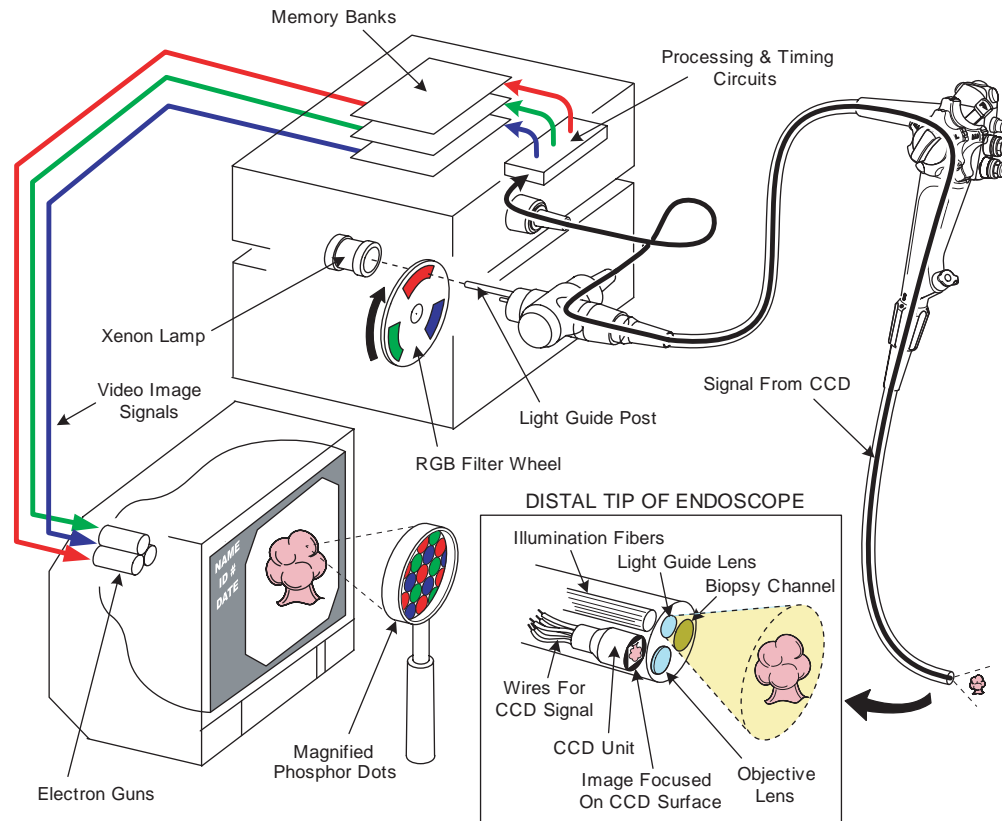


Fig. 22.16 Schematic representation of an RGB sequential endoscope imaging system. The rotating primary color filter wheel results in sequential monochromatic illumination of the view.

matches the rotation of the filter wheel with the read-out of the CCD, and sequences the switching circuit to direct each new image to the proper memory bank (see Fig. 22.23).

Color-chip video imaging

A color-chip CCD is essentially a black-and-white image sensor with a custom-fabricated, multicolored filter bonded to its surface. This filter allows the CCD to directly and simultaneously resolve the component colors of the image. Often, the term *instantaneous single-plate CCD* is used to emphasize that all three color components are obtained concurrently by a single plate, or CCD.

There are a variety of ways to construct a color CCD. One of the simpler methods is to cover the CCD with an RGB-stripped filter (Fig. 22.18). Alternate columns of pixels on the CCD are covered with precisely aligned red, green, and blue strips of filter material. When an image is projected onto the face of such a CCD, pixels behind the red filter segments capture the red component image directly. Likewise, pixels located behind the

green and blue filter strips allow reconstruction of the green and blue component images respectively.

Conceptually, the components of the RGB sequential video system (described earlier) and the RGB-stripped color chip system are the same, except for the fact that the filter segments that were previously mounted on a rotating filter wheel and placed in the illumination system have now been miniaturized, cut into thin strips, and bonded to the surface of the CCD. Rather than coloring the endoscope's illumination, they now act to filter the image before it hits the photosensitive surface of the CCD.

Although RGB-stripped CCDs are used in other camera applications, they are not commonly used in endoscopes. Endoscopes typically use a color-mosaic filter of the type shown in Fig. 22.19. It is possible to design a mosaic filter with a number of different color configurations; however, the color choices and the corresponding algorithm shown in Fig. 22.19 are by far the most common. The colors used in this filter are yellow, cyan, and white (no filter). These segments are arranged in a 2×2 pixel box pattern that regularly repeats over the face of the CCD. Since the final-output signals to be sent to the observation monitor must be the standard red, green, and blue component images, the image produced behind this yellow/cyan/white filter must first be converted into its primary red, green, and blue components prior to display.

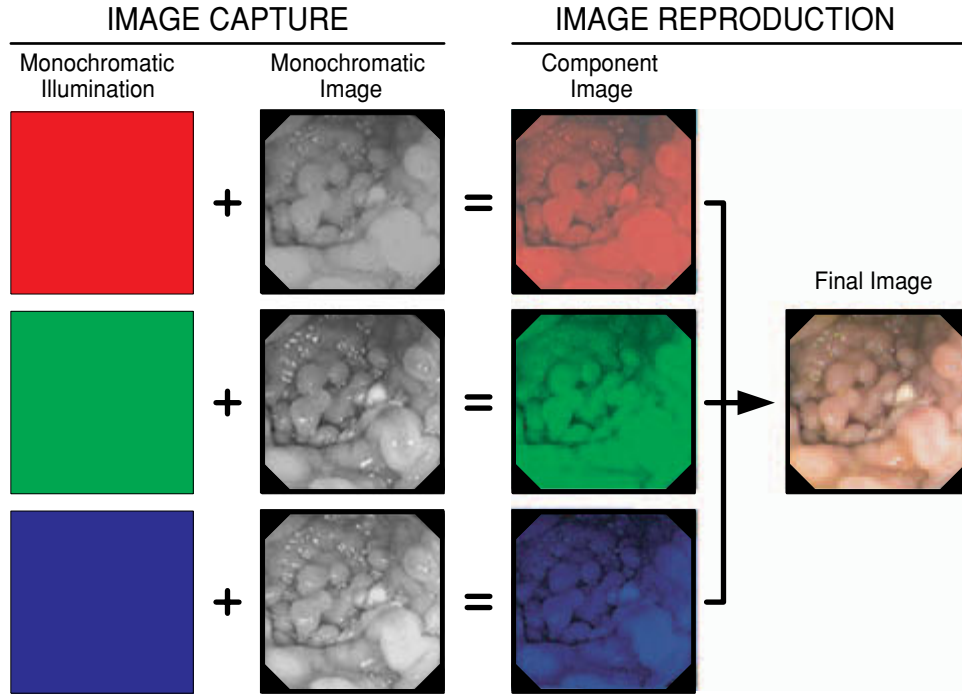


Fig. 22.17 RGB sequential imaging system. The tissue is sequentially illuminated by red, green, and blue light while monochromatic (black and white) images are captured in sequence. These component images are then fed to a video monitor, which generates RGB component images that the observer’s eye fuses into a full-color image.

The processing algorithm for doing this is also illustrated in Fig. 22.19 and works as follows. Yellow filter elements absorb blue light, but pass red and green (see Fig. 22.15). This enables the pixels behind all yellow filter elements to receive both red and green information. Likewise, pixels behind cyan filter elements receive both the blue and the green portions of the color spectrum (see Fig. 22.15). The filter-free white pixels receive light covering all three primary colors. In a representative block of four pixels (one yellow, one cyan, and two white), three pixels receive red information, four pixels receive green information, and three pixels receive blue information (Fig. 22.19). By adding or subtracting the information obtained from adjacent pixels using an appropriate algorithm, it is possible to derive the individual red, green, and blue component values for each block of (four) pixels. For example, if the voltage of the cyan pixel is subtracted from the voltage of the adjacent white pixel (Fig. 22.19, step 1), the result is the intensity of the red component for that pixel block. In a similar fashion, subtracting the voltages of adjacent yellow and white pixels will yield the intensity of the blue component in the pixel block (Fig. 22.19, step 2). Once the values for red and blue have been calculated, they can be subtracted from the voltage of an adjacent white pixel in order to calculate the green component value (Fig. 22.19, step 3). At this point, each of the red, green, and blue intensities is known for the 2×2 block of pixels being analyzed. This process is then repeated for all 2×2 blocks of pixels across the CCD face, thus generating the required RGB components of the original image.

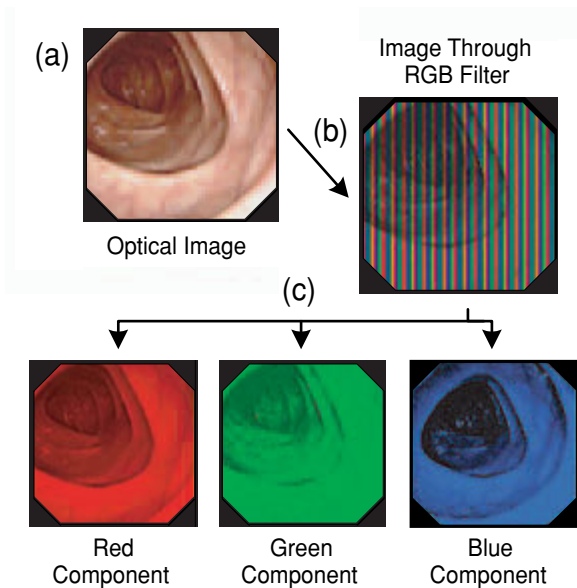


Fig. 22.18 An RGB-striped CCD captures all three color components simultaneously.

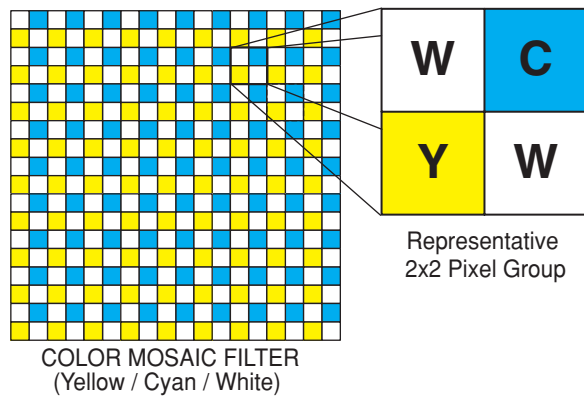


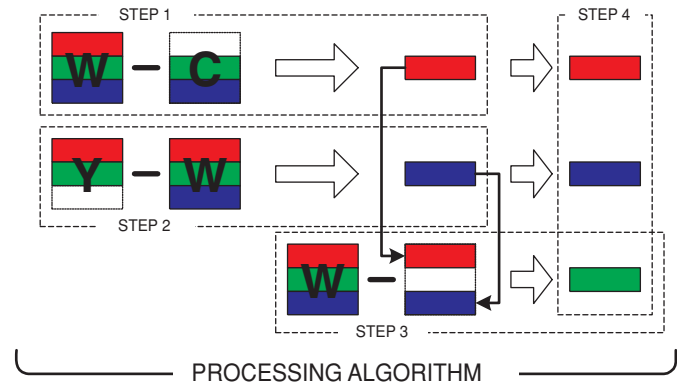
Fig. 22.19 A color mosaic CCD captures light filtered through yellow, cyan, and white filter segments. The resulting image replica is then processed to produce the standard RGB component images.

Why is it necessary to go through this extended process if using an RGB-striped filter will yield the RGB component values directly, without calculation? The answer lies in the fact that a yellow/cyan/white mosaic filter has a significant advantage in brightness over an RGB-striped filter. When red, green, and blue filter segments are used, each pixel is filtered to receive only one of the three primary colors. A cyan-filtered pixel, on the other hand, is exposed to both blue and green light. It is therefore more heavily illuminated than a pure blue or pure green pixel. Likewise, pixels behind a yellow filter (red and green) or a white filter (no filtration = red, green and blue) receive more photons (light) than pixels behind a pure red, green, or blue filter.

Because of the increased light intensity passing through a yellow/cyan/white mosaic filter, a CCD with this construction exhibits far greater light sensitivity than an RGB-striped CCD. The increase in brightness achieved by using nonprimary-colored filters is obtained at the expense of the additional processing required to later separate the mixed color signals into their primary components. However, due to the increased light sensitivity, color mosaic CCDs allow the videoscope designer to construct an endoscope with a smaller light-guide fiber bundle, to maximize the endoscope's angle of view, and to increase the endoscope's depth of field. All these characteristics improve optical performance but require additional light. For this reason all commercial color-chip endoscopes use color mosaic CCDs.

Color image display

The preceding sections explain the techniques used to capture images with an RGB sequential imaging system and a color-chip imaging system. However, display of the resulting image is common to all video systems.



The face of a color video monitor is actually composed of thousands of red, green, and blue phosphor dots, typically arranged in a repeated triangular matrix. The monitor also contains three electron guns, each of which scans over the face of the picture tube in an orderly manner (see Fig. 22.16). The physical arrangement of the “red” gun will allow it to hit and activate only the red phosphor dots. The “green” and “blue” guns are restricted to hitting and illuminating only the green and blue phosphor dots respectively.

By feeding the signal from the red memory bank of the video processor to the red electron gun in the monitor (see Fig. 22.16), the monitor will reproduce an image of the colon wall as it appears under red illumination. This is illustrated by the red component image depicted in Fig. 22.17. Likewise, feeding the images from the green and blue memory banks to the green and blue electron guns respectively will reproduce the green and blue components of the original image. Although three guns are described here, some monitors achieve the same end result using a single electron gun.

It is a phenomenon of human vision that when two or more sources of color are placed close together, but not overlapping, and are viewed from a sufficient distance, the colors will blend together to form a third color. This third color is the color predicted by the theory of trichromatic vision. This fusion of color sources is referred to as the *juxtaposition of color sources*. Because of this phenomenon, the three intertwined RGB images on the video monitor appear to fuse together into a single, full-colored, natural-appearing image, rather than appearing to be a confusing collection of intermixed colored dots.

Reproduction of motion

The color-chip videoscope has an inherent advantage over the RGB sequential videoscope in reproducing motion. The filter wheel in current RGB sequential video processors typically rotates at 20–30 rps. Since each of the color component images is captured individually in sequence, it takes 1/30 s (with a 30-rps filter wheel) to

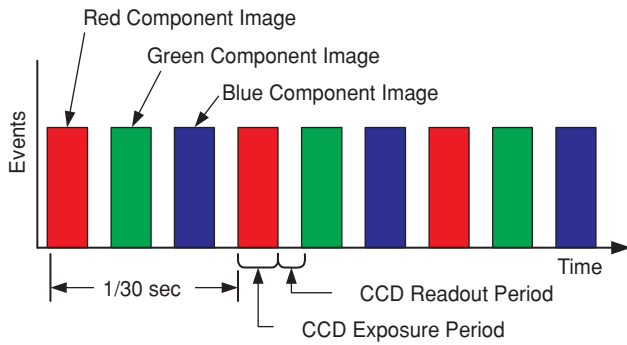


Fig. 22.20 Sequence of events in an RGB sequential imaging system.

capture the three component images that make up a single video image (Fig. 22.20). If there is relative motion between the endoscope and the object being viewed, as often occurs during endoscopy, the three component images may differ slightly with respect to object size and position. When these three RGB images are subsequently superimposed on the video monitor, it is likely that they will be misaligned. This misalignment will be clearly visible if the endoscopist happens to freeze the image while it is moving rapidly. This color separation is present, to a greater or lesser extent, continuously throughout the entire examination. It gives the images an unnatural, highly colorful, stroboscopic appearance whenever there is rapid motion of the endoscope, the object being viewed, or both. This type of color separation is especially apparent when the endoscopist feeds water to clean the objective lens. The water droplets produce a colorful but very distracting flicker across the endoscopic image.

Second-generation RGB sequential video processors are engineered to reduce the problem of color separation on captured images. These processors incorporate an anticolor-slip circuit to analyze the video signal in real time and to freeze the image at the moment when color separation is at a minimum (Fig. 22.21). In early RGB systems, the processor “froze” the image that was displayed on the monitor at the exact instant the image-capture function was activated (i.e. the “freeze” button was depressed). Instead of capturing this initial image, activation of the freeze function on these newer RGB video processors (e.g. Olympus EVIS model CV-240) triggers a special capture circuit that analyzes the stream of incoming images for the next 0.25 s, i.e. during the next five rotations of the filter wheel (Fig. 22.21). From these five complete images (a total of 15 RGB component images), the circuit selects the set of RGB component images that exhibits the least amount of color separation. In the example shown in Fig. 22.21, the capture circuit has found that relative motion was minimal during RGB component images 7, 8, and 9, these being the third set of images captured after the “freeze” button was

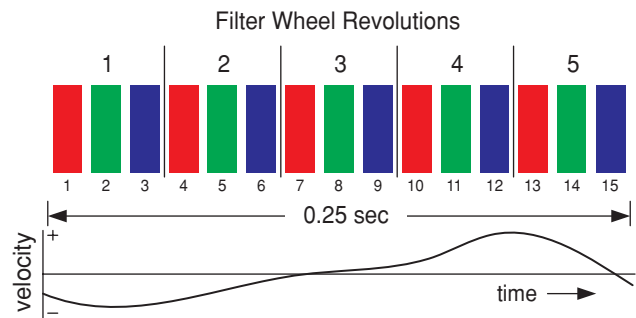


Fig. 22.21 An “antislip” image capture system identifies the set of images obtained during the capture period which has the least amount of color slip due to motion.

depressed. The circuit then holds these three RGB component images in memory and displays them on the observation monitor as the best possible still image of the mucosa. Even though the system is able to choose only from images obtained within a 0.25-s period after the freeze button is depressed, the circuit is remarkably effective in reducing color separation within captured still images. This system does not reduce the strobing, color separation, and water-droplet flicker observed during real-time endoscopy.

While the RGB sequential videoscope has difficulty reproducing motion, the color-chip videoscope has inherent advantages in imaging moving tissue. Because a color-chip endoscope captures all three color components of the image simultaneously, there is never any color separation with either moving or “frozen” images. Since illumination is continuous and unstrobed, and the frame rate is consistent with contemporary TV standards, reproduction of moving images is always smooth and always appears natural.

Another unique advantage of the color-chip videoscope is a feature that allows its effective shutter speed to be shortened to increase the sharpness of frozen images. The color-chip system normally captures a new video field every 1/60 s (Fig. 22.22). Even though this time period is relatively short, quickly moving subjects that are “frozen” may appear to be slightly blurred (but with

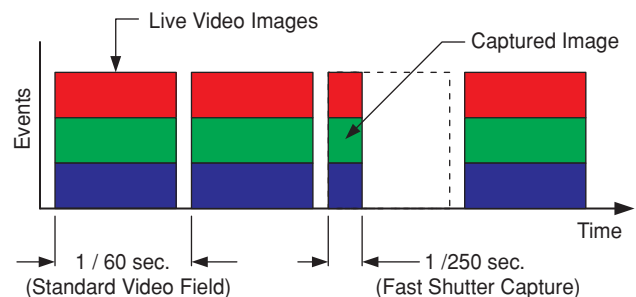


Fig. 22.22 Color-chip imaging systems often have a “fast-shutter” mode to reduce blur on still images.

no color separation) owing to movement during the capture period. To reduce this blur, it is advantageous to shorten the electronic capture period to a fraction of its normal time (e.g. from 1/60 s to 1/250 s). As in traditional film photography, the shorter the exposure period, the sharper the subject, but the more brightly the subject must be illuminated to prevent underexposure. The fast-shutter mode may not provide enough light for distant panoramic images but in situations where it is truly needed, the fast-shutter capture mode is very effective at producing bright, sharp, frozen images, i.e. close-up stills of quickly moving mucosa.

Advantages of color-chip videoscope

The color-chip videoscope has several inherent advantages over the RGB sequential system. Those discussed previously include:

- 1 smooth, natural reproduction of motion;
- 2 absence of color separation on frozen images; and
- 3 a fast-shutter mode that prevents image blur of even the fastest moving subject.

Additional advantages include:

- 4 compatibility with standard (nonstrobing) xenon light sources;
- 5 increased transillumination; and
- 6 superior performance during laser therapy.

With RGB sequential endoscopes, transillumination is problematic since its strobed light output is substantially weaker than that of nonstrobed systems. Many RGB sequential light sources have a means for temporarily removing the spinning filter wheel from the light path during the "transillumination" mode. This produces a steady intense white light ideal for transillumination. However, once the filter wheel is removed, the image is lost, since in most cases the illumination is so intense that it saturates the CCD, thus producing a totally white screen. Even if an image is visible, it will be in black and white, since the filter wheel must be in its proper position to reproduce color.

Advantages of RGB sequential videoscope

Having considered the advantages of the color-chip videoscope, it is appropriate to look at the advantages of the RGB sequential videoscope. One of its major advantages is the opportunity for increased resolution. Image resolution is heavily dependent on the number of pixels in the original image. The color-chip system requires information from several different pixels, which is then processed via an algorithm, to obtain the red, green, and blue component values for a single point within the image (see Fig. 22.19).

In the RGB sequential system, each pixel is illuminated by red, green, and blue light sequentially. Each

pixel thus provides information on each of the three color components in turn. The fact that a single pixel can provide all three color components is an advantage for small imaging devices like endoscopes. The physical size of an endoscopic CCD is restricted to the space available within the distal tip of the endoscope. This limits the size of the CCD and the number of pixels it can contain. Since the color-chip CCD uses several pixels to provide the same information obtained from a single pixel in the RGB system, the RGB system can theoretically produce the greatest image resolution (based on equivalent numbers of pixels). In practice, this advantage is not significant when designing a video colonoscope, but is a significant advantage when the thinnest possible endoscope is required (e.g. video choledochoscopy).

Because the RGB sequential videoscope uses primary-color filters and since the color components are isolated, captured, and processed separately within the video processor, this type of videoscope provides very accurate color information. Although both systems produce natural-appearing images, the RGB sequential system can theoretically produce a truer color signal. Again, this potential advantage is not apparent with routine colonoscopy. However, the RGB sequential system has the upper hand in image analysis research.

Laser therapy

No video endoscope can be effectively used with any laser that operates within the visible spectrum. The intense laser light would totally saturate the CCD sensor and overpower the endoscopic image, making observation of laser therapy impossible. However, it is possible to effectively adapt video endoscopes for use with lasers that operate outside the visible spectrum. As an example, the neodymium: yttrium-aluminum-garnet (Nd:YAG) laser, which produces near-infrared light at 1060 nm, is compatible with appropriately modified videoscopes. Since the Nd:YAG laser output is outside the visible spectrum, endoscope manufacturers commonly protect the CCD by covering it with a filter that transmits visible light (the image) but heavily absorbs reflected laser light (near-infrared light). Whenever the laser is fired within the endoscopic field, the filter prevents the laser output from reaching the CCD, leaving the image undisturbed.

Even with such a filter, RGB sequential videoscopes have other problems when used with nonvisible lasers. The first is a loss of the true color of the aiming beam. The helium-neon aiming beam used in almost all Nd:YAG lasers appears as a red spot when observed with a fiberscope or color-chip videoscope. When observed by an RGB sequential videoscope, however, the beam is always white. This is due to the fact that the red aiming beam is on continuously and therefore appears equally bright to the CCD during all portions of the RGB imag-

ing cycle. As a result, the video processor interprets the helium–neon beam as being white. Because of this color loss, the bright artificially white aiming beam displayed on the monitor obscures the tissue effect produced by the Nd:YAG laser and impairs observation of the laser’s action. The loss of aiming beam color can be avoided by strobing the aiming beam in synchrony with the light source filter wheel. However, this modification is complex and costly.

Another disadvantage of the RGB sequential endoscope is the relatively low brightness of its strobed illumination. This causes two problems.

1 The intensity of the laser aiming beam must be reduced because medical lasers have been traditionally designed to work with the intense illumination produced by fiberoptic endoscopes.

2 During periods of concentrated treatment, the tissue may glow at the point of laser impact. Since the burning tissue may be brighter than the videoscope’s background illumination, the glowing tissue may cause the CCD to bloom and mask the local tissue effect of the laser.

In contrast, the color-chip videoscope offers advantages for laser use because it provides intense, non-strobed white light illumination, similar to that used with fiberscopes. The aiming beam retains its red color, and its intensity is usually not a problem. The result is a view similar to that seen through fiberscopes. Because of these factors, the color-chip videoscope is the better choice for endoscopic laser therapy.

Functions of a typical video processor

Figure 22.23 schematically illustrates the functions of the various electrical circuits within a typical RGB sequential video processor. The CCD image sensor (located in the distal end of the endoscope) receives both power and timing signals from the video processor. The timing signals control the readout of the CCD and the transfer of charges to and from the horizontal shift register (see earlier). From the shift register, the image signal is fed through an amplifier on the CCD and then into the pre-process circuitry of the video processor.

The preprocess circuitry is responsible for electrically isolating the patient from the potentially dangerous high-voltage circuitry of the video processor, for initiating automatic brightness control, and for adjusting the chroma (color) and white balance of the image. The preprocess circuitry further amplifies the signal and often performs additional image processing functions such as edge or structure enhancement.

The signal then passes through an analog-to-digital (A/D) converter, changing the signal from an analog to a digital format. The digitized image is then directed through a switching circuit for storage in one of the

red, green, or blue image memory arrays. Images from the digital memories are next passed through a size-adjustment circuit that scales the relative size of the endoscopic image for presentation on the video monitor. A second circuit then adjusts the relative position of the endoscopic image, and sizes and positions any sub-screen image that may be added to the screen along with the main image. An example of a typical subscreen image is a reduced display of the real-time endoscopic image, added to the screen whenever the main image is frozen.

At this point, the developing image is still in a digital format but has been adjusted in size and position, with subscreen images (if any) added. The image then passes through a digital-to-analog (D/A) converter to change the image back to an analog format. A masking circuit then adds a mask (typically black) around the image(s) to provide a uniform background color. Finally, the image passes through a postprocessing circuit that encodes the video signal to conform with a recognized video signal standard, allowing the image to be displayed on any standard video monitor.

Figure 22.23 also schematically illustrates some of the mechanical components of the video processor and light source. Light from the light-source lamp first passes through an infrared filter to remove nonvisible heat rays. The light then passes through a lens that focuses it on the tip of the fiberoptic light-guide bundle within the universal cord of the endoscope. An iris in the light path controls the brightness of the light transmitted to the endoscope, and a filter wheel modifies the color of the light (described earlier). The motor rotating the filter wheel is regulated by a control circuit to ensure that the wheel spins at the precise speed required by the video processor. Detectors placed adjacent to the filter wheel identify which filter segment (red, green, or blue) is currently in the light path.

Figure 22.23 also illustrates the synchronization circuitry which ensures that all functions of the video processor and light source are coordinated with the video output signal. These functions include synchronization of filter wheel rotation, exposure and readout of the CCD, memory transfers within the video processor, and image freeze control. Video processors also generally require endoscope identification circuitry to identify the model (or type) of endoscope connected to the processor. Endoscope identification allows the system to compensate for differences in endoscope length and CCD type.

A major portion of the circuitry within a video processor is designed around the specific CCD(s) with which the processor is intended to operate. First-generation videoscopes used the same CCD for all model endoscopes, from the largest colonoscope to the slimmest gastroscope. Current video processors are designed to drive a family of CCDs, each of which differs in size

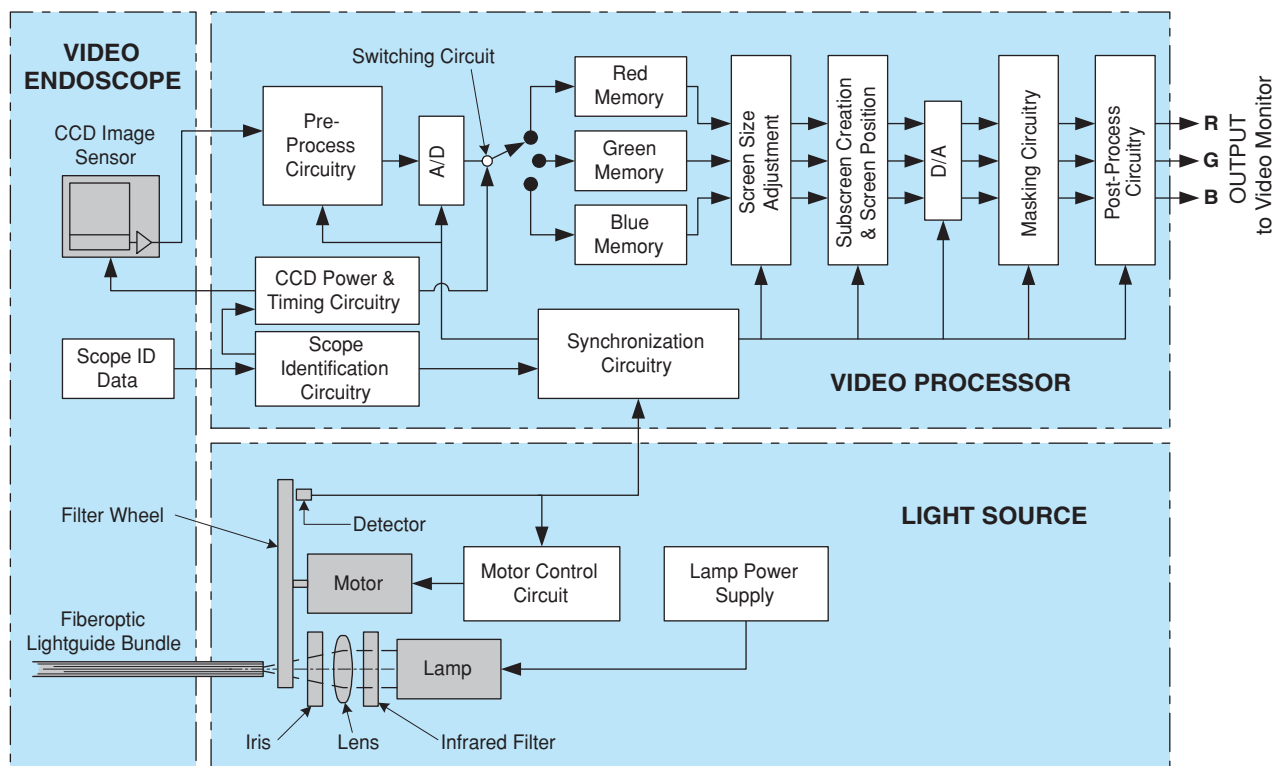


Fig. 22.23 Schematic representation of an RGB sequential light source and video processor.

and image resolution capability (see Fig. 22.12). An advantage of this strategy is that a family of compatible CCDs allows a wide range of videoscopes, old and new (including large-diameter high-resolution instruments, specialty endoscopes, thin pediatric endoscopes, and large-channeled therapeutic instruments), to be compatible with the same video processor. For a single video processor to drive several different CCDs, the various CCDs must have similar electrical and physical characteristics. In particular, the video processor must specifically compensate for differences in pixel number, illumination requirements, data transfer rates, and drive circuitry. Despite the range of CCDs available for current video processors, there are no video processors that are compatible with both color-chip and RGB sequential endoscopes; nor is it possible to interchange endoscopes or processors made by different manufacturers. Endoscopy units typically select one type of system from a single manufacturer. To do otherwise would require the purchase of additional video processors and would result in the accumulation of incompatible equipment.

Although Fig. 22.23 summarizes many of the basic functions of a video processor, some standard functions are not illustrated for the sake of simplicity. These include connections to an external keyboard for text input, circuitry for superimposing text on the monitor

image, and circuitry for communicating with external computers, printers, and image documentation devices.

Field vs. frame capture

The distinction between a video field and a video frame is significant when images of rapidly moving subjects are captured. In extreme conditions, the image may shift significantly during the time it takes ($1/30$ s) to capture both fields of the video image. Because the fields are captured sequentially, the image captured by the first video field may be slightly displaced from the image captured by the second field. This offset may cause the edges of objects within the image to appear ragged when the two images are interlaced. The faster an object is moving, the greater the difference between the images in the two fields.

When these two frozen offset fields are displayed together, there may also be a disturbing flicker in the image as the monitor alternately reproduces the two displaced fields. Flicker can be reduced in a “frozen image” by switching the documentation device from the frame-capture mode to the field-capture mode. In field mode, only every other line of the image is displayed (the second field is removed from the display), resulting in a single, crisp, nonflickering image from the first field. Since the displayed image lacks the second field, vertical image resolution drops accordingly. Most video processors offer the option of field vs. frame image capture.

It is often better to operate the videoscope in frame mode and, if flickering occurs, to take a second photo while endoscope movement is minimized.

Video standards

All cathode-ray tube monitors, whether used for computer or video applications, “paint” an image on the face of the monitor with a scanning electron beam. This beam typically starts in the monitor’s upper left corner and scans the monitor horizontally, line by line, from top to bottom. The energy of this electron beam causes the RGB phosphor dots applied to the back of the screen to glow briefly, thus creating an image (see Fig. 22.16). Broadcast and closed-circuit TV systems employ a system of interlace scan. The picture tube first scans all of the odd horizontal lines (1, 3, 5, etc.) and then goes back to complete the image by scanning the even lines (2, 4, 6, etc.). The odd lines represent the first “field” of the image; the even lines represent the second field. Together, the two fields paint the entire screen once and create a single video “frame,” or image. The process then starts over again, first one field, then the other, until a second complete picture or video frame is displayed.

The specifications for this interlace system were standardized (RS-170A Standard) by the Electronic Institute of America (EIA) and adopted by the U.S. Federal Communications Commission in 1941. In 1953, the National Television System Committee (NTSC) proposed a color-encoding method that expanded on the RS-170A standard to create the first black-and-white-compatible, color TV standard for public broadcasting. The NTSC standard is still the universal color-encoding method used in the USA, Canada, and Japan. (Most European countries conform to the incompatible PAL or SECAM color TV standards.) The NTSC video signal is a “composite” video signal, i.e. the luminance (brightness) and chrominance (color) information are combined in one signal. (Black-and-white video systems only use the luminance portion of the signal.) Although a composite signal is convenient for broadcasting, image quality deteriorates as the color information is encoded into and decoded from the brightness signal. Because all common ancillary equipment (video monitors, video-cassette recorders, etc.) accept NTSC composite video signals, all video endoscope processors have NTSC composite output connectors on their rear panels.

In addition to an NTSC composite output, current video processors also have a second set of connectors allowing for the output of the image in a luminance/chrominance (Y/C) video format (also called Super Video or S-Video). Y/C video connections maintain the brightness and chrominance information on two separate wires. Monitors, videocassette recorders, and other peripheral equipment communicating with Y/C signals

provide better image reproduction than composite video equipment.

A third method of connecting video equipment is to use four separate red, green, blue, sync (RGSB) cables. This video interconnection method is the ideal means for preserving the original video image quality. Since the RGB image components and the synchronization signals are carried over four separate wires, this information is never mixed. Most videoscopes provide the option of using any or all of these three video connection methods (NTSC composite, Y/C, or RGSB). Most video monitors used for endoscopy also have inputs for all three types of signals and allow the user to select from these various configurations. (For a more complete discussion of the video standards used in endoscopy, see reference 4.)

Factors to consider when evaluating a video-image colonoscope

The video-image endoscope is a technologically advanced and complex clinical tool. When these instruments first entered the market, published comparison reports of various commercially available models were common [6–8]. Now that the technology of video endoscopy has matured, such published comparisons are rare. It is difficult to identify any single design criterion as the deciding factor in selecting the best videoscope for a particular clinical application. When evaluating a video colonoscope, the following criteria should be considered.

- 1 *Image quality.* Does the instrument have a sufficiently wide angle of view, with good depth of field, high image resolution, good image contrast, accurate color, clear frozen images, and a wide dynamic range (ability to see clearly in both light and dark areas of the image)?
- 2 *Illumination characteristics.* Does the instrument have adequate image brightness under all clinical conditions? Is illumination evenly distributed from image center to image edge? Does the system have responsive automatic brightness adjustment as viewing distances change?
- 3 *Basic endoscope functions.* Does the instrument have responsive handling and appropriate insertion tube characteristics? Does it have smooth tip angulation, a control section of appropriate shape and weight, conveniently positioned angulation knobs and valves, and good suction, insufflation, and lens washing performance?
- 4 *Basic specifications.* Does the manufacturer have a full range of instrument models, with a variety of insertion tube diameters and biopsy channel capacities?
- 5 *Suitability for special therapeutic procedures.* Is the colonoscope well protected against image noise from electrosurgical generators? Is image quality acceptable when using lasers?
- 6 *System features.* Are the video processor controls easy to understand? Are the endoscope switches for

the control of remote devices easily accessible? Does the size and weight of the equipment allow for easy transportation?

7 System expansion and integration. Is the system capable of easily interfacing with hard-copy devices, videotape recorders, and computerized image management systems?

Summary

During the 1990s, the video-image colonoscope supplanted the fiberoptic colonoscope as the preferred instrument for colonoscopy. The availability of two distinct technologies for generating color images (color-chip vs. RGB sequential) provides the endoscopist with a choice of basic systems, each with its own advantages and disadvantages. Although the basic shape and function of the instrument have remained unchanged, recent advancements (including the development of smaller-diameter insertion tubes, instruments with adjustable stiffness, improvements in image resolution, and advanced video processor features) have continued the evolution of the colonoscope.

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Chapter 23

The Colonoscope Insertion Tube

Douglas A. Howell

Introduction

The colonoscope insertion tube is the largest contributor to overall endoscope performance. Individual practitioners develop a preference for individual instruments and develop skill and techniques for their use. Many choose soft flexible insertion tubes for their ability to maneuver through the sigmoid colon easily. However, advancement beyond the splenic flexure can prove challenging, requiring a variety of maneuvers, including patient positioning and counterpressure. Alternatively, stiffer instruments may be preferred for the opposite reason. Some endoscopists accept a more difficult sigmoid negotiation with stiffer instruments in order to permit easier cecal access once the splenic flexure has been negotiated. Examinations with stiffer instruments understandably may require more patient sedation, but there has not been a higher perforation rate reported with their use.

Various instruments

Pediatric-diameter long-length colonoscopies were introduced in the late 1980s and reports of successful use in adults soon followed. In 70 of 72 cases where the sigmoid could not be negotiated using standard colonoscopes, Bat and Williams [1] reported success with pediatric instruments. Reasons for initial failures included strictures, severe diverticular disease, and postoperative adhesions.

Several authors have now concluded that women are more difficult to examine at colonoscopy, especially if they have undergone hysterectomy, and are most likely to benefit from the use of pediatric endoscopes [2,3]. In a randomized trial of 100 women with hysterectomies, Marshall and colleagues [4] reported successful entry into the cecum in 96% when using pediatric colonoscopes compared with only 71% where standard colonoscopes were employed. When these failures with standard colonoscopes were then attempted with pediatric instruments, more than half could be successfully completed. Nevertheless, most endoscopists who use pediatric colonoscopes have observed that keeping the instrument straight and advancing beyond the

splenic flexure may be difficult. This should not be unexpected in view of the thin flexible insertion shaft of pediatric instruments.

When the more flexible endoscopes loop and bend during intubation, counterpressure and/or patient repositioning are the most frequently employed maneuvers to help advance the instrument. While these techniques do not add stiffness to the colonoscope shaft, counterpressure does result in compression of loops to transfer forward motion of the instrument to the tip [5]. Placing the patient on the back or right side can similarly affect insertion, and positional changes are frequently employed when using pediatric equipment. However, these techniques may be ineffective due to patient body habitus, incorrect placement of pressure, adhesions, and looping under the ribcage in either the splenic or hepatic flexures.

On occasion, the push enteroscope has been employed in an attempt to complete a failed colonoscopy. The largest experience was reported after failure with a standard-diameter colonoscope. In 32 such cases, the enteroscope was advanced to the cecum in 22 (68.7%), raising the authors' overall success rate to 96.4%. Of note, the authors did not attempt these patients with pediatric equipment and their report predates the availability of variable-stiffness technology [6].

The enteroscope probably does have a role in colonoscopy on occasion. In a 2002 report, Rex and Goodwine [7] used the enteroscope with a straightener or the colonoscope with a straightener to successfully study 2 of 42 consecutive patients with failed prior colonoscopies. In my personal experience, patients with extremely long colons with redundant sigmoids are the group in whom previously failed colonoscopy will be successfully completed with an enteroscope. One report of the routine use of an enteroscope rather than a colonoscope to specifically examine the terminal ileum had disappointing results, in that the technical failure rate for ileal intubation was 33%, attributed to the length of the scope, its smaller diameter, and its tendency to continuously form loops [8].

Some authors have described the use of gastroscopes in colonoscopy but, in general, only for special circumstances and almost always for left colon examinations

[7]. Gastroscopes have short bending segments, short transition zones, and stiff short insertion tubes, making them poor instruments for colonoscopy. Very slim pediatric gastroscopes are useful for performing retroflexion endoscopy in the rectum and distal sigmoid to assist in difficult polypectomy but advancement beyond the splenic flexure has rarely been reported. Perhaps the most frequent use of small-caliber gastroscopes is negotiation through severe diverticular disease, with tortuosity of the colonic lumen, narrowing, and rigidity.

A short bending segment colonoscope in prototype form (Olympus, Japan) has been developed to attempt to take advantage of the tight U-turn capability of gastroscopes. With a pediatric insertion tube and a bending section similar to a pediatric gastroscope, the prototype can be easily retroflexed virtually anywhere in the colon including in the cecum. Whether this instrument can be as successfully passed to the cecum and whether this ability will add to diagnostic yields or polypectomy success will require further study.

Stiffeners

Devices to add stiffness to assist in negotiating beyond the splenic flexure have a long history. These include external overtubes and internal biopsy channel devices.

Overtubes were introduced in 1983 to splint the sigmoid colon. Made of rigid tubular plastic, these devices proved painful, cumbersome, and dangerous. A major disadvantage was the need to withdraw the colonoscope to load the earliest overtubes and then repeat the insertion to the splenic flexure. A split overtube was marketed to avoid this specific disadvantage but the original drawbacks remained, resulting in abandonment of the technique. Overtubes for colonoscopy are no longer marketed.

Internal stiffening devices were initially tightly closed biopsy forceps, which did not add sufficient additional stiffness to reliably improve success during colon intubation. First appearing in 1972, several stainless steel cable devices where tension could be varied with a twist-wheel were produced and marketed (Fig. 23.1). Although often of benefit in performing a successful procedure, the devices were cumbersome, blocked suction capabilities, and were hard to clean. Despite their limited success in stiffening the colonoscope shaft, they were abandoned because of their potential to cause endoscope damage [9]. The last such device (Sullivan Stiffener, Wilson-Cook Medical, Winston-Salem, NC) is no longer manufactured but still exists in many units [10].

Some endoscopists prefer a double-channel colonoscope for a stiffer insertion tube, offered by all three major endoscopy manufacturers. The second channel adds approximately 1 mm to the overall diameter but increases the stiffness considerably. The additional



Fig. 23.1 Early cable internal stiffening device.

channel can be used to ensure suction capabilities when the first channel is occluded by a device. Several second-channel techniques have been used to assist in polypectomy, especially collecting resected polyp specimens while additional polyps are being removed. Never popular, these endoscopes have largely been abandoned with the advent of graduated stiffness insertion tubes and newer innovations that permit increasing stiffness during colonoscopy. Nevertheless, double-channel colonoscopes are still produced and are currently available.

Variable-stiffness colonoscopes

Since no one stiffness is appropriate in all settings, the development of variable-stiffness adjustment in colonoscopes was greeted as a welcome new innovation in endoscope engineering. Marketed by Olympus America (Melville, NY) as Innoflex® (i.e. “innovation in flexibility”), this new colonoscope series permits adjustment of the instrument during the procedure from flexible to stiff using a hand dial (Fig. 23.2). The details of the engineering and manufacture are outlined in Chapter 22 but, in summary, these instruments permit adjustment in the range from the most flexible to the stiffest colonoscopes currently in use (Fig. 23.3). It is important to note that the variable-stiffness cable within the insertion tube connects at 16 cm behind the tip. Tightening the internal cable does not change the characteristics of the bending section or the adjacent transition section (present in all modern endoscopes). Insertion shafts have always been produced to be stiffer than the initial forward section of the colonoscope, producing so-called graduated stiffness. This is in contrast to the ability to vary the stiffness of the insertion shaft during the procedure by changing the tension on a variable-stiffness cable. Innoflex® colonoscopes are produced in both standard diameter



Fig. 23.2 Adjustable hand dial for adding stiffness.

(12.8 mm) and pediatric diameter (11.3 mm). The performance of these insertion tubes depends upon both the external diameter as well as length of bending section and the degree of stiffness dialed into the variable-stiffness portion of the insertion tube. The radius of the bending section is shorter in pediatric instruments,

which assists in negotiating sharp turns and contributes to its greater flexibility.

Technique for use of variable-stiffness instruments

The recommended technique for using the variable-stiffness colonoscope is as follows.

1 The instrument is inserted in its maximally flexible mode (dial set at zero). The sigmoid is negotiated until the splenic flexure is achieved and “hooked” by entering the transverse colon. Counterpressure and/or patient positioning may be needed during this phase.

2 The instrument is then straightened by withdrawal, generally with some clockwise torque until about 55–65 cm of colonoscope remains within the patient as measured at the anal verge.

3 The dial is then twisted, fully tensioning the dial to a setting of 3. Shaft stiffness is not a linear function so that a setting of 1 or 2 does little to affect the character of the insertion tube.

4 Once fully straightened and stiffened, advancement should be facilitated. Even with the instrument in the maximal-stiffness mode, loops can develop in the shaft during insertion. The standard “straightening by withdrawal” techniques should be performed frequently, after removing the tension on the stiffening apparatus.

5 Following straightening, the above procedures can be repeated.

Variable-stiffness colonoscopes have rapidly gained favor, although the literature addressing effectiveness has reported mixed results (Table 23.1). Earlier reports suggested that the variable-stiffness instrument significantly reduced insertion time and was more comfortable

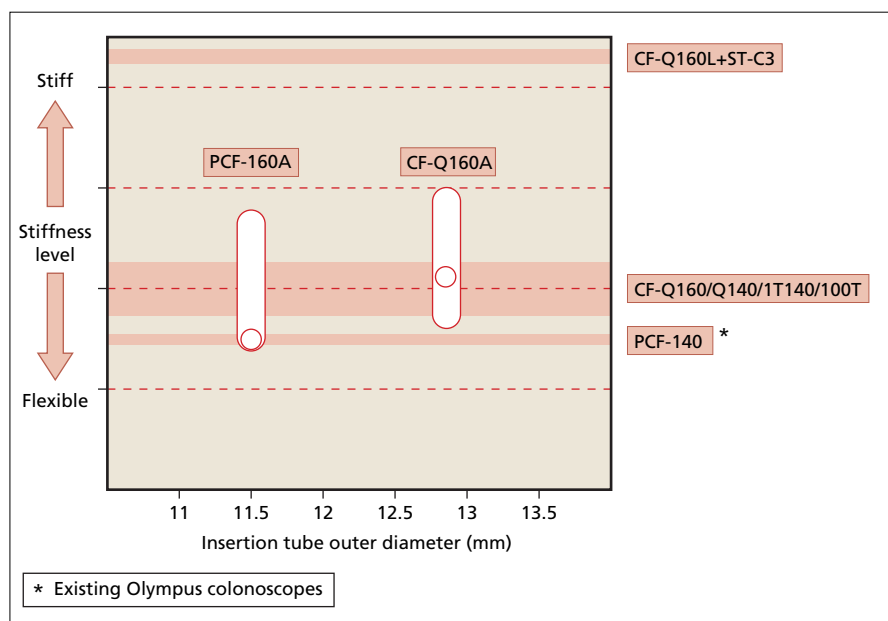


Fig. 23.3 Variable-stiffness graph of pediatric (PCF160A) and standard (CF-O160A) colonoscopes.

Table 23.1 Variable-stiffness compared with regular colonoscopes.

Reference	Patients	Trial	Loop control*	Pain scores	Time to cecum
Brooker <i>et al.</i> [11]	100	VSS vs. SC	NA	Less	Less
Sorbi <i>et al.</i> [13]	50	VSS vs. SC	Improved	Less	Same
Rex [15]	358	VSS vs. VSP vs. SC vs. PC	Same	Same	Same
Howell <i>et al.</i> [16]	600	VSS vs. VSP vs. SC vs. PC	Improved	Least with PC	Same
Shumaker <i>et al.</i> [17]	363	VSP vs. SC vs. PC	Same	Same	Same
Yoshikawa <i>et al.</i> [18]	467	VSS vs. SC	Same	Less	Less

NA, not available; PC, pediatric colonoscopy; SC, standard colonoscopy; VSP, variable stiffness pediatric; VSS, variable stiffness standard diameter.

*Need for counterpressure or patient repositioning.

compared with conventional colonoscopes [11,12]. Some later reports have agreed that counterpressure and positioning is less often needed, supporting the concept that variable-stiffness instruments do control loop formation; however, their use did not shorten insertion time or improve success [13,14]. Rex [15] reported a series of patients where success and speed to the cecum was not improved with variable-stiffness colonoscopes, but judged the effectiveness of the stiffening device to be very useful in 40% of cases when he used the standard-diameter variable-stiffness colonoscopy and 54% of pediatric variable stiffness cases.

Howell and colleagues [16] compared standard and pediatric colonoscopes with variable-stiffness standard-diameter and pediatric-diameter colonoscopes in 600 patients. Consecutive patients were examined with either instrument as equipment became available. The results again demonstrated that women were more difficult to examine and had more discomfort than men during colonoscopy but fared better with pediatric equipment. The use of variable-stiffness colonoscopes resulted in less loop formation as assessed by decreased need for counterpressure. Patients who had undergone prior colonoscopy with a standard adult colonoscopy rated the pediatric and variable-stiffness equipment most favorably (Fig. 23.4). In addition, the pediatric variable-stiffness colonoscopy was given the best rating by the author, as measured by the subjective score used.

Shumaker and colleagues [17], using a similar study protocol, did not find any significant advantages to using

variable-stiffness colonoscopy compared with standard instruments. Nevertheless, they reported that the variable-stiffness colonoscopes performed well and concluded that further study might identify subgroups in whom the variable-stiffness instruments would be of benefit. Most recently, Yoshikawa and colleagues [18] studied patients undergoing sedationless colonoscopy and reported a significant reduction in pain scores when using variable-stiffness pediatric colonoscopes. In this setting cecal intubation times by the less experienced colonoscopists were shorter than with conventional instruments.

Recently, the newly released magnetic endoscope imaging (MEI) device (see Chapter 24) has been used with variable-stiffness colonoscopes. The examinations performed with MEI demonstrated surprisingly effective control of sigmoid loop reformation after straightening and applying stiffness when the tip was at the splenic flexure. Despite the control of looping in the sigmoid colon, some examinations may remain challenging due to splenic flexure looping or transverse colon redundancy. Combining variable-stiffness technology with MEI is likely to be a major step toward more effective, more comfortable colonoscopy.

Choice of instruments

Now that many variations of insertion tubes are available, how does an endoscopist select an instrument which is most likely to be successful for cecal intubation

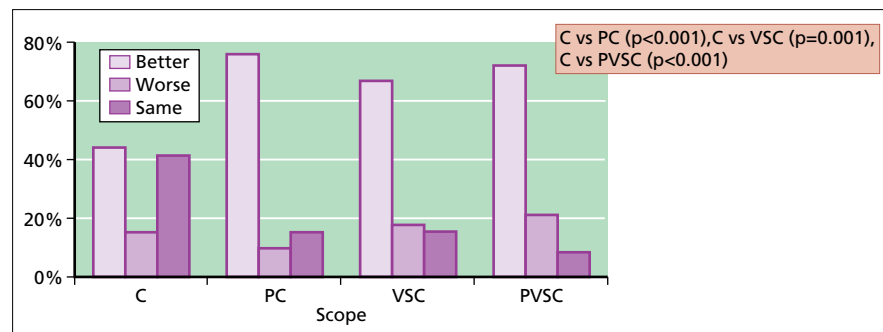


Fig. 23.4 Patient comparison to their prior colonoscopy.

and provide the greatest patient comfort? Anderson and colleagues [19] recently studied 802 consecutive patients in an attempt to define factors that might predict a difficult colonoscopy. The parameters of female sex, low body mass, diverticular disease (at least in women), and older age all resulted in somewhat more difficult examinations. Large body size was associated with a somewhat easier examination.

In our endoscopy unit, pelvic surgery in thin women causes us to select pediatric equipment, but we still anticipate a somewhat more difficult examination and a higher risk of failure. Conversely, obese patients are somewhat easier to examine, probably because intra-abdominal fat separates bowel loops, widening the radius of sharp bends. However, the presence of a very large panniculus often prevents effective counterpressure when a loop is encountered. In addition, very large individuals not unexpectedly have very large colons, which may make intubation proximal to the splenic flexure particularly challenging. We would choose the stiffest instrument available for use in these patients. Our choice is a standard-diameter variable-stiffness colonoscope when the patient's body mass index is greater than 30.

Most patients tolerate colonoscopy very well providing that the technique employed is gentle, with frequent straightening of early loop formation. Therefore in the average sedated adult patient, the selection of the insertion tube does not appear to make a critical difference.

What would be the ideal insertion tube of the future? A colonoscope ultimately adjustable throughout its length to permit painless and therefore sedationless colonoscopy should be the future goal. Avoiding medication shortens procedure and recovery time, avoids adverse effects of medication, and should reduce costs. As in sigmoidoscopy, patients can drive and resume their daily routine following sedationless colonoscopy, greatly easing the burden to the patient and placing colonoscopy more in line with the requirements of screening. However, unsedated colonoscopy that results in pain risks patient dissatisfaction. Clearly progress toward this possibility has been made [14,18]. The capability of stiffening a specific region of the instrument (to control looping) while simultaneously adding more flexibility in another region (to negotiate sharp flexures) may become possible. MEI may be required to guide this type of alternating variable stiffness. Automatic stiffness adjustments using internal pressure sensors might some day be developed [20]. However, more engineering will be required if painless colonoscopy is to be performed uniformly and predictably in the future.

Summary

Many changes in colonoscope insertion tube design have been developed since colonoscopy was first intro-

duced. The shaft of the instruments have become thinner and torque stability has increased. A wide variety of performance characteristics have been built into the insertion tube, most of which are invisible to the user. The variety of degrees of stiffness, the ability to vary the flexibility of the shaft, and the choice of various diameters is associated with new dilemmas for the colonoscopist. Which instrument is best for any particular patient, and if only one is to be purchased which one should it be? Engineering has not yet provided the ideal instrument but advances are made frequently. Variable-stiffness instruments are the harbingers of a future generation of colonoscopes that will make the procedure easier, safer, and better tolerated.

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Chapter 24

Magnetic Imaging of Colonoscopy

Brian P. Saunders and Syed G. Shah

Introduction

“Seeing is believing” is a saying pertinent to the colonoscopist. The amazingly detailed views obtained during video colonoscopy have dramatically improved our understanding and management of many colonic diseases. Understandably, much emphasis has been placed on the development of the fiberoptic and then video color image to identify and accurately document colonic pathology. However, it is perhaps surprising that it has taken until the 21st century to develop an effective method to image and guide endoscope insertion through the often tortuous intestine. Magnetic endoscope imaging, now commercially available as Scope-guide (Olympus Optical Company), for the first time provides real-time three-dimensional views of the colonoscope shaft during insertion and imparts a new understanding for the endoscopist of the procedure and all its attendant difficulties. It does not make a difficult colonoscopy immediately easy and is no substitute for good technique, but does show the exact problem encountered and gives the endoscopist a new insight into the likely maneuvers required to straighten the endoscope and ensure total colonoscopy.

Need for imaging

Colonoscopy is established as the procedure of choice for investigating patients with colonic symptoms and for screening patients considered at risk for colorectal cancer. In recent years it has also emerged as a viable method for population screening, with recommendations for a colonoscopy every 10 years from age 50 years [1]. This imparts a burgeoning colonoscopic workload and imposes a heavy duty of care on the endoscopist, who must provide a complete, safe, and accurate examination. Expert centers for colonoscopy report completion rates, corrected to exclude obstructing lesions and failed bowel preparation, of 97–99%, with very few if any complications from routine insertion. However less skilled endoscopists fare considerably worse and a recent audit from the British Society of Gastroenterology of 9000 procedures has shown cecal intubation rates of just 55–77% with perforation rates of 1 in 1000 pro-

cedures (O. Epstein, personal communication). These results are unlikely to be only a British phenomenon and are probably representative of “average” practice throughout the world. Even experienced colonoscopists find colonoscopy technically difficult in 10–20% of patients [2]. The most common cause of difficulty is recurrent shaft looping within a long and mobile colon [3]. Without imaging, the correct maneuvers to straighten the colonoscope must be arrived at by instinctive feel and essentially trial and error. This can make colonoscopy time-consuming, uncomfortable for the patient, and result in a need for heavy sedation. Imaging of the colonoscope tip is also important to confirm the anatomic location of lesions encountered and document successful cecal intubation [4].

Colonic anatomy

To understand why colonoscopy can be so difficult and why it is helpful to be able to see the shaft configuration during insertion, it is important to have an understanding of colonic anatomy and mesenteric attachments. The human colon varies considerably in length between approximately 68 and 159 cm, as measured at laparotomy [5]. Usually the sigmoid and transverse colon are free on mesocolons and therefore can greatly increase or decrease in length and mobility according to the action of the colonoscope. Most looping during colonoscope insertion is seen within these segments. Looping of the transverse colon deep into the pelvis may be more common in female patients, who appear to have a longer transverse segment than men [6]. The descending and ascending colon are usually located in a relatively fixed position along left and right paravertebral gutters; however, in 8% of western patients the descending colon remains mobile on a persisting descending mesocolon and in 20% the splenic flexure is also particularly mobile, thus predisposing to atypical (counterclockwise) colonoscope looping in the left colon [5]. Approximately 17% of patients attending for colonoscopy will have adhesions in the sigmoid colon producing a fixed pelvic loop [5]. Adhesions may be congenital or acquired secondary to diverticular disease or pelvic surgery.

Difficult colonoscopy

Several studies have looked specifically at what causes difficulty at colonoscopy. One study included 500 patients in whom fluoroscopic imaging was used during colonoscopy performed by expert endoscopists [3]. A difficult examination (defined as no advancement of the colonoscope tip for at least 5 min) was observed in 16% of cases. Difficulty was due to recurrent looping in the majority of patients (80%) and to sigmoid adhesions in the remainder. Endoscopists were frequently incorrect in identifying the site of looping and were mistaken in their assessment as to whether the tip of the colonoscope was in the proximal sigmoid colon or splenic flexure in 30% of patients. Another study assessed barium enema films of patients in whom colonoscopy was considered to have been technically difficult and found that difficulty correlated with the presence of a long transverse colon or sigmoid colon adhesions [7]. Either of these factors may explain why colonoscopy was considered to be difficult in a significantly greater percentage of women (31 vs. 16%) [6]. Another study identified gender as a major factor in difficulty at colonoscopy [8]. Colonoscopy was particularly difficult in slim female patients. In the same study, older female patients with diverticular disease (adhesions producing a fixed sigmoid colon) and constipated male patients (long redundant colon) were also groups identified with technical difficulties at colonoscopy.

Colonoscope imaging using fluoroscopy

The early pioneers of colonoscopy had no knowledge of intraluminal landmarks to assess their position in the colon and routinely performed colonoscopy in the X-ray suite with fluoroscopy [9]. With the expansion of endoscopy services in the 1970s and 1980s, dedicated endoscopy units were developed, often without access to fluoroscopy. By this time colonoscopists had gained experience with the technique and some considered imaging as only of benefit in the learning phase [10]. Today's generation of colonoscopists have developed skills without fluoroscopy and therefore are largely unaware of its potential advantages, particularly in the 10–20% of patients where recurrent looping occurs and the procedure becomes difficult. However, fluoroscopy as an imaging technique for colonoscopy is fundamentally flawed. Fluoroscopy equipment is expensive, as is the initial financial outlay to lead-line the endoscopy room. The views are two-dimensional, fleeting, and localized, only showing a portion of the abdomen at any one time. In addition, there is a radiation risk, necessitating staff to wear cumbersome protective clothing.

Magnetic imaging system

In view of the problems associated with the use of fluoroscopy and the realization that positional imaging may sometimes be of benefit, a nonradiographic real-time method of colonoscope imaging was sought by two independent groups of researchers based in the UK [11,12]. Both groups considered several approaches, eventually developing similar systems in 1993 based on the principles of magnetic field position sensing.

Prototype imaging system

Method of position sensing

The basic principle operates by determining the position and orientation of discrete points along the colonoscope and uses this information to produce an image of the colonoscope configuration on a display unit (Fig. 24.1) [13]. In the first working prototype, three generator coil assemblies, each comprising three orthogonal coils, situated below the patient sequentially produced pulsed (low frequency), low-strength magnetic fields external to the patient. The low-frequency (10 kHz) fields render the patient and endoscope transparent, while the use of low-strength fields (about 1×10^{-6} that of the energy of a magnetic resonance scan) ensures safety [12,14]. The magnetic fields were detected by miniature sensor coils mounted within a catheter inserted down the instrument channel of the endoscope. In response to each magnetic pulse an electrical current or signal is induced within the sensor coils, the magnitude of which is proportional to the distance from the generator coil. The point-location algorithm (a specifically designed software application) determines the three-dimensional position (x, y, z) and orientation of each sensor with reference to the plane in which the three generator assemblies lie (Fig. 24.2). For each point along the length of the colonoscope, the lengths of the position vectors R_0 , R_1 , and R_2 (the distances measured in a three-dimensional plane from each of the three generator assemblies to the sensor coil) are instantaneously calculated by computer. Each of the three generator assemblies contains three orthogonal coils aligned with the x, y, z axes of the reference plane. The x and y axes represent the horizontal and vertical boundaries of the plane, the z axis being perpendicular to this plane. The nine coils are sequentially energized and the induced voltages in the sensors are measured for each. Thus, from each generator assembly three measured voltages (V_x , V_y , and V_z) are obtained for a given sensor, from which the lengths of the position vectors can be determined. These distances can be considered as the radii of three spheres, the point of intersection of which gives the three-dimensional (x, y, z) position of the sensor coil (Fig. 24.3).

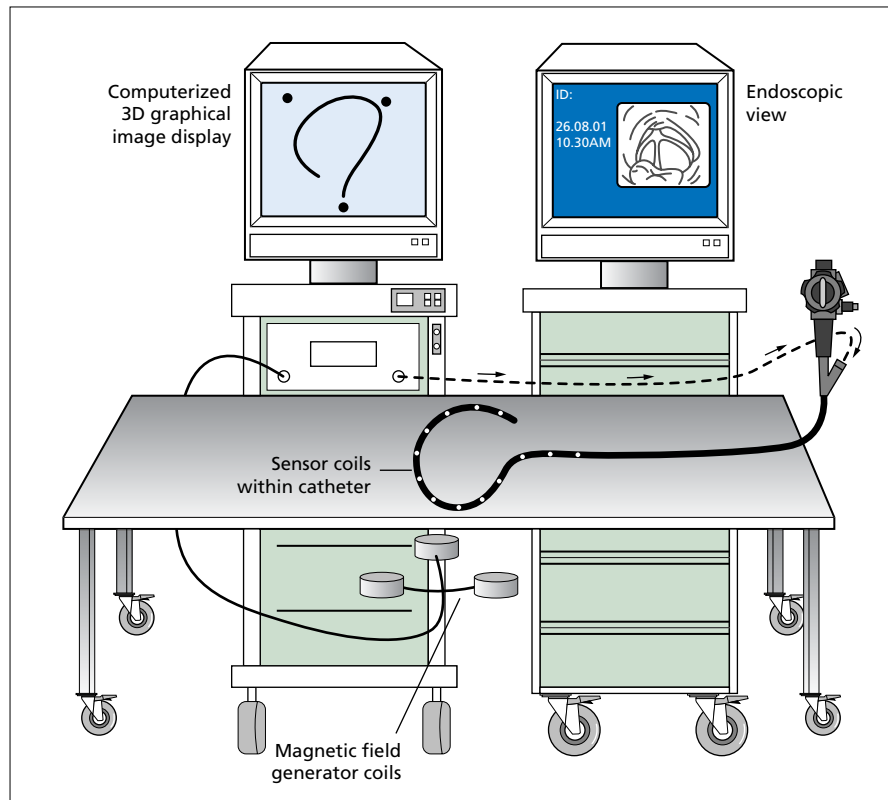


Fig. 24.1 Prototype magnetic imaging system incorporating magnetic field generator coils below a wooden bed with sensor coils situated within a catheter and passed through the biopsy channel of the endoscope.

Once the position of the sensor coils has been calculated, a smooth curve is fitted through each of the individual points by a computer graphics program incorporating the mechanical characteristics of the colonoscope tip and shaft. The curve-fitting algorithm uses the sensor orientation and position information and the fact that the exact distance between each equally spaced sensor coil along the length of the scope is known (usually 12 cm). A computer-generated image of the entire colonoscope shaft is thus displayed on a monitor. The positional data from each of the sensor coils is updated every 0.2 s, generating a real-time display.

Imager display

The representation of the colonoscope shaft on the computer monitor is rendered three-dimensional by using differential gray-scale shading, with those parts of the shaft furthest from the viewer being darker than those nearer the viewer (Fig. 24.4). The image display may be presented in anteroposterior (AP) view, lateral view, or a combination of both to aid in loop recognition. The imaging data of each procedure can be stored on the computer hard disk, but can also be transferred to CD-ROM or floppy disk and replayed for research or teaching purposes using purpose-designed viewing software. The viewing program allows precise meas-

urements to be taken between any sensor point, and also snapshot images to be taken for documentation purposes.

Unlike fluoroscopy, where the effects of abdominal hand compression are difficult to assess because of the necessity to wear heavy lead-protective gloves, the position of the endoscopy assistant's hand and its effect on any loop in the colonoscope shaft can be demonstrated easily using an additional external sensor coil attached to the assistant's hand. The position of the assistant's hand in relation to any loop that may have formed is displayed on-screen. The hand marker moves in real time as the hand is positioned and pressure applied and simultaneously with the representation of the colonoscope shaft.

Magnetic imager (Scope-guide) 2002

Since 1995, the magnetic imaging system has undergone further revision and continuing development. A number of key refinements have resulted in improved image representation and overall functionality, culminating in the launch of Scope-guide (Olympus Optical Company). Scope-guide is a portable stand-alone unit, positioned alongside the endoscopy couch, that has a single connection to either a dedicated colonoscope with in-built coils or to specifically designed imager catheters (Fig. 24.5)

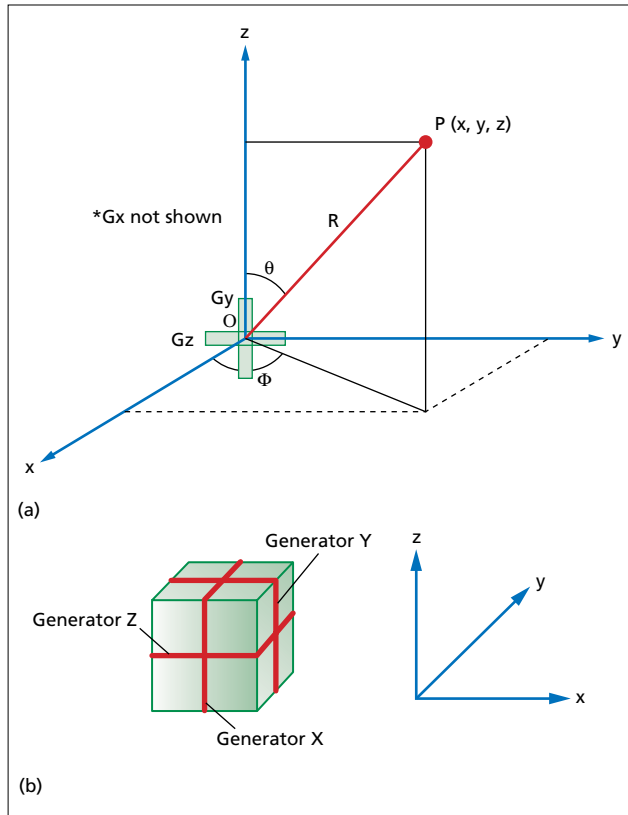


Fig. 24.2 Position (P) of a single sensor coil and a single orthogonal generator coil assembly (G_x, G_y, G_z), and the length of the position vector R (distance of point P from the origin O of the generator coil assembly). The angle of orientation θ is measured from the z axis and Φ is measured in the x, y plane.

that can be inserted through the entire length of the instrument via the instrumentation channel.

Generation of magnetic fields has been reversed in the current imager (Scope-guide) so that the endoscope coils act as generators and the receiver coils are situated within the receiver dish, which is positioned opposite the patient's abdomen (Fig. 24.6). The generator coils comprise a series of 12 insulated single copper wire coils wound around a core and mounted at fixed intervals, enclosed within a catheter or built into the insertion tube. The catheters are quite flexible and designed to resist damage from the bending forces applied to the colonoscope insertion tube. The use of dedicated instruments with in-built coils frees the instrumentation channel and improves the ability to aspirate air or fluid, a problem with catheter use unless a twin-channel or large-channel instrument (3.7 mm diameter or more) is used. At present, there is no dedicated small-diameter (pediatric) colonoscope available.

The magnetic fields are sequentially generated and detected by an array of four orthogonal sensor coils fixed in position and placed adjacent to the patient within the

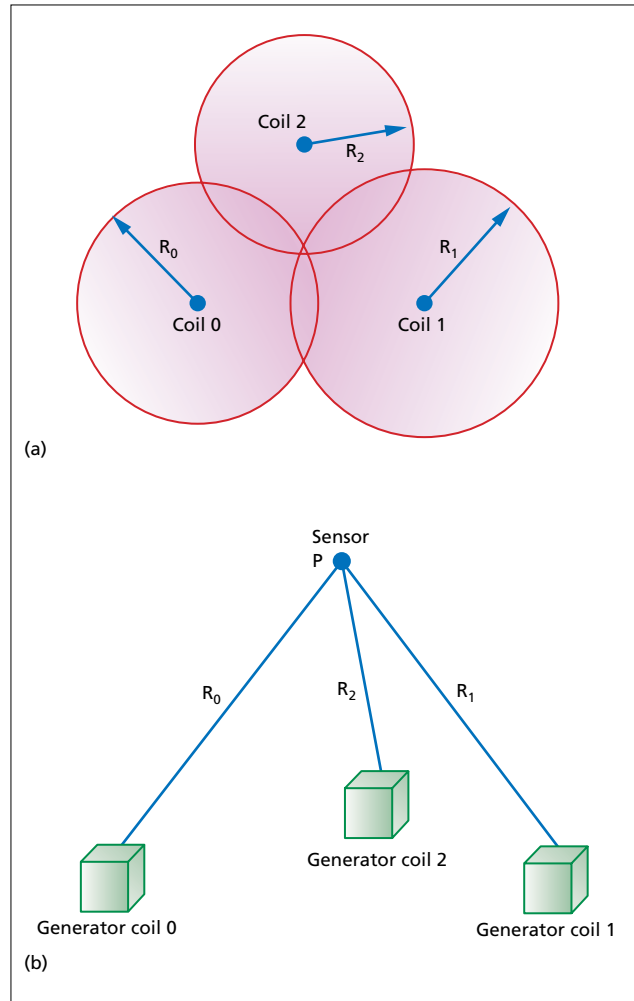


Fig. 24.3 Location (P) of the sensor lies at the intersection of the radial position vectors (distances R_0, R_1, R_2) from the generator coil assemblies (0, 1, 2).

receiver dish. The sensor coils thus form a reference coordinate (x, y, z) plane relative to which the position of each generator coil is calculated. As with earlier prototype imaging systems, the resultant electrical signal induced within each of the sensor coils is digitized, filtered to remove signal noise, amplified, and then fed to a computer processor, which calculates the three-dimensional position of each generator coil, as described earlier. The advantage of reversing the position of the field generators and sensor (receiver) coils is that it allows catheters of varying design (number and spacing of coils) to be used interchangeably with existing imaging software.

During colonoscope insertion (and withdrawal), patient position change is a crucial ancillary maneuver. With early prototypes of the imaging system, three anatomic markers were required to be set each time the patient moves position in order to maintain a true AP

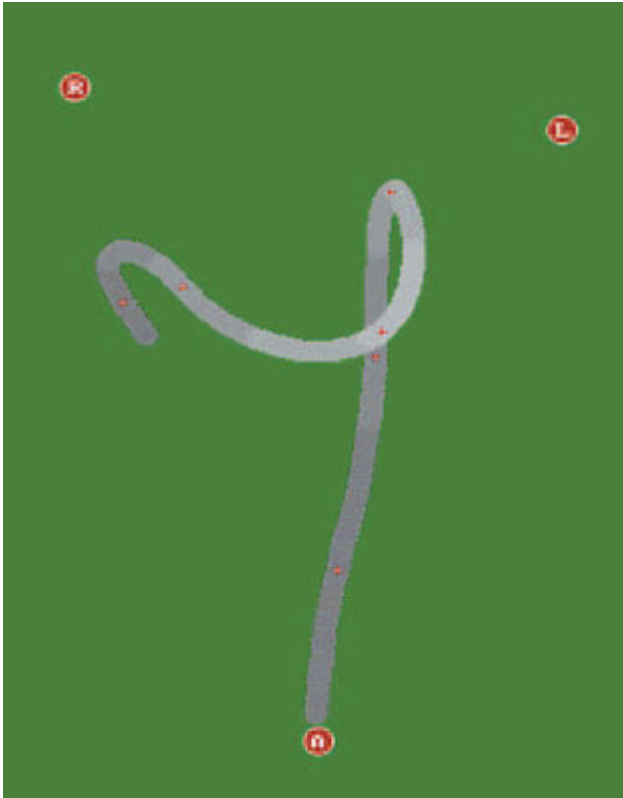


Fig. 24.4 Anteroposterior prototype imager view of colonoscope inserted to distal ascending colon. Anatomic markers represented on screen by the lettered red circles, corresponding to the rib margins and anal region. Note the three-dimensional effect created by gray-scale shading, with the regions of the colonoscope shaft closest to the viewer lightly shaded and those furthest away darker shaded. The red crosses represent the position of the sensor coils.

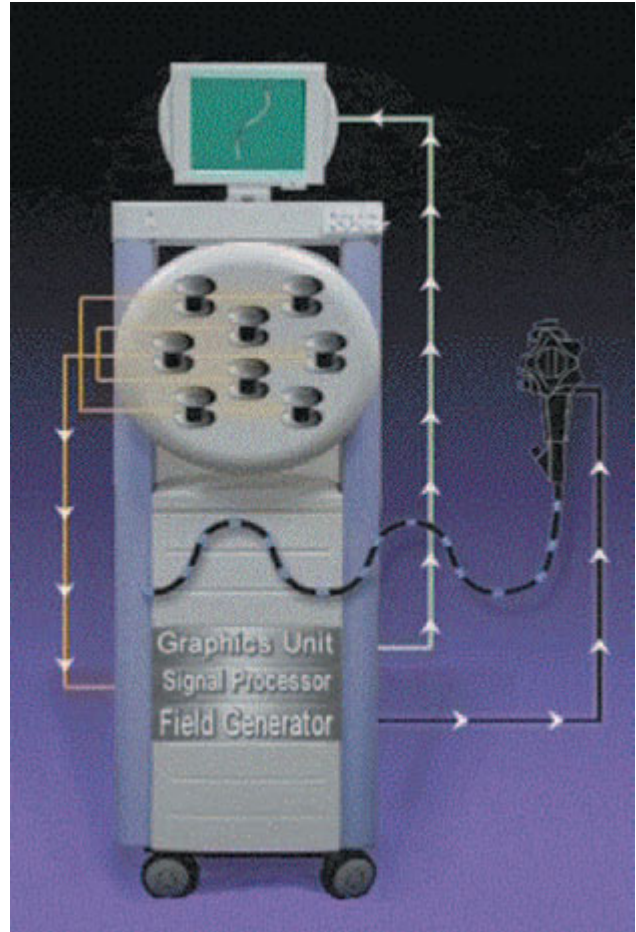


Fig. 24.5 Scope-guide system (semi-diagrammatic view) showing stand-alone unit and dedicated endoscope with in-built magnetic field generator coils.



Fig. 24.6 Set-up for using Scope-guide within the endoscopy unit. The Scope-guide unit is positioned opposite the patient couch with imager and endoscopic views easily seen by the colonoscopist.

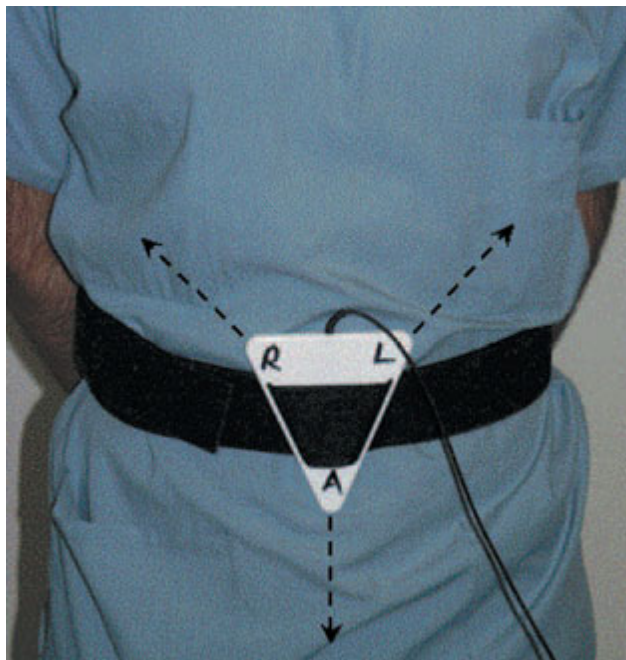


Fig. 24.7 Plate containing three additional sensor coils that sets the orientation of the Scope-guide view when the patient moves position.

view at all times of the procedure. This proved time-consuming and impractical and therefore a patient plate containing the three additional marker coils has been developed (Fig. 24.7). This can be attached to the patient by means of a Velcro belt and moves with the patient, recalibrating the system to maintain a true AP view as standard regardless of patient position. In reality only four patient positions are used during colonoscopy (left lateral, supine, right lateral, and prone) so an easier option that avoids the use of the patient marker plate is to have four preset patient positions identified by the system, which can be selected by a button on the Scope-guide unit (Fig. 24.8). An icon on the imager display indicates the current sensing position (one of four, Fig. 24.9) and a button on the Scope-guide unit allows appropriate selection according to patient position (Fig. 24.8). Thus a simple press of a button is necessary each time the patient changes position. Although the patient may not be at a perfect 90° angle, this matters little in overall interpretation of looping and approximate tip position. Once the endoscopist becomes familiar with this system, it becomes an easy automatic response to position change.

Another improvement in Scope-guide is the development of an ergonomically designed hand-pressure sensor (Fig. 24.10). Controls on the Scope-guide unit allow simultaneous AP and lateral viewing in a split-screen projection to aid accurate hand-pressure placement (Fig. 24.11).

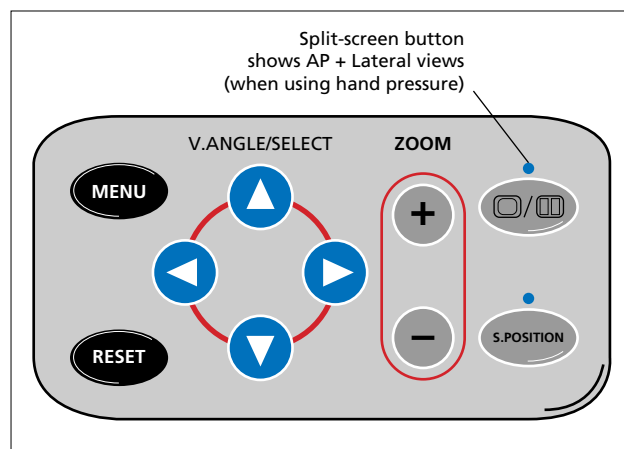


Fig. 24.8 Scope-guide control panel: menu, selects imager system functions; reset, return to default settings; V. ANGLE RESET, patient orientation button; ZOOM, increase or decrease size of image; s. position,

Scope-guide uses modern three-dimensional graphics applications to improve on the realism of the endoscope image. The technique of *polygon rendering* is used to create two-dimensional images, but with a three-dimensional appearance on a two-dimensional screen (computer monitor), generated from three-dimensional data. Polygon rendering is a mathematical technique in which a three-dimensional “wire frame” is initially constructed around points of interest onto which “polygons” are shaped to create the surfaces of the object being modeled (rendered). A polygon is made up of three or more edges, an edge being a line joining two points in a three-dimensional plane. Polygons are thus modeled to fit the wire frame and grouped together to fill and create a solid object—in the case of an endoscope, a cylinder. Differential shades of color (the nearer the viewer, the lighter the shade) and luminescence (light) add to the three-dimensional effect (see Figs 24.9 & 24.11).

Impact of magnetic imaging on colonoscopy practice

The results of the first clinical trials of magnetic endoscope imaging were reported in 1993 [11,12]. In a small number of patients an early prototype imaging system was shown to accurately display the entire configuration of the colonoscope in three dimensions, with close correlation with fluoroscopic images taken simultaneously. Since these early reports experience has been gained using the magnetic imaging system in over 2000 cases. This has provided a unique insight into the procedure of colonoscopy and has allowed comprehensive assessment of the likely benefits of magnetic imaging when it becomes more widely available.



Fig. 24.9 Scope-guide screen showing the typical question-mark appearance of cecal intubation with a straight scope. The octagonal symbol represents the position of the hand-pressure sensor and the Scope-guide icon (bottom right of the screen) shows an arrow pointing upwards from the patient couch demonstrating that the patient is in the supine position (arrow set to point in same direction as patient).



Fig. 24.10 Hand-pressure sensor with a finger grip that is easy to hold by the endoscopy assistant.

Understanding looping

In an audit of 100 consecutive colonoscopy cases performed by expert colonoscopists blinded to the magnetic imager view, the range of looping configurations that occur during routine practice were documented [14]. Typical and atypical loops were encountered and were described using new terminology to accurately indicate the looping state in order to aid straightening maneuvers (Figs 24.12 & 24.13). Despite application of the general principles of good insertion technique, loops occurred in most patients and in the sigmoid colon in 79%. The overall frequency of looping was similar in male and female patients, although atypical loops were more common in

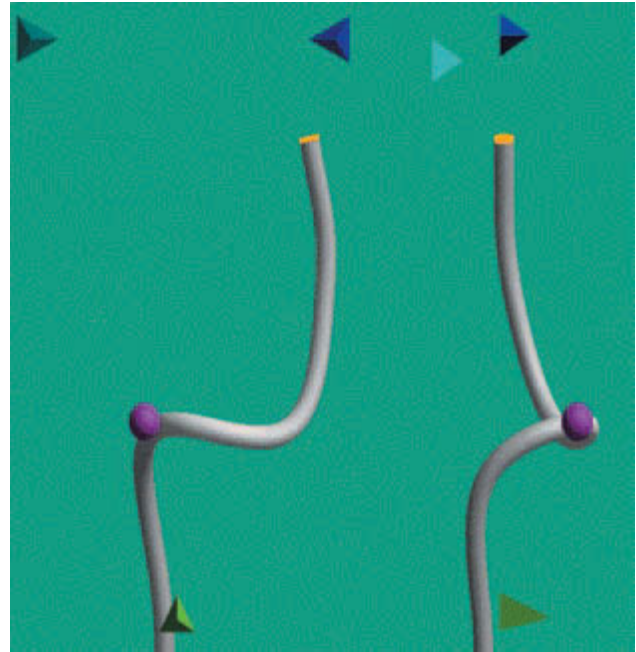


Fig. 24.11 Accurate hand-pressure placement. The loop is viewed in anteroposterior and lateral views to allow accurate positioning of the hand, which is represented by the hand-pressure sensor (purple sphere).

women. Loops were incorrectly diagnosed in 69% of cases; unusual loops, such as anticlockwise spiral loops (reverse splenic flexure, reverse alpha loop) and transverse gamma loops, were always incorrectly diagnosed. Complete colonoscopy was always achieved but in 6% the full 160 cm of the colonoscope was inserted to push through an uncontrollable loop prior to endoscope straightening. In the majority of cases, however, with good technique and frequent loop straightening, less than 100 cm was inserted at any one time. It was found that abdominal compression was generally inaccurate due to either hand misplacement away from the apex of the loop or inaccessible looping deep within the abdomen. In a separate study, pain episodes were documented to correspond directly with looping as demonstrated with magnetic imaging [15]. Looping in the sigmoid colon caused the most pain, particularly in female patients.

Accuracy of tip location

The imaging system accurately locates the colonoscope tip to aid in lesion recognition and cecal intubation. Comparison of contrast studies following imager-guided application of endoclips to predefined anatomic locations during insertion showed good correlation between the imager-defined and actual anatomic clip locations [16]. Imager snapshot views with corresponding endoscopic photos (with or without endoscopic tattooing)

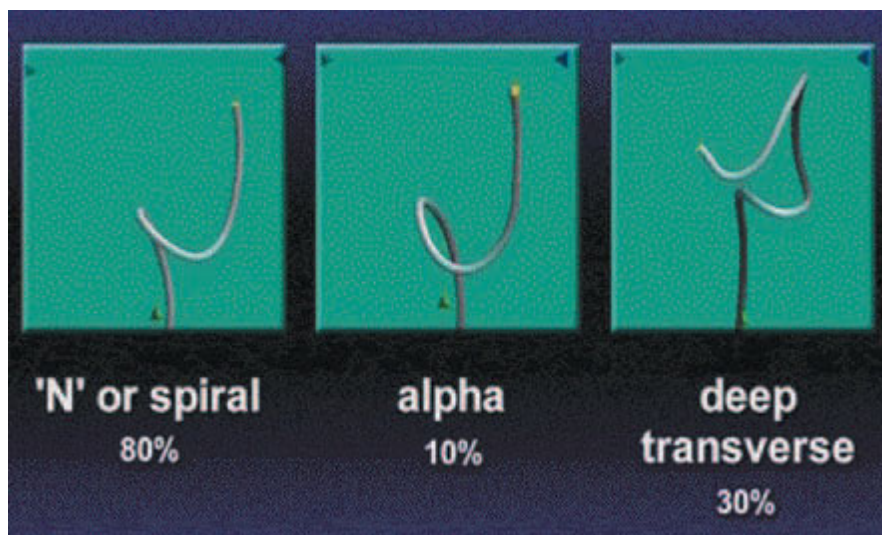


Fig. 24.12 Common loops seen during 100 consecutive routine colonoscopies [14].

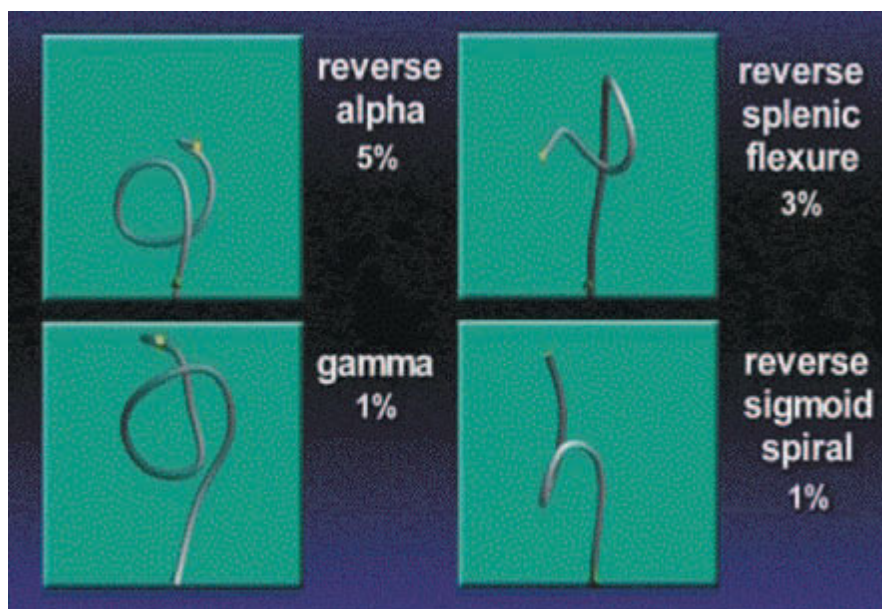


Fig. 24.13 Uncommon loops seen during consecutive routine colonoscopies [14].

represent the most convenient method of documenting colonic pathology to guide future endoscopic examinations or surgical intervention.

Colonoscopy performance

A series of randomized studies have now been published assessing the impact of magnetic imaging on colonoscopy performance. An early study of 55 consecutive patients undergoing colonoscopy by a single experienced endoscopist (1000 previous cases) with or without the imager view (early prototype) showed a reduction in the number of straightening attempts when the colonoscope shaft was looped, but without a corresponding decrease in the duration of loop formation or time taken

to reach the cecal pole [17]. Abdominal hand compression was significantly improved when the endoscopist and endoscopy assistant were able to visualize the imager view, the lateral view giving increased information as to the depth of looping and correct site for application of assistant hand compression. In a more recent study, the effect of magnetic imaging on the performance of colonoscopy was assessed in both trainee endoscopists (200 previous cases) and expert endoscopists (> 5000 previous cases) [18]. Significant improvements in cecal completion rate, insertion time, duration of colonoscope looping, number of straightening attempts, and accuracy of hand pressure were seen with the imaging system when used by the trainees. Similar, though less marked, benefits were recorded with the expert



Fig. 24.14 A variable-stiffness/imager colonoscope (prototype). Note the variable-stiffness dial situated below the instrument head and the additional umbilical that contains the imager electronics.

endoscopists, who found the imaging system dramatically shortened insertion times in technically difficult cases. No differences were seen in patient pain scores or sedation requirements, a finding that is not surprising given the universally low pain scores in the entire patient population. In a separate study assessing the impact of magnetic imaging on sedation requirements and using a patient-controlled analgesia system, no improvement in sedation requirements was seen with imaging to aid insertion, despite an objective improvement in loop handling [19].

There has been no direct testing of the magnetic endoscope imager in patients with implanted pacemakers or defibrillators and current advice is to avoid its use in these relatively rare circumstances.

Magnetic imaging and variable-stiffness colonoscopes

Variable-stiffness colonoscopes have recently been introduced that allow the endoscopist to change the shaft characteristics of the colonoscope at any time during insertion. This potentially allows easier passage through a fixed sigmoid colon, using a pediatric (increased flexibility) mode, and an enhanced ability to prevent recurrent looping by increasing shaft rigidity after successful passage into the proximal colon. Precise utilization of the variable-stiffness function is difficult to ascertain during insertion and its use is often by best guess and trial and error. Two studies have assessed the impact of magnetic imaging on use of the variable-stiffness colonoscope [20]. In the first, magnetic endoscope imaging was used

to evaluate the success of scope insertion during back-to-back proximal colon randomized insertions with and without the colonoscope maximally stiffened. Stiffening resulted in a more rapid proximal colon insertion, particularly around the splenic flexure and with less recourse to ancillary maneuvers such as hand pressure or position change. In the second study, an experienced endoscopist was randomized to perform consecutive examinations with a variable-stiffness scope with or without the benefit of the imager view. Not unsurprisingly, successful use of the variable-stiffness function was significantly more likely when the imager could be seen. New colonoscopes (CF-240 DL, Olympus Optical Company) are now available that combine the variable-stiffness function with in-built imager electronics (Fig. 24.14). These instruments appear to have major advantages over conventional colonoscopes, the new modalities in combination amounting to a greater overall benefit than would be expected by the simple addition of both factors.

Magnetic imaging and colonoscopy training

Colonoscopy training has changed little in the last 30 years and still relies heavily on an apprenticeship scheme, where an experienced colonoscopist hands down the “tricks of the trade” to the inexperienced trainee. Training is highly frustrating and unsatisfactory for all parties concerned. For the trainee it is difficult to appreciate why certain maneuvers are apparently beneficial and for the trainer it is difficult to assess why the trainee is stuck unless the scope is taken over by the

trainer and manipulated appropriately, by which time the teaching opportunity has often been lost. Magnetic imaging may address many of these frustrations by allowing a structured interaction between trainer and trainee, allowing the trainee to complete cases under supervision where previously the trainer would have needed to intervene, thus accelerating the trainee's learning curve and acquisition of hand-skills. In an initial pilot study, a single beginner colonoscopist (only 15 previous colonoscopies) performed procedures under supervision, with examinations randomized to be either with or without the imaging system [21]. Benefits in terms of loop management were seen with the imaging system in the initial stages of training, with a plateau seen at approximately 50 cases when a 90% completion rate to the cecum was seen. Thereafter no demonstrable difference was seen comparing cases with or without the imager, suggesting that imaging is particularly valuable early during the learning curve. Further work is required to define the longer-term impact on skill acquisition; however, it seems logical that future computer simulators teaching basic colonoscope hand-skills will incorporate simulated imager views that will lay the foundations for hands-on training with the imager in live cases. Performance assessment using a specific score from a combined video and magnetic imaging recorder may prove a robust tool for ensuring standards and charting trainees progress [22].

Tips on using magnetic imaging

It has taken 10 years since the first prototype imaging system was developed by Dr John Bladen [11] for a commercially produced, user-friendly system to become widely available. It remains to be seen whether endoscopists will embrace this new technology and reexamine their technique in the light of the new anatomic information that it provides. When the principal author first used the imaging system he was amazed (and at times horrified!) by the number and variety of loops that occur during routine practice; 30 cases were necessary to become comfortable with interpretation of the imager view and endoscopists new to the system must be patient and learn how to use it. A long and mobile colon will still be difficult to examine but imaging allows precise decisions to be made on the timing of loop withdrawal, application of hand pressure, timing of position changes, and accurate use of the variable-stiffness function. After nearly 1000 cases with the imaging system, the principal author has collected the following, hopefully useful, tips related to use of the imager for the difficult colonoscopy.

- A sigmoid loop can rarely be straightened fully until the tip of the colonoscope is in the descending colon and has been passed above the level of the highest point of the loop.

- Accurate assessment of hand-pressure location requires simultaneous visualization in AP and lateral views.

- When a long and acute N-spiral loop is encountered with difficult passage into the descending colon, withdraw to the distal sigmoid, change patient position to the right lateral, and then push inward with counterclockwise torque. This tends to manipulate a long sigmoid into a favorable alpha loop (alpha maneuver), which will pass easily to splenic flexure when scope straightening becomes easy.

- If a transverse gamma loop appears to be forming, immediate withdrawal to the splenic flexure with application of suction to shorten the transverse and inward push with clockwise torque countered by imager-directed transverse abdominal pressure may allow straighter passage across the transverse.

- Difficulty in passing the splenic flexure is nearly always made easier by position change to the right lateral.

Future developments

It seems likely that magnetic imaging will become a standard for colonoscopy practice. Initially teaching units will incorporate the technology as training becomes immediately transformed, even enjoyable, interactive, and more logical. Once the next generation of endoscopists becomes familiar with the imager, it will be seen as essential technology to improve completion rates in difficult cases and help document total colonoscopy. In particular, imager records will help endoscopists to assess their own performance and maintain standards within each endoscopy unit. The current Scope-guide system does not allow recording of cases and a software upgrade is in progress. Eventually, it will be possible to incorporate imager snapshots into the endoscopy report in the same way that endoscopic views help to document pathology and cecal intubation. A simple and potentially important future improvement will be to increase the degree of stiffness that can be imparted to the shaft of the new generation of variable-stiffness, imager scopes. The ability to see that the colonoscope shaft is straight will mean that the increased stiffening function can be applied entirely safely. Data from the imager will help in future colonoscope design and it is not beyond comprehension to envisage a semiautomatic endoscope that adapts to the degree of looping or which suggests maneuvers to help the endoscopist depending on shaft configuration.

Summary

Magnetic imaging of colonoscopy in the form of Scope-guide provides the endoscopist with important information that, if accurately interpreted, has the poten-

tial to dramatically improve procedure performance. As we move towards mass population screening by colonoscopy to prevent colorectal cancer, magnetic imaging would seem to be an essential tool in ensuring best practice and accurate documentation of the procedure. It represents an important step toward the ultimate goal of safe, painless, and complete colonoscopy.

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Chapter 25

Accessories

Gregory G. Ginsberg

Introduction

Accessories for colonoscopy are used for snare polypectomy, tissue sampling, endoscopic mucosal resection, object retrieval, size measurement, marking, image enhancement, hemostasis, ablation, and stenting. This chapter provides an overview of accessories used during colonoscopy. Specific applications of these accessories are detailed in their respective sections.

Polypectomy snares

The capacity to identify and remove colorectal polyps has enabled colonoscopy to prevent colorectal cancer and to become the preferred means for screening and surveillance of patients for colorectal neoplasia.

Polypectomy snares are available in a variety of shapes, sizes, and materials. Specialty snares are designed with special features for specific performance properties. Snares may be designed and marketed as disposable or reusable. Reusable snares must be designed so they can be disassembled for cleaning and sterilization and then reassembled, and in addition have properties that enable them to retain their configuration and performance through multiple use and cleaning cycles. These constraints, plus the availability of cheap materials and production costs, have promoted broad acceptance of disposable snares for colonoscopic polypectomy.

Colonoscopic polypectomy snares consist of an attached or continuous wire loop housed within a flexible synthetic polymer sheath. This device is passed through the accessory channel of the colonoscope. Sheaths are typically 7.0Fr in diameter, for a minimal channel size of 2.8 mm, and 230 cm in length. The wire and sheath are affixed to a moving-parts plastic handle at the operator end of the device (Fig. 25.1). The handle controls opening (extension) and closing (retraction) of the wire loop from and within the outer sheath. The snare wire couples to an electrical connector within the handle, which also has a socket for connecting an active cord to an electrosurgical unit.

Although bipolar snares have been developed, most snares are designed to be used with monopolar current. Bipolar snares are designed with each half of the snare



Fig. 25.1 Colonoscopic polypectomy snares consist of a continuous wire loop housed within a flexible synthetic polymer sheath and affixed to a plastic operator handle. (Courtesy of Olympus America, Inc., Melville, NY.)

loop functioning as an electrode so that current flows across the polyp [1]. In monopolar snares the current flows from the snare to a distant return electrode (grounding pad), generating local thermal energy for cutting and coagulation [2]. There are no comparative trials of bipolar vs. monopolar snares.

Braided stainless steel wire is the most commonly used material for polypectomy snares, owing to its strength, conduction properties, and configurational memory. The snare wire typically is 0.30–0.47 mm diameter. Nitinol wire snares may have superior configurational memory but lack sufficient stiffness, tending to be floppier than desired. Monofilament wire snares promote transection over coagulation and are largely limited for cold-snare polypectomy of small polyps in patients without coagulation disorders [3].

The standard shape of the snare loop is oval or elliptical (Fig. 25.2). Alternative configurations include round, crescent, or hexagonal (Fig. 25.3). Selection of snare configuration is based on personal preference. Experienced colonoscopists may choose specific snare shapes for the removal of individual lesions based on the lesion's location, orientation, size, and configuration. The standard size and shape snare suffices for the vast majority of instances. There are no comparisons of snare shapes to support superiority of any one configuration over others.



Fig. 25.2 The standard snare loop shape is oval or elliptical (Courtesy of Olympus America, Inc., Melville, NY.)

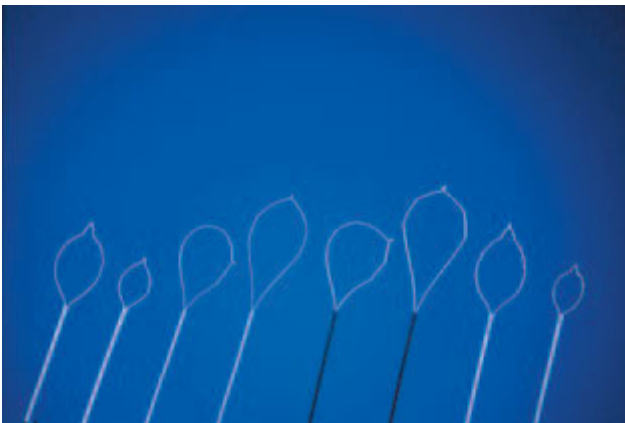


Fig. 25.3 Alternative snare loop configurations include round, crescent, or hexagonal shaped. (Courtesy of Olympus America, Inc., Melville, NY.)

While there is some variability among the manufacturers, standard size snare loops are typically 2.0–2.5 cm in diameter and the length of the loop varies from 5 to 6 cm. Minisnares have loop diameters 1.0–1.5 cm and length of 2–3 cm and are used for completion resection of residual adenoma following mucosectomy of a sessile lesion and for resection of smaller polyps [4].

Other specialty snares have been developed to enhance success when circumstances prove challenging to the characteristics of ordinary snares. While specialty snares may offer advantages in specific instances, most experienced colonoscopists do quite well with standard-loop snares along with the occasional use of mini- and jumbo-snares. Nonetheless, a familiarity with and limited stock of specialty snares may ensure success when faced with the occasional defiant polyp. Duck-bill® (Wilson-Cook Medical, Winston-Salem, NC) and multi-angled (Fig. 25.4) snares are intended for lesions difficult to access based on their wall location with respect to the tip of the colonoscope. Rotatable snares can be adjusted so that the snare loop opens in an orientation favorable to polyp entrapment (Fig. 25.5).

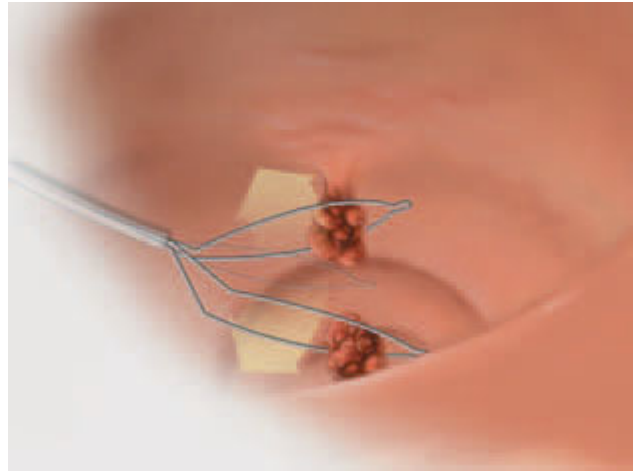


Fig. 25.4 The multiangled snares are intended for lesions difficult to access based on their wall location with respect to the tip of the colonoscope. (Courtesy of Wilson-Cook Medical, Winston-Salem, NC.)

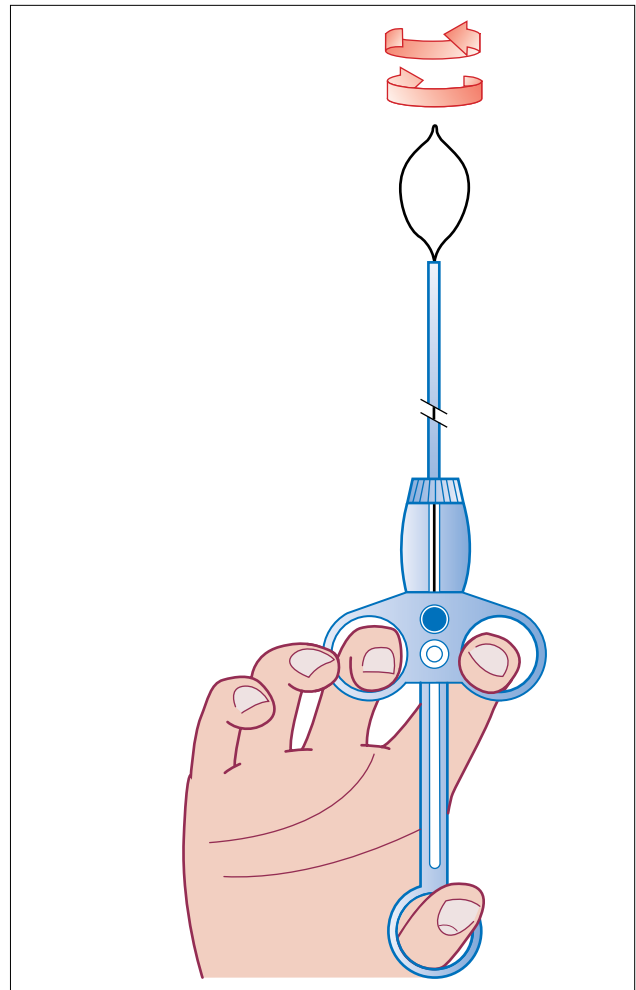


Fig. 25.5 Rotatable snares can be adjusted so that the snare loop opens in an orientation favorable to polyp entrapment. (Courtesy of US Endoscopy Group, Mentor, OH.)



Fig. 25.6 Needle- or anchor-tipped snares have a short, pointed barb at the tip of the snare intended to stabilize the snare for polyp capture. (Courtesy of Wilson-Cook Medical, Winston-Salem, NC.)

Needle- or anchor-tipped snares have a short, pointed barb at the tip of the snare (Fig. 25.6). The modified tip is intended to aid in stabilizing the snare for polyp capture. By impaling the barbed tip into the bowel wall just beyond the lesion, the snare tip can be fixed in place while the loop is being flexed to open over and around the polyp.

A variety of snares have been developed and marketed for the removal of sessile polyps. These iterations include barbed, spiral, and “hairy” snares (Fig. 25.7).



Fig. 25.7 Barbed snares have tiny barbs on the wire loop intended to grasp the leading edge of sessile polyps.

Each is designed to grip the edges of low-profile sessile lesions. There are no studies to indicate superiority of modified over standard snares for the resection of sessile colon polyps.

Retrieval devices

An assortment of retrieval devices has been developed for the extraction of polyps and foreign objects from the colon. These include a variety of graspers, baskets, and nets [5]. Polyp retrieval is discussed in detail in Chapter 37.

Biopsy forceps (see Chapter 27)

Biopsy forceps are used to sample colonic mucosa and mucosal-based lesions. Colonoscopic biopsy forceps consist of a flexible, metal-coil outer sheath that houses a steel cable connecting a two-piece plastic handle to opposing metal biopsy cups (Fig. 25.8). Some biopsy forceps are coated with a synthetic polymer to improve passage through the colonoscope accessory channel.

Single-bite cold-biopsy forceps allow sampling of only a single specimen at a time. Double-bite cold-biopsy forceps (most commonly employed) are equipped with a needle-spike between the opposing biopsy cups. The needle-spike serves several purposes: the spike can be used to impale the tissue of interest, thus stabilizing the forceps cups for selected tissue sampling; deeper biopsies can be obtained than with nonneedle versions [6]; the spike secures the first specimen on the device while a second specimen is obtained. Without the spike, attempts at multiple tissue sampling with single-bite forceps may result in the loss of specimens and crush artifact.



Fig. 25.8 This forceps is equipped with a needle-spike between the opposing biopsy cups to impale tissue. (Courtesy of Olympus America, Inc., Melville, NY.)

Biopsy cup jaws may be standard oval or elongated, fenestrated or nonfenestrated, and smooth or serrated. Large-capacity cup or “jumbo” biopsy forceps, popular in upper endoscopy applications, are not routinely employed in colonoscopy.

Multibite forceps have been developed that can obtain up to four or more specimens on a single pass. In a prospective, partially blinded, randomized trial of multibite forceps vs. conventional forceps, the multibite forceps compared equivalently for diagnostic quality [7]. The multibite forceps has the potential to contribute time saving when a large number of specimens are needed to be obtained, such as in surveillance of patients with ulcerative colitis.

Other specialty forceps include a variety of innovations for challenging circumstances. “Swing-jaw” forceps feature a rocking cup assembly action intended to direct the jaws of the forceps toward the tissue of interest; “rotatable” forceps are designed to do that with variable degrees of control. “Angled” forceps assume a 90-degree orientation to the long access of the scope once extended from the accessory channel.

Monopolar hot biopsy forceps were developed for simultaneous tissue biopsy and coagulation. Thermal energy is generated when current, passed through an insulated shaft is introduced to the tissue at the blunted edges of the forceps jaws [8]. Heat energy is regulated and determined by generator voltage and waveform, current density, and application time [2]. Bipolar hot biopsy forceps have also been developed. Bipolar forceps have insulated biopsy cups except for the cup edges that are the electrodes [2]. Tissue injury is deeper with monopolar as compared to bipolar hot biopsy forceps [8].

Hot biopsy became popular for biopsy resection of diminutive colonic polyps. The rationale for coagulative tissue sampling is to destroy neoplastic tissue, thereby preventing residual or recurrent adenoma and the potential for subsequent development of carcinoma. There is insufficient data to indicate that excisional hot biopsy forceps removal reduces the incidence of colorectal cancer or even complete eradication of neoplastic tissue treated [8–10]. Complications of hot biopsy forceps include hemorrhage, perforation, and postcoagulation (transmural burn) syndrome [8].

The relative virtues of reusable vs. disposable biopsy forceps can be debated. Arguments focus on cost, operational performance, and infection control. Two prospective, randomized, pathologist-blinded trials showed no differences in quality of specimen for histologic diagnosis between a variety of commercially available reusable and disposable biopsy forceps [11,12].

Yang *et al.* prospectively measured cost and operational performance of disposable and reusable forceps in 200 biopsy sessions [13]. Costs were factored in acqui-

sition and reprocessing. They found that malfunction of reusable forceps increased with number of uses. At 15–20 uses, reusable and disposable forceps costs are similar, when the cost of disposable forceps is around \$40.00. When reusable forceps are used more than 20 times, they are less expensive. However, this study showed that the performance of reusable forceps deteriorated significantly in the range from 15 to 20 uses. Deprez *et al.* in a much larger study (7740 sessions) using similar design and the lowest available purchase price for disposable forceps at the time (\$26.90) reported that total purchase and reprocessing costs for reusable forceps were 25% less than disposable devices [14]. Further, an average of 315 biopsy sessions were performed with a reusable forceps extending their mean life to 3 years.

In a third study, disposable forceps outperformed their reusable counterparts and offered a cost advantage [15]. These authors also reported a concern over residual proteinaceous material observed in reusable forceps, raising an infection control risk. This charge was countered, however, by a study by Kozarek *et al.* who performed an *ex vivo* evaluation of cleaning, and *in vivo* evaluation of function, performance, and durability of reusable forceps [16]. Their analysis concluded that reusable biopsy forceps can be confidently sterilized and reused when accepted cleaning and sterilization protocols are followed. Sterilized reusable biopsy forceps were used a mean 91 times, rendering the potential for significant cost saving, again, depending on acquisition and reprocessing costs. All published cases of transmission of infection associated with reusable biopsy forceps have been attributed to breaches in accepted standards of device reprocessing [17].

The functional performance of reusable biopsy forceps will ultimately deteriorate with increased number of uses. The durability can be extended with care in use and reprocessing. Cost comparisons depend mainly on the cost of disposable devices. Users should also factor in the cost of medical waste disposal and environmental impact associated with the disposal of single-use devices.

Injection needles

Injection needles are devices passed through the accessory channel of the colonoscope to enable injection of a solution into tissue. Injection needles are used in colonoscopy for injection-assisted polypectomy, hemostasis (variceal, nonvariceal, and hemorrhoidal), and tattooing.

Injection needles consist of an outer sheath (plastic, Teflon, or stainless steel coil) and an inner hollow core needle (21–25G) (Fig. 25.9a,b) [18]. The needle tip is typically beveled. Needle-tip length should be sufficient to routinely penetrate into the submucosa and not so long

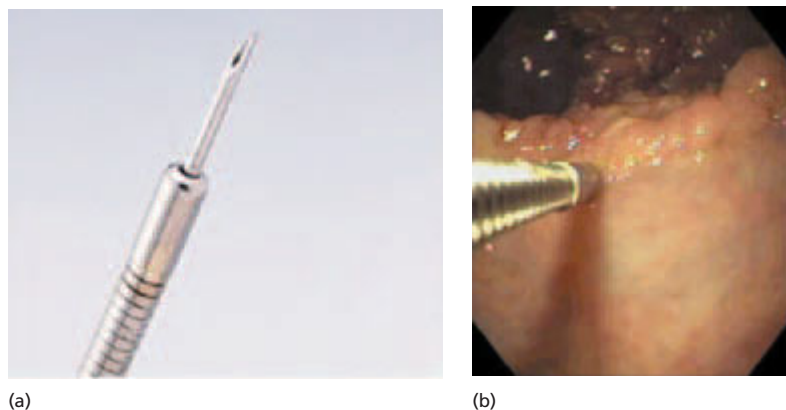


Fig. 25.9 (a) Injection needles consist of an outer sheath (in this case stainless steel coil) and an inner hollow core needle. An operating handle controls the advance and withdrawal of the needle. (b) Needle placed for injection to elevate a polyp. ((a) Courtesy of Olympus America, Inc., Melville, NY.)

as to routinely penetrate through the colon serosa. The outside diameter varies from 2.3 to 2.8 mm. A metal and plastic luer lock handle controls needle extension and retraction to fixed or variable lengths. Some versions allow the needle to be preferentially locked in the extended position. Most commercially available injection needles are single-use disposable. One manufacturer markets disposable needles with a reusable sheath that can be sterilized.

Metal coil sheathed needles may offer advantages over their plastic sheathed counterparts in that they are less likely to kink and are more apt to remain fully functional when passed through the channel of a coiled colonoscope. This allows use even when there is excessive looping of the colonoscope or when operating with a retroflexed colonoscope position. Metal coil sheaths are also less likely to allow unintended needle puncture through the sheath with the associated risk of scope injury. However, there are no published trials comparing various injection catheters for colonoscopic applications.

An injection needle has also been incorporated into a multipolar electrocautery device. This device allows combination injection and contact-thermal hemostatic therapy for nonvariceal bleeding.

Spray catheters

Spray catheters are used for performing chromoendoscopy (see Chapters 41–43). Chromoendoscopy employs a colored dye to enhance the mucosal surface pattern in order to enhance the detection or discrimination of dysplastic epithelia [19]. Chromic agents may be vital stains or contrast agents. Vital stains are selectively taken up by epithelial cell cytoplasm, whereas contrast agents coat the epithelial surface enhancing the contour relief pattern. Contrast agents are commonly employed when performing high-resolution and high-magnification colonoscopy [20].

Spray catheters are disposable, flexible, hollow plastic sheaths, with a plastic luer lock handle, and a metal spray nozzle tip (Fig. 25.10a,b). Alternatives to dedicated spray catheters are injection needles, ERCP catheters, and simple injection through the accessory port itself. Spray catheters generally allow the most controlled, precise, and tidy application of chromoendoscopy.

Endoscopic clips (see Chapter 26)

The application of metallic clips via flexible endoscopes has had considerable appeal. The most experience has

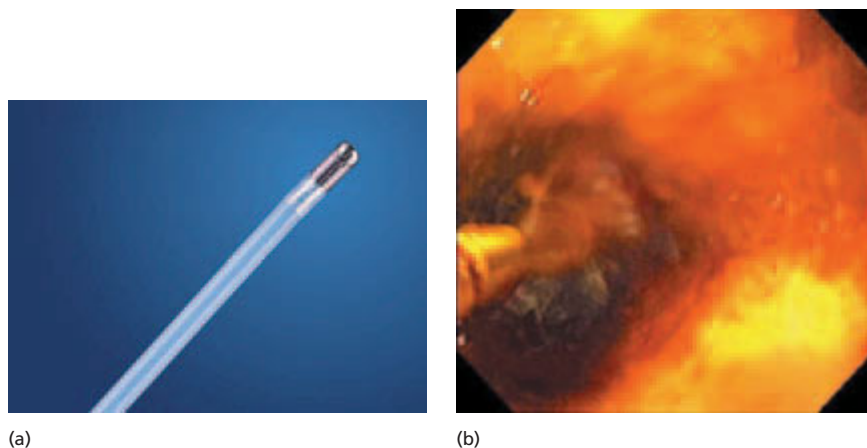


Fig. 25.10 (a) Spray catheters are disposable, flexible, hollow plastic sheaths, with a plastic luer lock handle, and a metal spray nozzle tip. (b) Dye being expelled from the catheter. ((a) Courtesy of Wilson-Cook Medical, Winston-Salem, NC.)

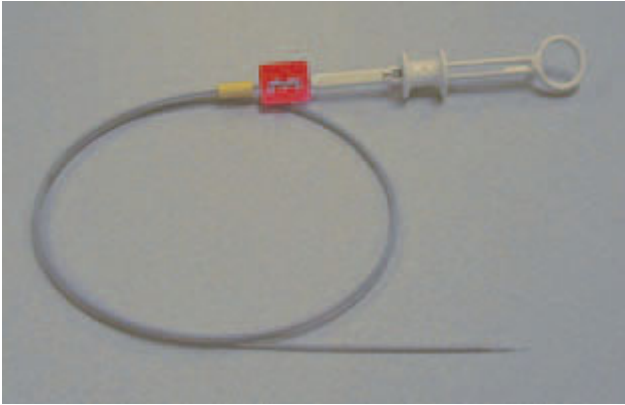


Fig. 25.11 This disposable clip-fixing device consists of a control section and an insertion tube. The control section incorporates movable plastic parts that manipulate clip loading and deployment. The insertion tube is made up of a metal coil sheath contained within an outer plastic sheath. A metal cable moves within the coil sheath. (Courtesy of Olympus America, Inc., Melville, NY.)

been with the HX series of endoscopic clip fixing devices (Olympus Corp., Tokyo Japan). This device was first conceived for hemostasis of nonvariceal bleeding sources. Colonoscopic clip application has been used effectively for hemostasis of immediate and delayed bleeding from polypectomy and hot biopsy forceps sites, diverticulosis, arteriovenous malformations, colorectal variceal bleeding, and prophylaxis of postpolypectomy bleeding pre- and post-snare resection. Such mechanical hemostasis allows localized, directed, and specific therapy, while minimizing tissue injury at the treatment site. Other applications have included lesion marking (bleeding or tumor site), fixation of endoscopically placed decompression tubes, and primary closure of resection sites and perforation. The clip-fixing device has evolved from its first inception to a relatively easy to use, reliable, and now rotatable delivery device [21,22]. A single-use, preloaded iteration is also available. Clips typically slough off in 3–4 weeks and pass uneventfully in the stool.

The clip-fixing device consists of a control section and an insertion tube (Fig. 25.11). The control section incorporates movable plastic parts that manipulate clip loading and deployment. The insertion tube is made up of a metal coil sheath contained within an outer plastic sheath. A metal cable moves within the coil sheath. At the distal end of the cable is a hooking apparatus to which the clip is attached. The insertion tube is compatible with an endoscope accessory channel of 2.8 mm or larger. Sheath lengths are available up to 230 cm.

The clips themselves are configured from a multiangled stainless steel ribbon (Fig. 25.12). Clips are available in a limited variety of lengths and configurations. Standard hemoclips (MD850) have prongs that meas-



Fig. 25.12 The clips themselves are configured of a multiangled stainless steel ribbon. When fully opened, the predeployment distance between the clip prongs measures 7 mm (Courtesy of Olympus America, Inc., Melville, NY.)

ure 6 mm in length and 1.2 mm in width. When fully opened, the predeployment distance between the clip prongs measures 7 mm. A “clip connector” enables loading of the clip on to the hooking cable. Predeployment and actual deployment is facilitated by a cylindrical “clip pipe.” A stepwise, controlled progression of the clip pipe over the clip promotes full opening and subsequent closure of the clip.

In practice, the clip is loaded on to the hooking cable and withdrawn into the outer plastic tube sheath. This procedure is unnecessary when using the preloaded ready-to-use version. The delivery device insertion tube is then passed through the endoscope-working channel. With the target lesion in view, deployment is initiated by exposing the clip from within the tube sheath. Withdrawing the cable within the tube sheath slides the pipe clip up the clip itself fully opening the clip. With the rotatable version, a rotator-disc located on the control section may be used to turn the clip to the desired orientation. The insertion tube is then advanced so the teeth of the clip engage the target tissue, whereupon further sliding of the pipe clip closes the clip and completes deployment detaching the clip from the clip connector.

Becoming facile with loading and deployment of endoscopic clips requires practice and regular use. Clips deploy with equal reliability in the en face as well as in retroflexed scope positions. The most recent models (HX-5LR-1, HX-5QR-1, HX-6UR-1) are equipped with the rotating wheel that works surprisingly well. The clip can usually be rotated to the desired orientation. The rotator feature and improved durability are clear advantages over earlier clip designs. An unlimited number of clips can be placed during a single session. Mechanical cleaning followed by gas sterilization can reprocess the reusable model delivery device.

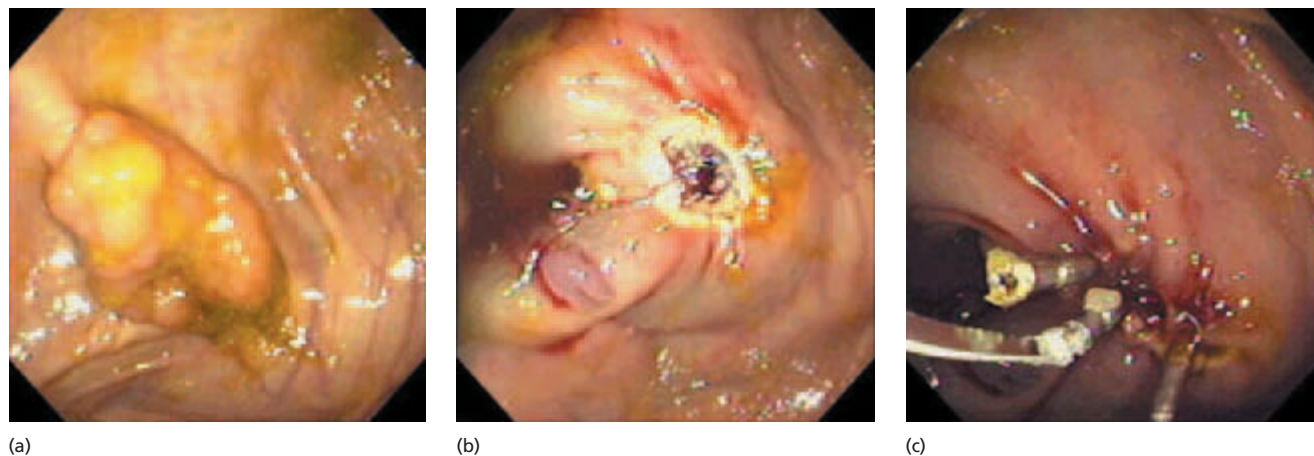


Fig. 25.13 A large sessile polyp is identified in the cecum in a patient requiring anticoagulation therapy (a). Following saline-assisted polypectomy, there is oozing from the pigmented center of the resection site (b). Primary closure of the resection site and durable hemostasis is achieved with three clips (c).

Endoscopic mucosal clips are highly effective for prophylactic hemostasis of polypectomy and mucosectomy sites and for primary or secondary hemostasis of postpolypectomy bleeding [23,24]. Endoscopic hemoclips promote durable hemostasis and do not incur additive tissue injury as is the case with thermal or injection techniques. Among 72 cases of colonoscopic immediate postpolypectomy ($n = 45$) and delayed postpolypectomy ($n = 18$) and postbiopsy ($n = 9$) bleeding, effective and durable clip hemostasis was achieved in all but one case [25]. There were no episodes of recurrent bleeding or need for surgery related to bleeding.

Marking with clips is effective for lesions benefiting from precise localization preoperatively including tumors and bleeding sites (e.g. diverticulum). Clips can readily be palpated or located with fluoroscopy at the time of surgery. Clips may be used for the fixation of colonic decompression tubes to prevent tube migration. Lastly, endoscopic mucosal clips have been used to achieve transient tissue remodeling to oppose surrounding tissue at a resection site or luminal defect (Fig. 25.13a,b,c) [26]. The latter application should be limited for use in highly selected instances. A three-pronged clip has recently become available (triclip) from Wilson-Cook, Inc.

Detachable loops (see Chapter 26)

Detachable loop snares have been developed for the prevention and management of bleeding from polypectomy sites. Such bleeding is reported to occur in 2% of all polypectomies. Bleeding occurs more frequently with the removal of large polyps with thick stalks and in

patients who have underlying coagulopathies or in those taking anticoagulation therapy or nonsteroidal antiinflammatory drugs. The detachable loop snare ligature was developed a little more than a decade ago for primary or secondary prophylactic therapy for postpolypectomy bleeding, or as primary or secondary treatment of active or recent postpolypectomy hemorrhage [27–30]. The detachable snare or “endoloop” (Olympus HX-20Q, Olympus Corp., Tokyo) is composed of an operating apparatus (MH-489) and an attachable loop of nylon thread (MH-477) (Fig. 25.14). The operating apparatus consists of a Teflon sheath 2.5 mm in diameter and 1950 mm in working length, a stainless steel coil sheath 1.9 mm in diameter, a hook wire, and the handle. The nylon loop is nonconductive and consists of a heat-treated circular or elliptically shaped nylon thread and a silicon-rubber stopper that maintains the tightness of the loop.

The optimal application of this device for prevention and management of polypectomy bleeding is yet to be determined. When used for primary prophylaxis, the flexibility of the loop makes it difficult to encircle the



Fig. 25.14 The detachable snare or “endoloop” (Olympus HX-20Q, Olympus Corp., Tokyo). The nylon loop is nonconductive and consists of a heat-treated circular or elliptically shaped nylon thread and a silicon-rubber stopper that maintains the tightness of the loop. (Courtesy of Olympus America, Inc, Melville, NY.)

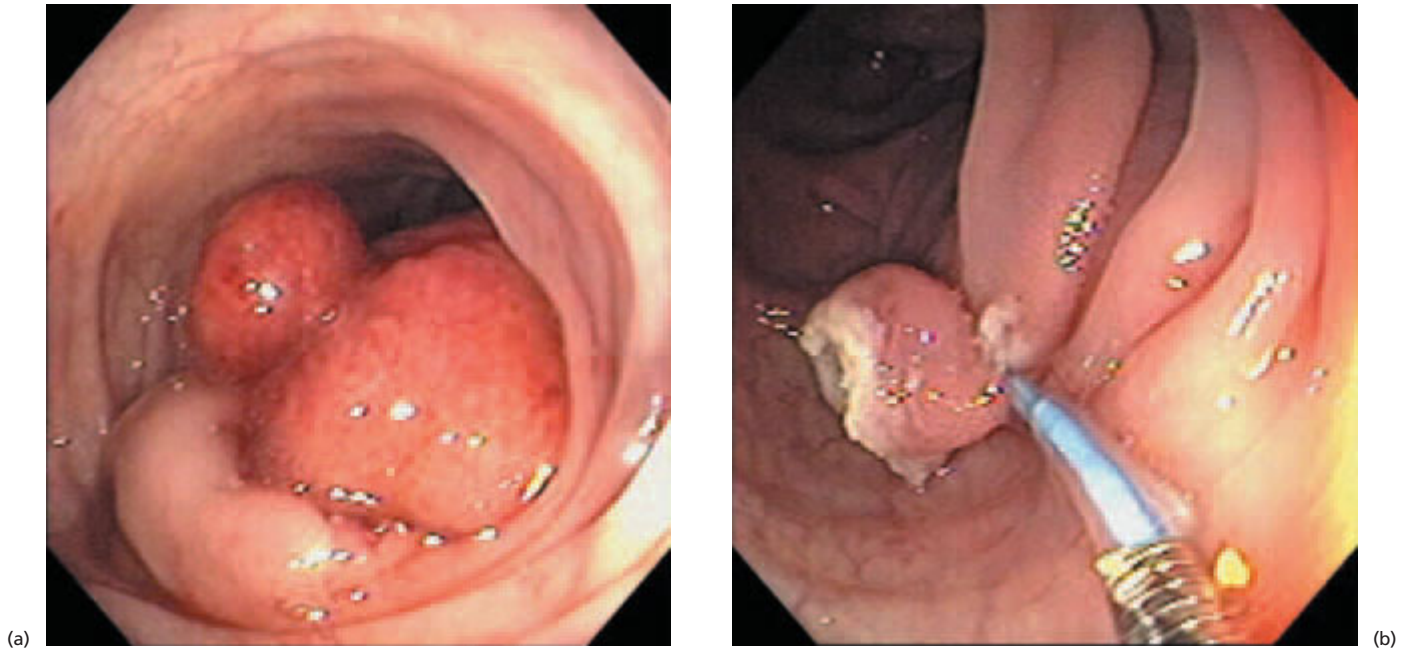


Fig. 25.15 Following snare resection of the large pedunculated polyp (a), a detachable loop was applied (b) to prevent delayed bleeding.

large polyps where its use would be most desirable. Entanglement of the subsequent electrocautery snare with the previously placed nylon loop may be a source of frustration. Unintentional transection of the polyp stalk with the detachable loop snare resulting in a frank hemorrhage is a risk in the hands of an inexperienced assistant. When used as secondary prophylaxis against postpolypectomy bleeding, the loop is placed over the residual pedicle immediately postpolypectomy (Fig. 25.15a,b). This, too, can be challenging in all but the most prominent of residual stalks.

Matsushita *et al.* summarized their experience. They reported primary prophylactic use of a detachable snare for colonoscopic polypectomy of 20 large polyps in 18 patients and secondary prophylactic placement following conventional polypectomy of five polyps in five patients [31]. Four of the 20 polyps were semipedunculated and the loop slipped off after polypectomy in three of the four. Among the 16 pedunculated polyps, bleeding occurred in four cases, because of: transection by the loop of the stalk before polypectomy in one, slipping-off of the loop in one, and insufficient tightening of the loop in two. Among the five patients in whom the loop placement was attempted following conventional polypectomy, the residual stalk could not be ligated in three of the five lesions because of flattening. These authors concluded that the detachable snare is difficult to apply and subject to operator-dependent error. For the treatment of active bleeding from a polypectomy

site again the loop was only effective when there was a sufficient pedicle to allow ensnarement. Iishi *et al.* report a more favorable experience [32].

Secondary loop ligation for treatment of postpolypectomy hemorrhage is most apt to occur in the immediate postpolypectomy setting before the stalk has had a chance to flatten. In most instances of delayed postpolypectomy hemorrhage, bleeding or adherent clot obscures view. Initial attempts at hemostasis with injection of epinephrine or alcohol solution may achieve partial hemostasis and improve visualization. If a sufficient residual stalk is present, loops may be applied; however, alternatives include additional electrocautery, placement of endoscopic hemostatic clips, or even the placement of a variceal rubber band ligator.

Contact and noncontact thermal devices

(see Chapter 34)

Thermal devices are used for coagulative hemostasis and ablation. Contact thermal devices include the heater probe and multipolar electrocautery (MPEC) probes [33]. Noncontact thermal devices include laser fibers and argon plasma or beam coagulators [33].

The heater probe (Olympus America, Melville, NY) consists of a Teflon-coated hollow aluminum cylinder with an inner heating coil at the tip of a flexible shaft. A thermocoupling device at the tip of the probe allows maintenance of a predetermined and constant temperature once the pulse has been initiated and for a predetermined duration. The mechanism of tissue coagulation is heat transfer. Water for irrigation and cleansing the target tissue passes through a central port. A foot

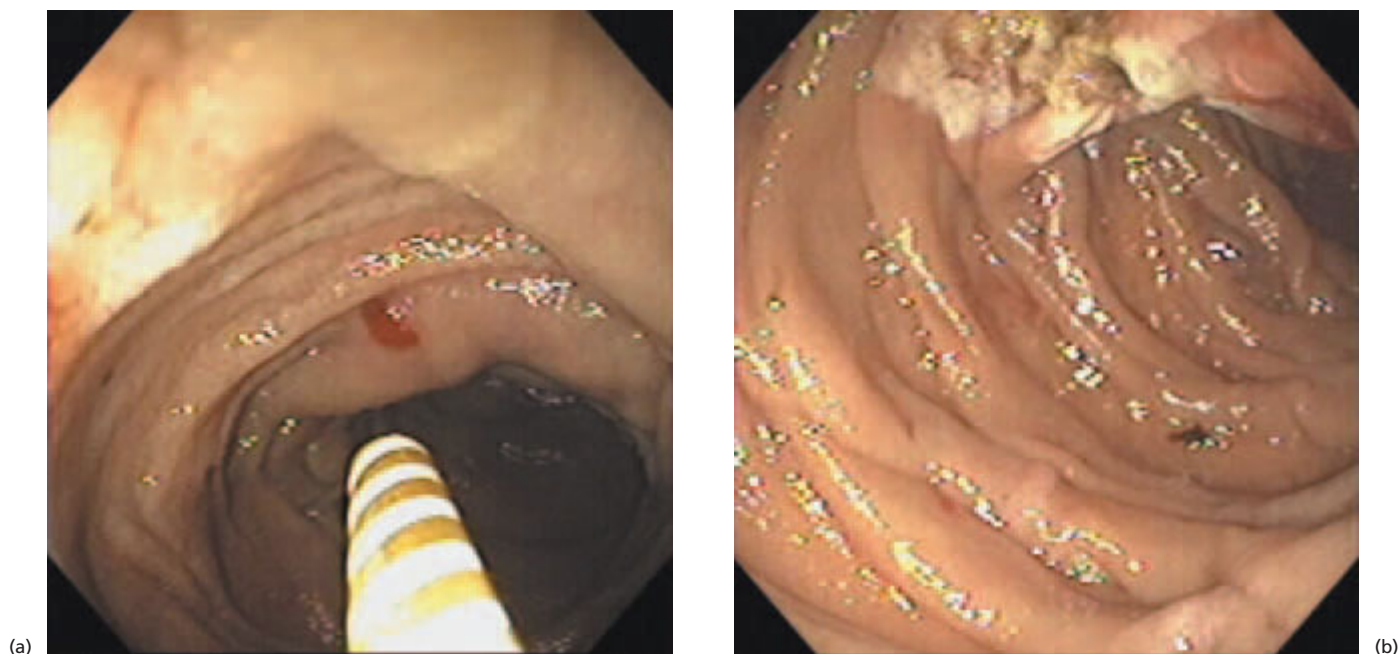


Fig. 25.16 (a) Multipolar electrocautery probes and an angiodysplastic lesion. (b) Tissue after cautery application.

pedal controls coagulation and irrigation. MPEC probes deliver thermal energy by completion of an electrical circuit between two or more electrodes on a probe at the tip of a flexible shaft [34]. The electrodes may be arrayed linearly or in a spiral fashion (Fig. 25.16a,b). The circuit is completed locally and ceases with loss of conductivity as tissue desiccates, limiting maximum temperature (100°C) and depth and breadth of tissue injury. There is a central port for irrigation of water. Foot pedal control is standard. A variety of MPEC probes in colonoscopic lengths are available from endoscope device manufacturers with similar specifications but varied characteristics. One device combines an injection needle with the MPEC probe. Both the heater and MPEC probes can be used tangentially and en face.

Laser fibers transmit collimated highly energized light energy, emitting a focused monochromatic beam [35]. They are flexible glass fibers with coated shafts. The laser light, delivered from a focal distance of ~ 10 mm from the tissue, results in coagulation or vaporization. The argon plasma beam coagulator is a noncontact electrocoagulation device [36]. Monopolar current is conducted to the target tissue through an ionized argon gas (argon plasma). As it is monopolar current, a grounding pad is required to complete the circuit. Electrical energy flows through the plasma from the probe tip to the target tissue. Coagulation occurs at the plasma–tissue surface interface. As the target tissue desiccates, the plasma steam shifts to adjacent, nondesiccated tissue. The probes consist of a flexible Teflon tube as a shaft, with a

tungsten electrode contained in a ceramic nozzle at its distal tip [37]. The operative distance of the probe from the target tissue is 2–8 mm. While mode-specific probes are available, the arc of energized argon plasma to the tissue enables en face or tangential coagulation/ablation with the standard probe. An argon plasma beam coagulation unit (ERBE USA, Marietta, GA; ConMed Electrosurgery, Englewood, CO) includes a high-frequency electrosurgical generator, source of argon gas, gas flow meter, flexible delivery catheter, grounding pad, and foot switch to activate both gas and energy.

Contact and noncontact thermal devices are used for hemostasis of colonic bleeding attributed to immediate and recent polypectomy, arteriovenous malformations, radiation proctopathy, and diverticulosis [33]. Contact and noncontact thermal devices are also used to ablate residual adenomatous-appearing mucosa at the margins of snare resection of sessile polyps and for ablation of lesions unamenable to colonoscopic or surgical resection [38–40]. Noncontact thermal devices have been used to ablate obstructing colorectal cancer to achieve recannulation of the colonic lumen and for hemostasis of inoperable colorectal cancers.

Transparent cap

Plastic transparent caps that affix to and overhang the tip of the endoscope may be used to enhance colonic visualization and to facilitate endoscopic mucosal resection (EMR) [41]. These caps are modifications of devices initially used for endoscopic band ligation therapy. The cap consists of a hollow cylinder of fixed or flexible plastic and a snug-fitting adaptor that slides over and is affixed



Fig. 25.17 Plastic transparent cap to enhance colonic visualization and to facilitate endoscopic mucosal resection (EMR).

to the tip of the colonoscope (Fig. 25.17) [42]. Those devised for cap-assisted EMR may have a built-in rim to house a predeployed specially designed snare. A commonly used cap size is 16 mm in outer diameter with 2 mm wall thickness, and 15 mm in length. However, they are available in a variety of sizes and configurations, including straight or oblique angled opening, depending on the intended purpose and colonoscope being used (Olympus America Inc., Melville, NY).

For cap-assisted EMR, submucosal injection of saline or other sterile solution is performed to “lift” the mucosal-based lesion on a submucosal cushion. The scope tip with the attached cap is then placed over the lesion. By applying suction, the cap cylinder becomes a vacuum chamber, drawing the target tissue into a pseudopolyp within. The predeployed snare is then closed and standard electrocautery excision is performed. This technique has been described for lesions throughout the colon and is safe and effective in experienced hands [43]. Cap-assisted EMR may also be used for completion resection of flat rectal or submucosal lesions unamenable to other mucosectomy techniques [44]. Such may be the case for very distal rectal lesions and for rectal lesions in which prior electrocautery has been introduced that prevents submucosal injection techniques alone due to “nonlifting”. Because of the potential to draw in deeper layers of the colonic wall, cap-assisted EMR is generally restricted to lesions below the retroperitoneal reflection in my practice.

The transparent cap may also be used to enhance mucosal imaging during colonoscope withdrawal. Using this technique, the semilunar folds can be flattened out for improved inspection. In two series, use of the cap did not interfere with colonoscope insertion or terminal ileal intubation, and enabled identification of small polyps not seen on standard colonoscopy [45,46].

Summary

An extensive array of accessory devices has been developed and adopted for diagnostic and therapeutic colonoscopy. These innovations and adaptations have enabled the expansion of minimally invasive colonoscopic therapies for benign and neoplastic diseases of the colorectum. Countless lives have been saved, surgical procedures avoided, and societal benefits accrued as a result of the development and dissemination of colonoscopic accessories and the techniques they enable. We are indebted to the legions of physician endoscopists and their industry counterparts who contributed to device development and evaluation. Continuous creative innovation ensure the further advancement of these tools.

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Chapter 26

Clips, Loops, and Bands: Applications in the Colon

Michael J. Bourke and Stephen J. Williams

Introduction

Throughout the gastrointestinal tract, clips and loops have varied endoscopic applications; however, within the colon they are primarily used as hemostatic tools. These modalities are not part of routine endoscopic practice but are reserved for unique or uncommon therapeutic challenges. They can be employed in either a prophylactic setting, such as ligation of a large polyp stalk prior to electrosurgical transection, or in an emergency setting to arrest bleeding, e.g. postpolypectomy hemorrhage. Endoscopic band ligation can also be used in this latter situation. These techniques form a discrete subclass within the endoscopic hemostatic therapies, namely “mechanical hemostasis,” which is both conceptually appealing and theoretically advantageous when compared with other techniques. The ability to arrest hemorrhage is due to direct mechanical ligation of the responsible vessel. The captured tissue usually includes not only the vessel walls but also the surrounding tissue. The more conventional hemostatic techniques, such as injection therapy, contact thermal electrocoagulation (bipolar, heater probe) or noncontact thermal electro-

coagulation (laser, argon plasma coagulation), rely on some degree of tissue destruction, coagulation, transient tamponade, or vasoconstriction to achieve the hemostatic effect. Rebleeding may ensue due to treatment-induced ulceration, coagulopathy, large vessel size, or poor tissue quality. Within the thin-walled colon, the risk of perforation with tissue destructive techniques, such as electrothermal devices, is also a major consideration.

Clips and loops have a number of additional reported or potential applications within the lower gastrointestinal tract. These are summarized in Table 26.1. Each of these modalities is discussed in turn.

Clips

Technical considerations

Metallic clips are routinely used in both open and laparoscopic abdominal surgery. The clip is made of stainless steel and does not induce a tissue reaction [1]. The result is analogous to the application of a surgical ligature; successful deployment of the clip for hemostasis is self-evident, with immediate and complete cessation

Table 26.1 Potential or reported applications of clips and loops within the lower gastrointestinal tract.

Potential or reported applications	Ease of use	
	Device	Endoscopic
<i>Clips</i>		
Prophylactic stalk clipping before large pedunculated polypectomy	Difficult but readily learned	Moderately difficult
Intraluminal marking device for fluoroscopic procedures, e.g. colonic tumor margins for expandable stent placement, marking for laparoscopic colonic resection for small lesions		
Closure of recognized perforation following polypectomy		
<i>Loops</i>		
Prophylactic stalk snaring before large pedunculated polypectomy	Not difficult	Not difficult, similar to conventional polypectomy
Temporary mechanical hemostasis for large, broad-based lesions before surgery, e.g. bleeding leiomyoma/lipoma		
<i>Bands</i>		
Stalk bleeding post polypectomy	Easy	Easily learned
Colonic variceal or Dieulafoy hemorrhage		
Aid to sessile polypectomy particularly left colon		

of bleeding. One potential disadvantage of the hemoclip in hemostasis is that precise targeting is required, in contrast to epinephrine injection, where an injection in the general region will often suffice. In major hemorrhage where brisk bleeding may obscure the view, preinjection with epinephrine will usually slow bleeding sufficiently to allow accurate clip deployment. The inability to wash the bleeding point and treat with the same device, as can be done with thermal probes, is a potential disadvantage. An endoscope with a working channel of 3.7 or 4.2 mm is preferred to allow both suctioning of secretions and blood alongside the device and free movement of the device within the channel, which is particularly important where acute angulation of the endoscope tip is required to target lesions (e.g. retroflexion in the rectum or cardia of the stomach).

If a standard polypectomy snare can be considered as a “two-layered” system, comprising an inner stainless steel snare and the covering plastic sheath, then the

endoscopic clipping device is a “three-layered” system (Fig. 26.1). It is composed of an outer plastic sheath, an inner metal coil sheath, and a central cable with a hook at its tip to which the clip is attached. The hemoclip is connected to the hook by a joint plate and the base of the clip is then juxtaposed against the end of the metal coil sheath. The articulated clip and metal coil sheath complex is then drawn back into the plastic sheath and is ready for insertion into the working channel of the endoscope. The handle consists of two sliding components; moving these components toward one another will project the clip forward from the plastic sheath. Partial closure of the handle will allow the prongs of the clip to fully open. The clip is then applied firmly to the target and with complete closure of the handle the mechanism fires, a “click” indicating detachment of the clip from its hooked end. The clip should now be closed and attached to the target.

The technique of clipping is heavily dependent on the topographic features, location, and nature of the lesion. The working channel of most endoscopes exits the instrument at the 5–7 o’clock position so that alignment of the target in this position greatly enhances successful clip placement. In cases of gastrointestinal bleeding the endoscopist should endeavor to capture not only the responsible vessel but also a portion of the surrounding tissue, which results in more secure anchoring of the clip. Applying suction at the critical moment just prior to clip closure can facilitate this. Another option is to apply suction using a large mucosal resection aspiration cap (the larger cap allows the clip to open completely) prior to deploying the clip. Several clips may be necessary to adequately treat a large polyp stalk or an actively bleeding vessel.

A wide range of clips and applicator devices are available (Table 26.2). These include both single-use and reusable devices. The authors prefer the reusable, autoclavable, rotatable clip applicators due to their greater maneuverability and stronger mechanism. They are also compatible with a wide range of clips of different characteristics, including the long MH-858 clip. In the authors’ experience this is the preferred clip for most cases of colonoscopic hemostasis, polyp stalk ligation, and mucosal defect closure. The shorter MD-850 may have advantages in hemostasis of firm tissues but this is not the usual case in the colon. A selection of clip applicators of variable length are available (1650 mm, HX-5L; 1950 mm, HX-5QR-1; 2300 mm, HX6UR-1) to suit the length of the endoscope to be used.

Clinical experience

The metallic clip as a means of endoscopic hemostasis was first introduced by Hayashi in Japan in 1975 [2]. Initial experience was disappointing due to the com-

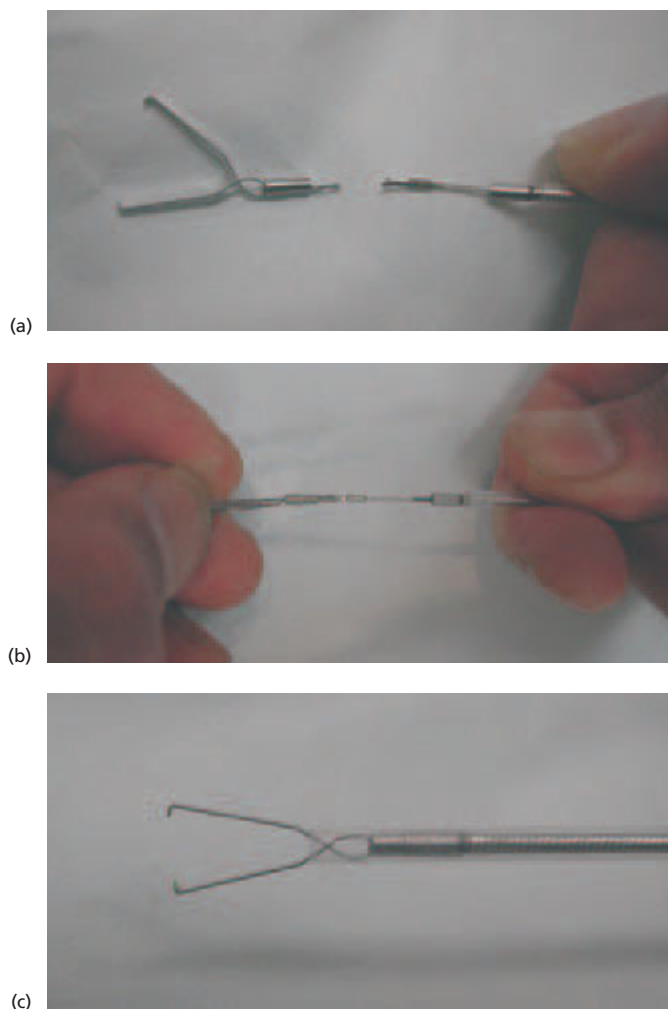


Fig. 26.1 (a) Hemoclip and the “three-layered” clipping device. (b) Hemoclip attached to hook. (c) Hemoclip partially drawn into the plastic sheath.

Table 26.2 Range of clips and applicator devices that are commercially available.

Clip	MD-59	MD-850	MH-858	MH-859	MAJ-458	MAJ-459
Jaws angle	90°	135°	90°	90°	90°	135°
Clip arm length (mm)	7	7	8.5	5	5	5
Opening width (mm)	6–12	6–12	8–15	4–8	4–8	4–8
Preferred tissue consistency	Soft	Soft or hard	Soft	Marking	Marking	Soft or hard

Table 26.3 Experience with acute hemorrhage in the lower digestive tract.

Reference	Number of patients	Source	Active bleeding	Initial control	Rebleeding
Parra-Blanco <i>et al.</i> [10]	72	Immediate PP (45) Delayed PP (18) Post biopsy (9)	58/72 (81%)	71/72 (99%)	0
Binmoeller <i>et al.</i> [11]	45	PP (42) Diverticula (1) Solitary rectal ulcer (1) Hemorrhoids (1)	100%	100%	1/45
Hachisu <i>et al.</i> [12]	7	PP (5) Colonic diverticula (2)	100%	100%	0
Rino <i>et al.</i> [13]	1	Diverticula	100%	100%	0

PP, post polypectomy.

plex method of deployment and low clip retention rates. Subsequent improvements in the design of both the delivery system and the clips have led to an expanding literature reporting applications throughout the gastrointestinal tract.

In gastrointestinal bleeding, most of the published experience has been accumulated in the upper digestive tract and predominantly in peptic ulcer hemorrhage. When compared with the established techniques of endoscopic hemostasis in ulcer bleeding, namely injection or heater probe, two of the four studies reported have demonstrated superior results for the hemoclip in terms of rebleeding and need for surgery [3,4]. Rebleeding was reduced by at least 80% in both series. This is despite the fact that the peptic ulcer base is often suboptimal tissue for clip placement due to the fibrous cicatricial nature of most chronic ulcers, which may not allow adequate clip closure. The hemoclip has also been used successfully in bleeding related to Dieulafoy lesions, duodenal diverticula, and Mallory–Weiss tears [5–9]. The hemoclip is ideally suited for treatment of bleeding Mallory–Weiss tears as the sequential placement of clips along the length of the tear will close the mucosal defect and arrest bleeding.

Table 26.3 summarizes the experience with acute hemorrhage in the lower digestive tract. Parra-Blanco and colleagues [10] reported their experience in 72 patients with lower gastrointestinal bleeding derived

from a consecutive series of 9555 colonoscopies accumulated over a 3-year period at Fujigaoka Hospital, Yokohama, Japan. Postpolypectomy bleeding occurred in 63 patients (45 immediate, 18 delayed), while nine others had postbiopsy bleeding. Initial hemostasis was successful (Fig. 26.2) in all but one patient, who later stopped with conservative management after additional heater probe therapy failed to arrest oozing hemorrhage following piecemeal resection of a 25-mm sessile villous adenoma. There were no complications in this series. Binmoeller and colleagues [11] report a similar experience in 45 patients, 27 of whom had spurting hemorrhage. Postpolypectomy bleeding accounted for the majority, with one case each of solitary rectal ulcer bleeding, hemorrhoidal bleeding, and diverticular bleeding. Initial hemostasis was successful in all 45 patients, with a mean of 2.9 clips per patient, and there was only one episode of rebleeding, which was managed with further clip placement without sequelae. Patients with spurting arterial bleeding required more clips to achieve hemostasis when compared to those with an oozing bleed. Active colonic diverticular hemorrhage has also been treated successfully with the hemoclip, although published experience includes only three patients [12,13].

The hemoclip can also be used to protect against postpolypectomy hemorrhage, where the lesion to be removed is large (> 3 cm), the stalk is abnormally thick (1 cm or greater) or in patients with coagulopathy

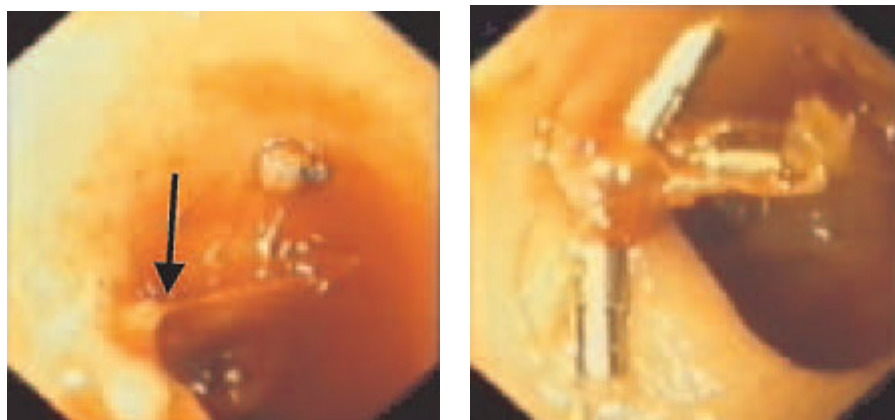
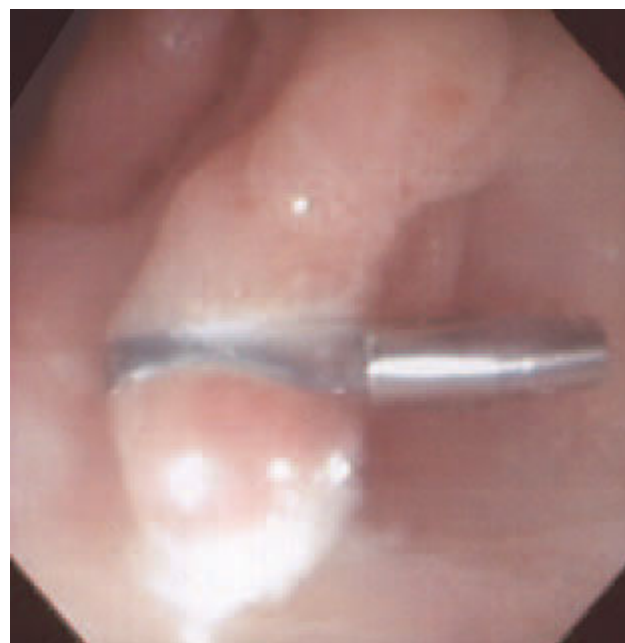


Fig. 26.2 Active post-polypectomy bleeding (arrow) treated with three hemoclips.



Fig. 26.3 Hemoclip on stalk of polyp before and after polypectomy in a patient with cogulopathy.

or other bleeding disorders who are at greater risk of post-polypectomy bleeding (Fig. 26.3). Cipolletta and colleagues [14] report their experience in four patients with giant pedunculated colonic polyps (mean size 4.8 cm, range 3–6 cm). In all cases the polyp heads were large and nearly occluded the lumen, making use of standard polypectomy techniques or placing an endoloop extremely difficult or impossible. Hence these workers describe an alternative technique of prior endoclip ligation of the stalk using the MH-858 long clip and HX-6UR-1 clip applicator followed by needle knife resection of the polyp. The procedure was successful in all cases and without complications. Follow-up colonoscopy at 8 weeks revealed that most of the clips had dislodged



spontaneously. Hemoclips can also be applied after polypectomy has been completed to avert subsequent delayed hemorrhage or close mucosal defects [15,16].

Iatrogenic perforations following polypectomy can be sealed using the hemoclip, although published experience with this technique is limited. Binmoeller and colleagues [17] published the first description of this technique to repair a 5-mm perforation complicating snare resection of a pedunculated gastric leiomyoma. Successful repair of a 4-mm perforation following endoscopic mucosal resection of a 10-mm descending colon adenoma has also been reported [18]. The technique obviated the need for surgery. The hemoclip has also been used successfully to close perforations elsewhere in the gastrointestinal tract, including postsurgical esophago-gastric anastomotic leaks, duodenal perforations secondary to biliary stents, endoscopic mucosal resection

or sphincterotomy, and esophageal perforation complicating fish-bone ingestion or pneumatic dilation for achalasia [19–25].

Timing is critical when iatrogenic perforations are being treated. In the colon, a nonoperative course of management can only be reasonably considered if the perforation is identified at the time of the index endoscopy (recognized perforation). Rapid and effective closure of the defect to prevent contamination of the peritoneal cavity is required. Broad-spectrum antibiotics are indicated, but if clinical evidence of diffuse peritonitis develops, laparotomy should be strongly considered.

Loops

Technical considerations

Detachable snares or loops are currently available in 20 and 30 mm diameters (MAJ-340 and MAJ-254). They are composed of nylon with a sliding plastic collar at the base and, along with the delivery system and handle, are fully autoclavable. The loop delivery device (HX-20), like the clipping device, is a three-layered system composed of an outer plastic sheath, a metal coil around a central cable with hook (Fig. 26.4). The detachable nylon loop can be fixed to the hook and closed until the metal coil sheath comes to rest against the plastic collar on the base of the loop. The loop/metal coil plus loop complex is then drawn back into the plastic sheath. The system is now ready for insertion into the working channel of the endoscope. An instrument with a minimum working channel of 2.8 mm diameter is required and those with larger channels are preferred. The target lesion should be positioned at the 5–7 o'clock position to facilitate successful loop placement. The loop is expressed by withdrawing the plastic sheath backward and is then placed over the target lesion. Placement is rehearsed by closing the plastic sheath over the loop without advancing the plastic collar along the loop (i.e. the handle of the device is not closed). If the endoscopist is satisfied with the positioning of the loop, it can be deployed by simultaneously withdrawing the outer plastic sheath while closing the handle of the device. This latter movement will slide the plastic collar over the loop and close it. The loop can now be released from the device by opening the handle. A cutting device (FS-5 L/Q/U-1) is available to transect the residual end of the loop after ligation has been performed, but this is rarely necessary.

In contrast to a conventional metal snare, loops have limited expansile force due to their nylon composition and thus can be challenging to place under circumstances where there is limited room for opening fully, either due to the large size of the target lesion or narrow luminal diameter. This is rarely a problem in the right

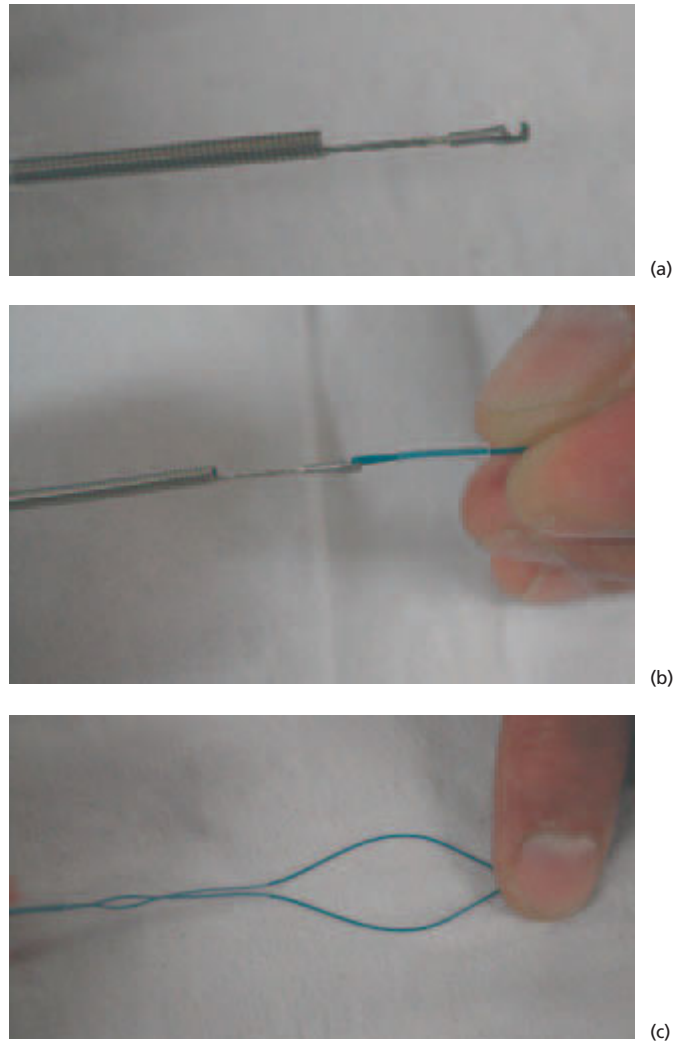


Fig. 26.4 (a) Loop delivery device. (b) Detachable nylon loop attached to the hook of the loop delivery device. (c) Loop partially drawn into the plastic sheath.

colon but can create significant technical difficulty in the left colon, particularly within severely stenotic diverticular disease or acute angulations. The use of a double-channel instrument could potentially overcome this problem. Akahoshi and colleagues [26] have described a technique using grasping forceps and a double-channel instrument in 10 patients with pedunculated polyps with heads 1 cm or greater. The grasping forceps are passed down one working channel and the endoloop device down the other. Once both devices have exited the end of the instrument and are in place, the grasping forceps are inserted through the detachable snare loop. The polyp head is then grasped and pulled through the loop, which is then closed on the stalk as described above and standard polypectomy is undertaken. This technique was successful in all cases. An alternative strategy for large pedunculated lesions is the application of one or several hemoclips to the base of the polyp stalk.



Fig. 26.5 (a) Colonic lipoma. (b) Loop in place around the base with snare secured above. Note the bluish discoloration of the looped tissue. (c) Lipoma removed leaving the loop *in situ*.

Clinical experience

Loops are generally used in the prophylaxis of post-polypectomy hemorrhage. The stalk or base of the polyp is first ligated as close to the mucosal surface as possible. Firm closure of the plastic sheath on the polyp base renders the polyp head relatively ischemic, indicated by a bluish discoloration of the polyp head (Fig. 26.5b). The tissue above the ligature is snared and removed in the conventional way, leaving the loop in place. Although anecdotal evidence suggests that the use of the endoloop is relatively widespread within specialist therapeutic endoscopy units [27], there are surprisingly few published reports describing this experience [28–33]. Iishi and colleagues [28] performed a randomized trial involving 89 patients with pedunculated colonic polyps 1 cm or greater in diameter. No bleeding occurred during or after polypectomy in the 47 patients who were assigned to the detachable snare group. Of the 42 patients who did not have a detachable snare applied, five (12%) sustained postpolypectomy bleeding. A significant advantage of prior loop ligation of a large polyp stalk or abnormally thick pedicle (e.g. colonic lipoma; Fig. 26.5a–c) is the ability to use greater electro-surgical generator power, including cutting or blended current, during polypectomy without fear of precipitating hemorrhage.

Detachables snares have also been used to achieve hemostasis in actively bleeding gastric and esophageal varices [34–36]. In theory, this device could be similarly employed in colonic variceal hemorrhage.

An endoloop has been used to remove a migrated self-expanding esophageal metal stent from the upper gastrointestinal tract [37]. The loop was closed over the leading aspect of the stent to reduce the diameter and then the stent was drawn back onto the tip of the endoscope and removed. A similar technique could be used for migrated stents in the lower gastrointestinal tract.

Bands

Band ligation has been proven to be the endoscopic therapy of choice in acute esophageal variceal hemorrhage [38] and is ideal for treatment of bleeding colonic varices (Fig. 26.6). It is a viable therapeutic strategy in certain cases of lower gastrointestinal hemorrhage. Our group first reported this application for nonvariceal, nonulcer hemorrhage throughout the gastrointestinal tract [39]. In this series of 18 patients, abnormalities treated included arteriovenous malformations, Dieulafoy

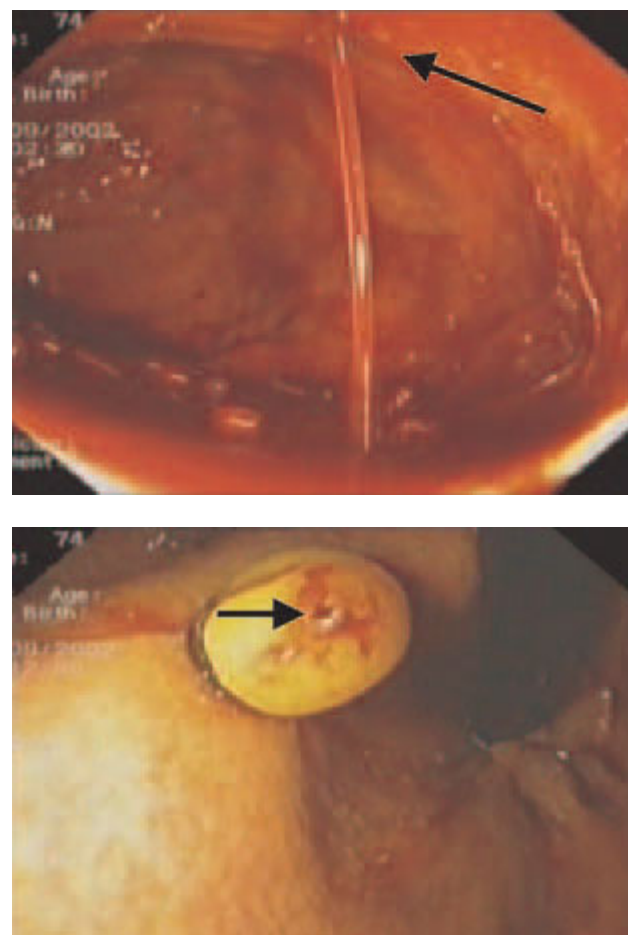


Fig. 26.6 Rectal variceal active bleeding (arrow) treated with band ligation. Following immediate cessation of bleeding, the bleeding point is seen at the apex of the banded varix (arrow).

lesions, Mallory–Weiss tears, and postpolypectomy bleeding. Two cases of delayed postpolypectomy hemorrhage following removal of pedunculated sigmoid colon polyps were managed by band ligation. The band was applied to the residual stalk, with immediate and permanent cessation of bleeding. The appeal of this modality is due to the rapid “single-shot” mechanism of hemostasis, analogous to the application of a surgical ligature. Published experience with this technique is limited, although it merits consideration in most forms of postpolypectomy hemorrhage, particularly where a residual stalk is evident [40,41]. It can also be safely used in the rectum and left colon for small (10 mm or less) bleeding cautery ulcers following polypectomy, where the entire lesion is aspirated into the device, the band applied, and hemostasis secured. In the right colon the risk of capture of the full thickness of the colonic wall, with subsequent necrosis and delayed perforation, generally precludes the use of this technique for nonelevated lesions. The necessity to “carry” the ligation apparatus, which limits the endoscopic view, to the bleeding source adds complexity to the treatment of lesions in the right colon.

Summary

Technologic advances in the design of the clipping, looping and banding devices have made their use in the colon relatively user-friendly and they should be part of the available accessories in all endoscopy units undertaking colonoscopy. Their application is mainly in the prevention and treatment of complications such as postpolypectomy hemorrhage. Appropriate use allows safer and more effective colonoscopic therapy.

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Chapter 27

Colonoscopic Biopsy

Wilfred M. Weinstein

Biopsy instruments

Pinch biopsy forceps

Large cup vs. conventional sized biopsy forceps

The term large cup rather than the more familiar “jumbo” will be used here. This is the preferred forceps when “tissue is the issue.” This forceps has been available for more than 30 years but is not used by most endoscopists. The main barrier to the use of the large cup forceps is that more than 80% of endoscopes sold in the USA have conventional-sized channels that can only accommodate a 2.8-mm-channel forceps. The term large cup forceps rather than “jumbo” is preferred because the term “jumbo” seems to have induced fear into the hearts of otherwise brave endoscopists.

The large cup forceps requires a large channel endoscope (biopsy channel 3.6 mm). The opened cups are 7–9 mm in the open span, actually not much greater than the conventional forceps, but the cups have a greater volume (Fig. 27.1). Biopsies yield two to three times the surface area but are not generally much deeper. We and a few other groups have used them extensively for more than 20 years. They appear to be as safe as any other biopsy forceps [1].

The large cup forceps makes it more likely that the endoscopist will obtain a high-quality biopsy, one that is much easier for the histotechnologist to orientate in the laboratory. Orientation for embedding in paraffin is

the key to maximizing the diagnostic yield from mucosal biopsies. Other advantages of the large cup forceps is that they contain proportionately less crush artifact, permit more precise evaluation of architecture, and are more likely to detect small, focal lesions.

Even more puzzling than the general lack of interest in using a forceps that yields superior specimens is the fact that arguments or studies are done to actually try to show that it is unnecessary [2], as if it represented some form of potential evil. Some studies have shown that the conventional-sized forceps may be adequate for diagnosis [2]; that is not in question. However for the majority of centers, the large cup biopsies make it much easier for the histotechnologist with average skills to orientate, embed, and section, and to thus provide better quality tissue specimens.

The multibite forceps

This refers to forceps that permit taking multiple biopsies with one pass of the forceps. In one model the biopsies are stored in the forceps sheathed channel. The main disadvantage in models marketed to date is the tiny size of each individual biopsy. It is true that if one lays the pieces end to end they add up to more than one can obtain with one conventional sized biopsy, and are about the size obtained by one to two large cup biopsies. However the fragments are just that, i.e. tiny, in the 1–2 mm range. Only select highly expert technologists can predictably orientate them properly.

Hot biopsy forceps

Hot biopsy refers to an insulated pinch biopsy forceps that has the capability to pass coagulation current through its jaws. The belief has been that hot biopsy leaves behind a burn that takes care of any residual adenoma not biopsied off. This view has been challenged in one study [3]. The cautery artifact induced by hot biopsy often makes the tissue uninterpretable histologically. Therefore if it is used to remove a cluster of small polyps, a few should be biopsied off with conventional forceps in order to obtain better quality histology. Hot biopsy appears to be safe in some hands [4] but



Fig. 27.1 Comparison of open span of biopsy forceps and (endoscope channel size); right to left: large cup (“jumbo” 3.5-mm channel); conventional sized (2.8 mm channel); pediatric sized (2.2 mm channel).

caution should be exercised when used in the right colon [5,6].

Suction biopsy

Suction biopsies are still sometimes used for biopsy in children. Their broadest application is in the diagnosis of Hirschsprung's disease where careful measurement of biopsy distance from the anal verge is essential [7].

Grasp biopsies

Grasp biopsies are taken through a rigid sigmoidoscope using an alligator-jaw cutting forceps. These instruments are rarely used but have an application for distal rectal tumors that are indurated and difficult to grasp with the endoscopic biopsy forceps.

Handling tissue specimens

Retrieval of biopsies from the forceps and getting them into fixative

The best way to remove biopsies from the forceps is to use a blunt dental probe or dissecting needle and scoop it out from the bottom of the opened forceps cups and place the specimen on a support material. If one approaches the biopsy from the top of the opened forceps and pushes it sideways into fixative there is more likely to be trauma to the surface epithelium with denudation or squash of the whole mucosa. A common practice is to shake the opened biopsy forceps in the formalin fixative solution until it floats out. Intuitively this is as unappealing as the preceding alternative because of the potential traumatic detachment of the surface epithelium.

Routine orientation of biopsies on support materials in the endoscopy unit is difficult to maintain at a high level, and is not necessary. The ability to orientate biopsies properly can be optimized in the pathology

laboratory by histotechnologists, with the intent being to embed the tissue "on edge" in paraffin.

Discarding inadequate biopsies

The endoscopy assistant should be empowered to tell us that a given biopsy is tiny, transparent (shallow) or not a biopsy (blood clot instead). In the process of taking biopsies a routine should be established whereby the endoscopy assistant calls out that a biopsy is adequate or not. This practice will, overnight, improve biopsy quality and reduce the unnecessary proportion of "inadequate" biopsies for interpretation. The reason for discarding these inadequate biopsies rather than putting them into fixative anyway is that mixing biopsy specimens of varying sizes in the same bottle makes it hard to have all of them orientated in the histology slides.

Never place more than four biopsies into a fixative bottle

All the biopsies that are put into a fixative bottle are embedded by the histotechnologist into a single tissue block. It is not usually possible to line up more than four biopsies in a tissue block during embedding and section them so that all are predictably represented with optimal orientation for interpretation. Although placing 10 or more biopsies in a single bottle reduces costs (because they all end up on one tissue slide), less than half of these 10 specimens may be fully interpretable (Fig. 27.2).

Handling polyps and endoscopic mucosal resection specimens

The central focus of this chapter is on biopsy, but a few comments regarding the tissue handling of polypectomy and endoscopic mucosal resection (EMR) specimens are relevant to the general handling of tissue specimens in the endoscopy unit. Quite commonly small polyps are

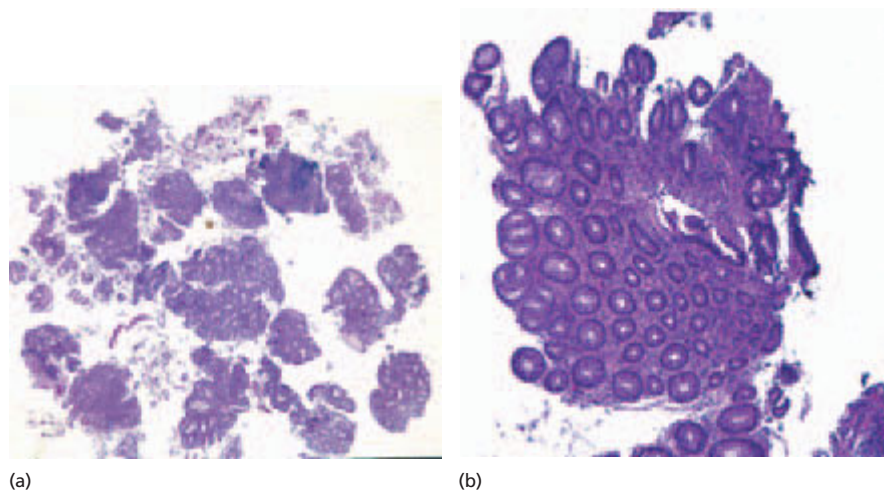


Fig. 27.2 Quality Issues. (a) Multiple biopsies were put into one fixative bottle. Then they were processed in one tissue block. Many of the pieces are tiny and should not have been put in as biopsies. Having multiple biopsies in one tissue block makes it impossible to orientate the biopsies for the accurate assessment of dysplasia, or even for IBD type or severity. (b) A typical totally tangential section. There are no test-tube-shaped crypts, just doughnut appearances of the crosscut crypts.

retrieved into a suction trap. It appears that this does not damage the tissue. One key to suction removal without getting the specimen stuck in the suction channel is to have the polyp in a pool of liquid prior to suctioning. If necessary, saline can be instilled first to create a pool.

Pedunculated polyps: identify the stalk region

To diagnose early cancer invasion of a pedunculated or semipedunculated polyp requires that the stalk zone be represented in the histologic sections. Although the stalk region looks distinct right after polypectomy, it commonly disappears after fixation because it shrinks in fixative and the whole polyp changes from pink-red to whitish after fixation in formalin. Identifying the stalk region immediately after polypectomy makes it possible for the histotechnologist to predictably provide sections right through the stalk zone rather than guessing and having the all-too-familiar situation in some cases of repeated recuts (see Chapter 33).

There are two ways to identify the stalk zone in the endoscopy unit. One is to insert a thin short needle (e.g. 25 gauge) into the line of resection with the needle point emerging at the most convex part of the tip of the polyp. An alternative technique, without the use of needles, is to mark the polyp stalk with India ink [8].

Endoscopic mucosal resection

Endoscopists and the pathologists who handle endoscopic biopsy tissue need to recognize that these specimens should be handled in an identical manner as any resections for cancer or possible cancer. They should not be regarded as the equivalent of handling a large biopsy. Shaving the lesions (either piecemeal resection or endoscopic mucosal resection—EMR) makes it very difficult for the pathologist to rule out cancer. The specimens should be orientated by the endoscopist or the pathologist in such a way that there is no doubt as to how to handle them during embedding in paraffin and subsequent sectioning. The best results are obtained when the specimen is pinned out first, before immersion in fixative. An interested pathologist should be brought in as a partner with the knowledge that the EMR specimens must be orientated so that multiple orientated step sections can be cut to look for focal cancer invasion. Once an approach is established with the pathologist, freshly resected specimens can be sent to the pathology laboratory so they can be orientated by the designated interested pathologist.

Piecemeal polypectomy

If piecemeal removal (shave biopsy) is absolutely unavoidable then the specimens need to be submitted with

the cut sides inked. The diagnosis of cancer requires the ability to be certain that the muscularis mucosae and upper submucosa are visualized. If the cut sides are marked and orientated then the pathologist may be able to reconstruct the picture of the adenoma. Adenomatous change of *any grade* that penetrates the muscularis mucosae is invasive cancer. If multiple fragments are submitted with no orientation then the pathology cannot provide reassurance that invasion is not present. In those instances it is only the intuition of the endoscopist that dictates whether the polypectomy was complete and that invasive cancer was not present.

Pinch biopsy techniques and tricks

How hard should the opened biopsy forceps be pressed against the intestinal wall?

The answer is: do not push the forceps too hard. More gentle apposition of the opened forceps against the wall helps get better quality biopsies. The lumen should be partially deflated beforehand or the opened forceps should gently touch the wall and then apply several rapid depressions of the suction trumpet valve. There is no need to thrust the opened forceps against the wall to indent it and then give another push to indent it even more, before closing it around the tissue. This is unnecessary and because of the added stretch effect on the wall it is possible that shallower rather than deeper biopsies are obtained. Even with the large cup forceps it is difficult to obtain submucosa in biopsies on a routine basis. This becomes a relevant issue when it comes to biopsy for amyloid, or a hunt for vasculitis (Table 27.1).

Table 27.1 Indications for colonic biopsy.

Biopsy removal of polyps
Biopsy of larger neoplasms for diagnosis
Undiagnosed diarrhea with either normal or abnormal colonic mucosa
In ulcerative colitis or Crohn's disease:
Differential diagnosis:
Assessing disease extent and activity
Established case but atypical course to rule out other contributor, e.g. CMV
Surveillance biopsy in inflammatory bowel disease for dysplasia or carcinoma
Lumps and bumps in inflammatory bowel disease
Biopsy of focal lesions with no apparent cause
Hirschsprung's disease
Biopsy of the colon in generalized gastrointestinal disease or in systemic disease
Examples include:
Amyloidosis
Graft-versus-host disease
Vasculitis

Double bites

Double bites refers to taking two biopsies with a single pass of the biopsy forceps. This can actually be done successfully in the colon and small bowel using the large cup (jumbo) forceps. With the conventional-sized forceps this double-bite technique usually yields a tiny second biopsy, a “macrocytology.”

In the small bowel and colon with the large cup forceps after the first biopsy is obtained, the closed forceps is then placed with slight pressure on the wall where the next biopsy is to be taken and the forceps is opened against a bit of pressure. This helps prevent the first biopsy from falling out into the lumen. After opening the forceps, a few rapid bursts of suction are applied and the forceps is quickly closed to obtain the second biopsy. Average success at getting a quality second biopsy is at least three out of four times. This double-bite large cup forceps technique works well in the colon, but not in the esophagus and stomach. In the esophagus it is difficult because of the need for angulation. In the stomach the biopsy size is so generous with the first biopsy that there is scant room in the large cup forceps for a second biopsy.

How close should you be to the biopsy site?

In surveillance biopsy or random sampling for the diagnosis of endoscopy-normal diarrhea it is not necessary to be up close to the colon wall, nor to have a pristine clean site. If there are no focal lesions it is not necessary to advance the endoscope each time to within a few centimeters and see the mucosal detail up close.

When flexible sigmoidoscopy is done in the evaluation of diarrhea and the endoscopy is normal, biopsies to rule out collagenous colitis are best done as proximally as possible because the yield is better as one approaches the proximal descending colon rather than near the sigmoid colon [9].

If colonoscopy is done for the diagnosis or differential diagnosis of inflammatory bowel disease and it is impossible to get into the terminal ileum, a forceps can sometimes be advanced in the closed position through the ileocecal valve and biopsies taken at the point where resistance is met. This should be done carefully so as not to press too hard on the nonvisualized ileum. Also it should not be done if there is evidence on the outside of the ileocecal valve of deformity and/or active inflammatory change.

The solution to surveillance biopsy antipathy: a second assistant in the room

Endoscopists tend to take too few rather than too many biopsies. In surveillance for inflammatory bowel disease for example, just when the cecum is reached and the

work should begin, endoscopists often start to rush. Part of this may be due to perceived drudgery of routine biopsy. One way to speed things up enormously in surveillance biopsy anywhere in the gastrointestinal tract is to have a second assistant in the room for the biopsy part of the procedure. One assistant watches the patient and opens/closes the forceps while the second assistant handles the biopsies, both getting them into fixative and recording biopsy sites and appearances.

Dialogue with the pathologist

(see Chapter 33)

Colonic biopsy to rule out inflammatory bowel disease (IBD) requires more correlative information between endoscopist and pathologist than for biopsies anywhere else in the gastrointestinal tract [10,11].

Inflammatory bowel disease encompasses a variety of inflammatory conditions, including: nonspecific inflammatory bowel disease; ulcerative colitis (UC) and Crohn’s disease; and also specific etiologies such as ischemia and infections such as amebiasis, etc. Thus when the endoscopist indicates on the pathology requisition to “rule out IBD” the pathologist should know that the question is whether there is any inflammatory disease evident, in the broadest sense.

When biopsies are taken in the workup of diarrhea to rule out IBD, the way to get a focused and intelligent differential diagnosis is to provide the pathologist with some specific information. This does not require sentences of prose, but rather important historical points and focused questions for the pathologist. A more detailed discussion of the pathologist–endoscopist interaction is available in [11].

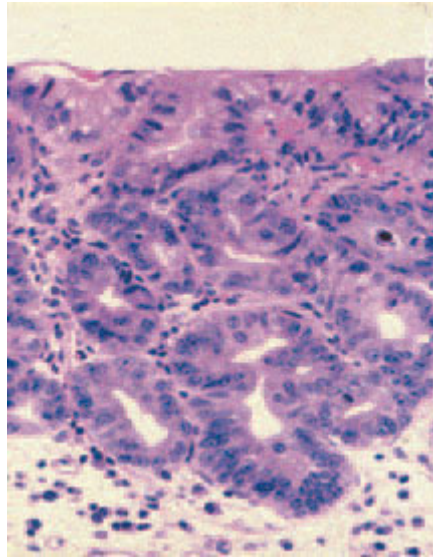
The key information required by the pathologist is the “gross pathology,” i.e. what was seen, and to label biopsy sites as normal or abnormal; to provide key historical information and then the question(s) for the pathologist. In turn the pathologist must be sufficiently versed in colonic disease to come up with a meaningful differential diagnosis.

The role of the pathologist*Better quality processing*

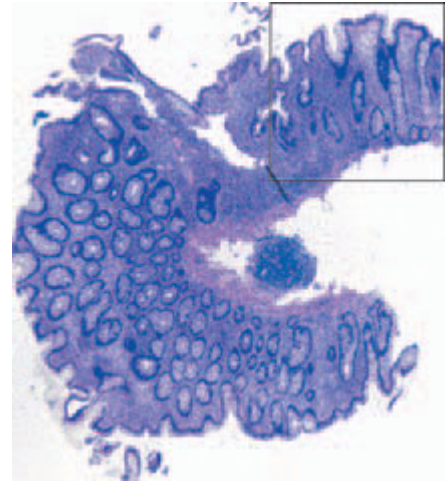
Unfortunately, processing of gastrointestinal biopsies is often poor with poorly orientated specimens. For example the rectal mucosal crypts should look like test tubes lined up next to each other. Too often they are crosscut and one sees the all too familiar “doughnut pattern” (Figs 27.2, 27.3). Crosscut crypts seriously affect the diagnosis of dysplasia in which architectural changes are one of the criteria for diagnosis (Figs 27.2, 27.3). Also, in the differential diagnosis of inflammatory bowel disease the

Fig. 27.3 High-grade dysplasia.

(a) There are two criteria, one is architectural disarray of intestinal crypts. The second is abnormal nuclear cytology. (Courtesy of the late Rodger Haggitt.) (b) This biopsy is mostly tangentially sectioned. Only the small portion within the square shows a few orientated colonic crypts. The rest is doughnut-hole-appearing, thus eliminating the use of architectural change as a diagnostic criterion and also cutting at only one plane somewhere along the vertical thickness of the biopsy.



(a)



(b)

findings of crypt branching and subcryptal inflammatory infiltrates cannot be seen if the biopsy is crosscut. One reason that biopsy processing quality may be poor in a given center is the reluctance to have one or two technologists designated as the "small piece" specialists.

The solution for chronically poor biopsy processing may be to send biopsies to central laboratories with good track records for quality processing of gastrointestinal mucosal biopsies. Sending poorly processed biopsy slides for second opinions is not a good alternative, because biopsy interpretation of poorly processed tissue remains compromised, irrespective of the expertise of the pathologist.

Know the truth and consequences

Pathologists must know the consequences of their diagnoses. Two important areas of truth and consequences are overdiagnosis of colitis (discussed below), and the overdiagnosis of "mixed adenomatous hyperplastic polyps." Some hyperplastic polyps have very reactive crypts that may mimic adenomatous change and thus result in this overdiagnosis of a mixed polyp. If a mixed polyp is the only one that puts patients and their subsequent generations into regular colonoscopic surveillance then a second pathologist opinion should be sought.

Pathologists often use a closing caveat in a report of "clinical correlation recommended." Those who do this argue that it is intended to let the clinician know there are some worrisome findings. In their defense they often point out that they do this for clinicians who never provide meaningful clinical information. How does one stop this dysfunctional cycle of communication? One point is that endoscopists have to provide the basic information to pathologists that is required for modern biopsy

diagnosis. Then the pathologist should be reminded that we give clinical correlations with every test we order, even urinalyses! If the pathologist is concerned about the implications of the biopsy findings then those concerns should be reflected in how the report is prepared, and in certain instances followed up with a phone call to the clinician.

Stop the universal reporting of "mild chronic inflammation" in biopsies that are normal

Most who read this would nod knowingly. Many endoscopists ignore "mild chronic inflammation" in biopsy reports and thus miss some bona fide cases of microscopic/lymphocytic colitis. The alternative for endoscopists is to believe each of these reports and subject patients to needless and expensive therapy, namely those patients who have never had colitis.

There are two reasons for pathologists to persist in this practice of reporting mild chronic inflammation. One is insecurity with what is normal. In clinical medicine we may use the equivalent term of "grossly normal." The other reason is that some pathologists believe that the endoscopist will get into trouble if too many biopsies are signed out as normal. This is reminiscent of the parallel of signing out appendectomy or cholecystectomy specimens as normal. Regarding insecurity with what is normal, pathologists need to realize that the overcall of normal biopsies may have long-term adverse implications for patients.

Use modern accepted terminology

Expressed in a different way the pathologist should not use terms for which there is no action plan. The best

Locations	Comment
Cecum and ascending colon	The cecum and ascending colon look histologically inflamed relative to left colon. Separate these sites from the rest of the biopsies
<i>Hepatic flexure region</i>	
Transverse colon	If multiple sites biopsied then designate as proximal, mid, distal
<i>Splenic flexure region</i>	
Descending and sigmoid colon	Note biopsy location as “descending,” or as sigmoid with centimeters from anal verge
Rectum	Describe as such or, if important focal rectal disease, as centimeters or relationship to the valves of Houston

Table 27.2 Standardized reporting of biopsy and lesion locations. (Modified from Weinstein [11].)

example is moderate dysplasia, a grade that does not exist in the modern classifications of dysplasia in either IBD [12] or Barrett’s esophagus [13].

Answer the questions from the endoscopist

The questions should be answered either in the body of the text of the report or in the final diagnosis section. In some disorders the pathologist may not be able to answer the question we ask. Hopefully the pathologist will be able to point us to a study or data that will educate us in this regard. For example, if we biopsy a vascular lesion to verify that it is vascular prior to ablation, the biopsy may not be positive in over 50% of cases [14]. The reasons for failure to document vascular lesions histologically include the fact that some are located in the submucosa, deeper than the biopsy forceps reaches, or that small mucosal vessels collapse and shrink in tissue fixatives.

Encourage feedback from pathologists

Endoscopists might have stopped doing multiple biopsies with a single pass of a forceps if the pathologist had told us decades ago that we are getting one good quality biopsy and one that is tiny and diagnostically useless much of the time. Another example of the desirability of feedback is when endoscopists put all the biopsies, e.g. 10–15, into one fixative bottle. Pathologists should tell the endoscopists that, when 10–15 biopsies are embedded into one tissue block, perhaps only half will come out as interpretable (Fig. 27.2).

What information should the endoscopist provide the pathologist?

When an X-ray is ordered, the radiologist is provided with the history and the question to answer. When biopsies are sent to pathology they often go unaccompanied by any information. This dysfunctional com-

munication should not continue in this era of easy and rapid information exchange.

All endoscopy units should use a standardized biopsy requisition that incorporates the key information given in Tables 27.2 and 27.3

This is probably the only way to overcome the lack of communication which in turn compromises the maximum potential for biopsy to aid in patient management. In regards to biopsy location and describing the mucosal

Table 27.3 Lesion descriptions, relevant medications, history, and question for the pathologist. (Modified from Weinstein [11].)

Lesion description

Simple language for mucosal abnormalities: thick folds rather than hypertrophic; define friability if used, i.e. petechiae on passing the area with a colonoscope or bleeding or spontaneous petechiae or oozing

Describe what was seen rather than an interpretive term such as colitis

Biopsy instrument

Detail type of instrument if different (e.g. hot biopsy forceps, electrocautery snare) than a pinch biopsy forceps

For polyps

Give size, whether sessile or pedunculated and instrument used, e.g. biopsy forceps, hot biopsy forceps, or electrocautery snare

Relevant medication

Colon: type of prep; enemas or oral, and type of oral medication; 5 ASA compounds or other IBD agents

For all sites in the GI tract: any NSAIDs, immunosuppressives, chemotherapy or radiotherapy (and time from last treatment)

History

Brief usually suffices. In patients with diarrhea: duration of diarrhea, bloody or nonbloody

Questions for the pathologist

Be as specific as possible—see Table 27.4 listing good vs. bad questions

biopsy site as normal or abnormal, the surrounding terrain may be important. For example if there appears to be focal inflammation between diverticula in the left colon the pathologist should be made aware of the fact and of how far from a diverticulum opening the biopsy came from [15,16].

The history

It should be very brief and relevant. Then there should be the question(s) for the pathologist. For example, when biopsies are taken in patients with diarrhea two key elements are the duration and whether the diarrhea is bloody or not. The duration is important to avoid putting a diagnosis of inflammatory bowel disease on a patient’s chart prematurely.

Not infrequently after biopsies are taken an infectious colitis may be diagnosed from the stool culture or examination studies. The pathologist should be notified to save them puzzlement time and irrelevant differential diagnoses on patients’ charts. Also if additional potentially relevant historical information is obtained after the biopsy is taken (e.g. recent radiation therapy, cohabitation with an amebiasis patient) but before the biopsies are signed out, call the pathologist with the information. Again the objective is to save the pathologists’ time and avert potentially irrelevant differential diagnoses for conditions already clinically diagnosed.

Some (including, sadly, some pathologists) still harbor the notion that it is good for the soul to keep information from the pathologist to preserve objectivity. That practice is equivalent to asking a physician to do a physical examination without any history. Prior review without any history may be an effective teaching tool for pathology residents to cover all the bases in examining tissue, but not for integrating information in modern medicine for patient management.

What medications does the patient take?

Table 27.3 outlines the information regarding drug or other therapy that can impact biopsy diagnosis in any

part of the gut and some that are site specific. For chemotherapy and radiotherapy it is essential to know when these were last administered because the early effects differ from the delayed effects histologically. Nonsteroidal inflammatory drugs (NSAIDs) are important to document, especially if unusual lesions are found virtually anywhere in the gut—cause and effect in such instances are difficult to prove but at least NSAIDs can be put into the differential diagnosis of an unusual colitis [17,18]. In lymphocytic or microscopic colitis it is likely that a host of drugs will be proven to be important in initiation and/or cause. It is not necessary to list all drugs a patient takes. The importance of some of the drugs a patient takes may only become apparent after review of the biopsies. For example, if ischemic colitis is suspected on the basis of the biopsy findings, then the drug history can be sought or amplified after the biopsies are interpreted; here one would want to know about cocaine use, oral contraceptives, etc.

The questions for the pathologist

Table 27.4 gives examples of some good and some bad questions that are discussed in this section. When a tumor that is destined for surgical resection is biopsied, the pathologist should be informed that the biopsy is only to be sure that there is not some other very rare cause of a similar appearance. Instead of asking whether it is cancer, it is better to ask if the biopsy shows adenomatous change. Otherwise the pathologist will feel compelled when appropriate to indicate “can’t exclude cancer, recommend rebiopsy.”

In ulcerative colitis (UC) biopsy helps most when it does not fit. Namely the best question is “it looks like UC but tell me if I might be wrong.” That alerts the pathologist to look for disorders that can mimic UC, like infections, or multifocal granulomas that would suggest Crohn’s disease [10].

In suspect Crohn’s disease, asking “is this compatible with Crohn’s” too often gets a yes because virtually any mucosal abnormality can be seen in Crohn’s. The question to ask is whether granulomas or multifocal

Table 27.4 Examples of good questions and bad questions.

Biopsy site	Bad question	Good question
Biopsy of large tumor scheduled for surgery	Rule out cancer	Rule out adenomatous change
Biopsy of apparent UC	Is it compatible with UC?	Looks like UC—is there anything to suggest another cause?
Biopsy of suspect Crohn’s	Is it compatible with Crohn’s disease?	Are there diagnostic features of Crohn’s disease?
Biopsy of normal mucosa in a patient with diarrhea	Is there mild colitis?	Exclude microscopic or collagenous colitis

inflammation are present. Of course neither of these findings clinch the diagnosis of Crohn's, but the question alerts the pathologist that you are looking for more solid evidence to suggest Crohn's disease rather than any small collection of inflammatory cells signed out as "compatible with Crohn's."

Finally the question of whether there is mild colitis is best replaced by questions that rule out microscopic or collagenous colitis or even rule out unequivocal inflammation. The reason for this defensive posture was discussed previously in regard to the pandemic of "mild chronic inflammation."

When and where to biopsy the colon

Table 27.1 gives the broad indications for colonic biopsy.

In the biopsy removal of sessile polyps, pathologists should be discouraged from making a diagnosis of "the margins are clear." The only way to make that diagnosis is to section the dome-shaped lesion entirely from front to back. The issue in larger lesions removed with EMR was discussed previously.

In biopsies for amyloidosis and Hirschsprung's disease, submucosa must be present in the biopsy in order to visualize submucosal vessels (amyloidosis) or ganglion cell presence or absence for Hirschsprung's disease. In these disorders it is not sufficient to sign cases out as negative if the submucosa is absent. The report should be specific, such as: "cannot rule out amyloidosis because submucosa is not present." The report and its interpretation require coordination between the clinician and the pathologist so that both understand the requirements, and that not meeting them means the biopsy is inadequate.

When graft-versus-host disease (GVHD) is suspected and the endoscopist is consulted to help make the diagnosis, there is a parallel need for coordination of information because in addition to ruling GVHD in or out it is essential to look for evidence of infection, especially with CMV. To rule out GVHD it may be useful also to do an upper endoscopy with small bowel and gastric biopsies as well as colonic biopsies. Sometimes the upper gastrointestinal tract is much more commonly affected [19].

Diarrhea with normal endoscopy

In patients with chronic diarrhea (assuming infection is ruled out) and a normal endoscopic appearance, important colonic disorders to exclude are collagenous and microscopic colitis [20,21]. Random biopsies in some patients with collagenous colitis may miss the subepithelial deposits and reveal only microscopic colitis. This is especially true in the rectosigmoid region [9]. Other findings in diarrhea with a normal endoscopy include amyloidosis and melanosis coli. Melanosis coli is commonly unassociated with any endoscopic evidence

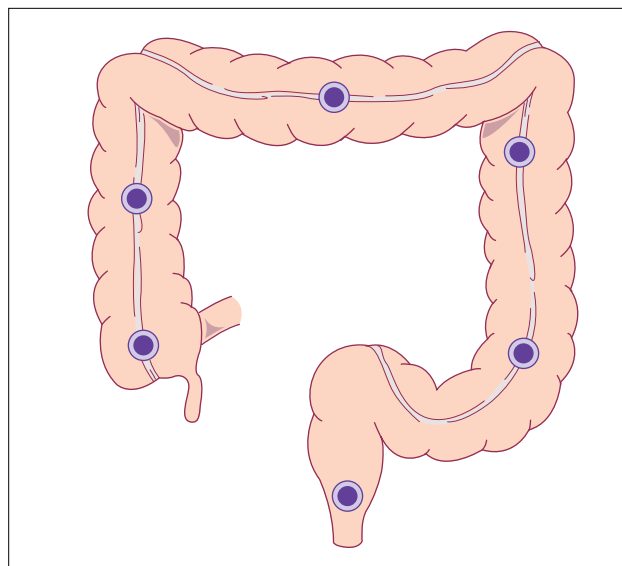


Fig. 27.4 Sample scheme for biopsy of the colon in diarrhea where endoscopy is normal or where there is a pan- or left-sided colitis, seen for the first time (two biopsies per site). Biopsies from the cecum and ascending colon should be separated from biopsies of the transverse colon and distally (see text).

that it is present and may predominate in the right colon. When found, it raises the question of a prior or recent history of laxative abuse.

Figure 27.4 is a sketch of the scheme for taking the biopsies, two per site, six sites. Four biopsies are grouped per fixative bottle and hence will be placed together in one tissue block: the cecum and ascending colon together; transverse and proximal descending colon; and the other two left-side sites together. Because the cecum and ascending colon can look inflamed in health relative to the left colon (Fig. 27.5), biopsies from those sites should be kept separate from all others. Figure 27.6 is a sketch of biopsies in special IBD circumstances. The distal part may also apply to biopsy of normal mucosa in diarrhea patients at flexible sigmoidoscopy; namely it is useful to obtain biopsies from three locations, descending colon, sigmoid, and rectum.

Some consider the number of biopsies suggested in Figure 27.4 to be a gargantuan task. However, the effort expended by the endoscopist is necessary to make the appropriate diagnosis. If the main reason for the examination is to find the cause of diarrhea it is difficult to argue that six sites is excessive in this vast expanse of mucosa.

Diarrhea and an abnormal endoscopy

Figure 27.6 highlights some issues related to biopsy in the wide range of inflammatory bowel diseases for the diagnosis and differential diagnosis and for focal

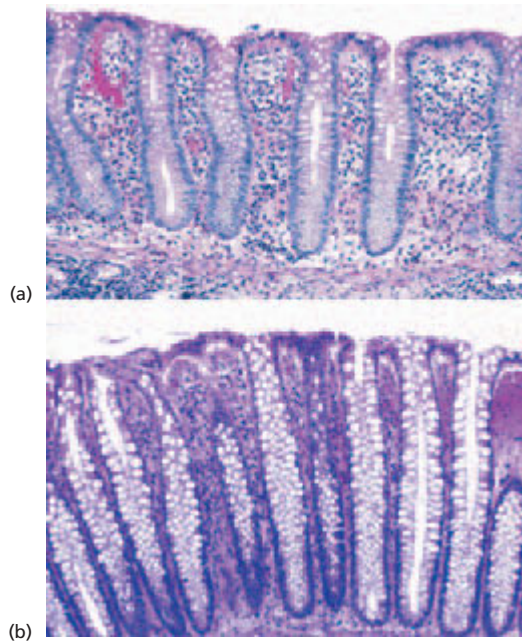


Fig. 27.5 In health the normal cecal mucosa (a) looks more cellular and inflamed than the normal sigmoid colon mucosa (b).

lesions throughout the gastrointestinal tract. Ulcerative proctitis should not be diagnosed solely on the basis of one biopsy from the abnormal rectum. A second biopsy about 10 cm proximal should be taken. Not uncommonly there is unequivocal histologic inflammatory change in the proximal biopsy from normal-appearing mucosa. That then makes it a case of putative left-sided colitis to be worked up later for extent.

If the 10-cm-above biopsy is normal then the patient can be informed about ulcerative proctitis, to include the facts that in 80% or more of cases the disease does not migrate proximally, and thus the risk of cancer is lower or nonexistent in bona fide cases. Perhaps the higher proximal migration rates reported by some are due to suboptimal classification at the outset, i.e. not taking proximal biopsies routinely to identify occult left-sided colitis cases [22] as there is no apparent increase in cancer risk assuming it stays as an ulcerative proctitis, etc.

Figure 27.6 also illustrates the key point regarding biopsy of a focal lesion and applies not just to the colon but also to focal lesions throughout the gastrointestinal tract. It is often useful for diagnosis and differential diagnosis to biopsy the focal lesion and also the adjacent mucosa within a centimeter away. The reasons for this recommendation include: (i) not infrequently what appears focal is not; (ii) sometimes the adjacent mucosa is more abnormal than the target lesion. Figure 27.7 illustrates the approach to a large unclassified type ulcer of the colon and its biopsy sites. If there is severe mucosal injury with ulceration, the aetiology may be more apparent in the less damaged non-ulcerated adjacent mucosa.

Whereas the biopsy of the ulcer may reveal only exudate, the fact that the ulcer might be CMV or ischemia may be evident only in the adjacent biopsies with typical cytomegalic cells in the case of CMV, or focal crypt necrosis (dropout) in the case of ischemia.

The biopsy scheme shown in Figure 27.4 for biopsy of the normal mucosa in diarrhea can also be used in the biopsy of the diffusely abnormal mucosa.

The best time for the pathologist to contribute to a diagnosis of ulcerative colitis or Crohn's disease is before therapy has been initiated while typical features are still preserved. Even thereafter, the issue is not whether a single biopsy session gives the answer. If the type of inflammation is unclear, the biopsies should be repeated at a later time. In some instances biopsy of the upper gastrointestinal tract may be used to look for surrogate evidence of Crohn's disease [23].

In centers with a large experience with inflammatory bowel diseases and where the endoscopists and pathologists communicate well it is likely that the numbers of cases of indeterminate colitis are small, i.e. less than 5%. This presupposes that the category of "indeterminate" is based upon all the methods of evaluation in a given patient, after at least 1 year and with at least one colonoscopic rebiopsy session. In puzzling cases it helps to review two or more sets of biopsies with the pathologist in the context of what the endoscopic and clinical findings were at the time of each examination.

Biopsies at the outset of, or in established, ulcerative colitis or Crohn's disease

Differential diagnosis and assessment of extent and disease activity

Assessment of established UC or Crohn's is usually done early in the presentation but not necessarily when the patient is very ill and the colitis is severe. In that instance a limited exam, e.g. left side colonoscopy and biopsies, may be taken to rule out other causes. The principles of biopsy are those given in the previous section. The terminal ileum should be examined in all new patients with UC or Crohn's disease. Both the normal and abnormal ileum should be biopsied in these instances but the yield from biopsy of a normal-appearing ileum in an IBD patient is small and there are concerns about prion transmission because of the concentration of lymphoid tissue. There are fewer histologic surprises in the terminal ileum than in the colon. Current practice in Europe is that, because of the concentration of lymphoid tissue in the terminal ileum, and possible risk of prion transmission, biopsies are not routinely taken from the terminal ileum unless they have a significant chance of contributing to the management of the patient concerned.

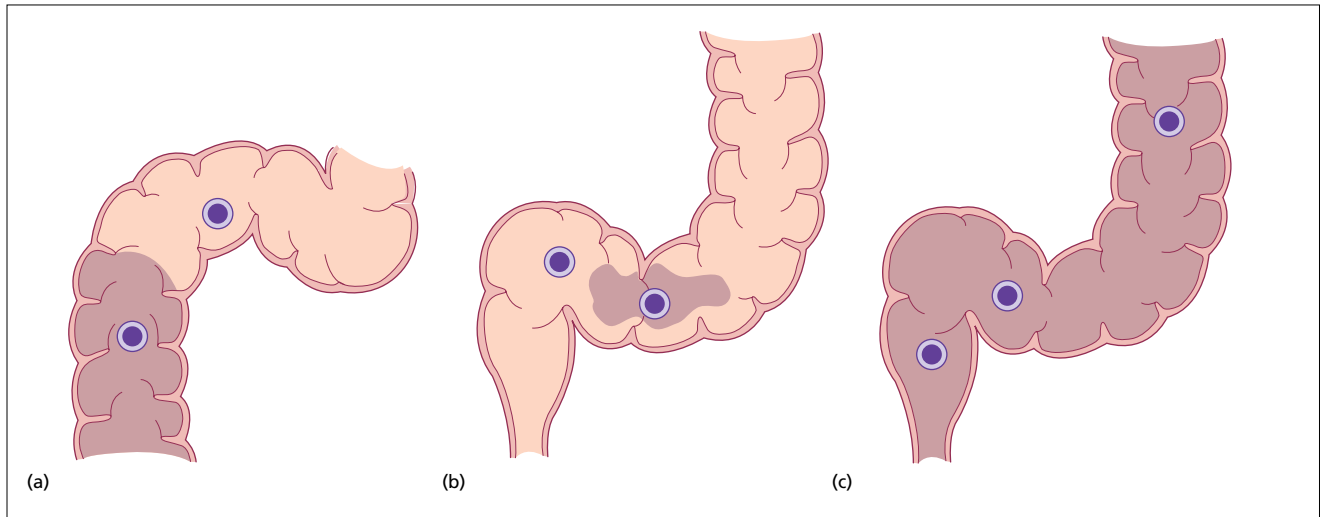


Fig. 27.6 Some principles of where to biopsy in IBD diagnosis. For ulcerative proctitis (a) one biopsy within the inflamed zone and one approximately 10 cm away (see text). For any focal lesion (b) biopsy the adjacent mucosa. For diffuse inflammation (c) at flexible sigmoidoscopy, biopsy the descending colon,

sigmoid colon, and rectum. This helps resolve whether the histology is patchy, verifies apparent diffuseness, and additional biopsies may help find a specific diagnosis. Note that this scheme of three biopsies also applies to normal mucosa in a diarrhea workup, at flexible sigmoidoscopy.

Established ulcerative colitis or Crohn’s disease but atypical course

When the patient fails to respond to the same therapy that was previously successful for flareups or maintenance, stool studies to rule out infection are indicated. If those are negative a repeat colonoscopy and biopsy should be done. The objective is to rule out a concomitant cause of poor responsiveness, such as more severe disease, coinfection with CMV, or development of ischemic colitis.

Surveillance for cancer (Fig. 27.8)

“Normal” surveillance frequency for the purposes of this discussion is annually for 2 years, then every 2 or 3 years up to 20 years of disease, and then annually thereafter [10]. The conventional recommendation is to biopsy four quadrants every 10 cm. However most patients do not have a featureless colon where 10 cm at a time is meaningful or accurate. Therefore focusing on landmarks in these patients is preferred. Thirty to

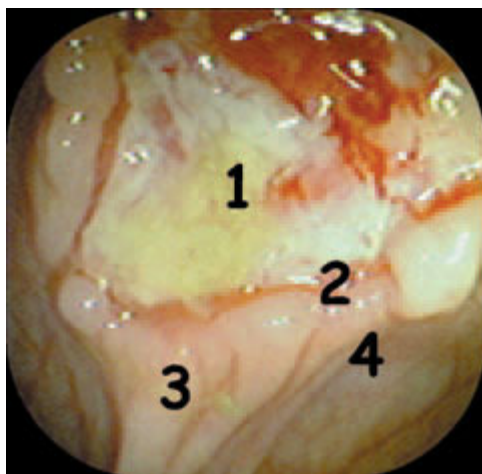


Fig. 27.7 Suggested biopsy scheme for a colonic ulcer of unknown cause. Focusing only on the center (biopsy site 1) might just yield non-specific exudate. The edges (2) are often high yield for specific processes associated with overlying exudate, e.g. infections (CMV), lymphoma. Biopsy sites (3) and (4) within 1 cm may be the ones that are diagnostic for CMV or other infections, or ischemia, with focal crypt dropout.

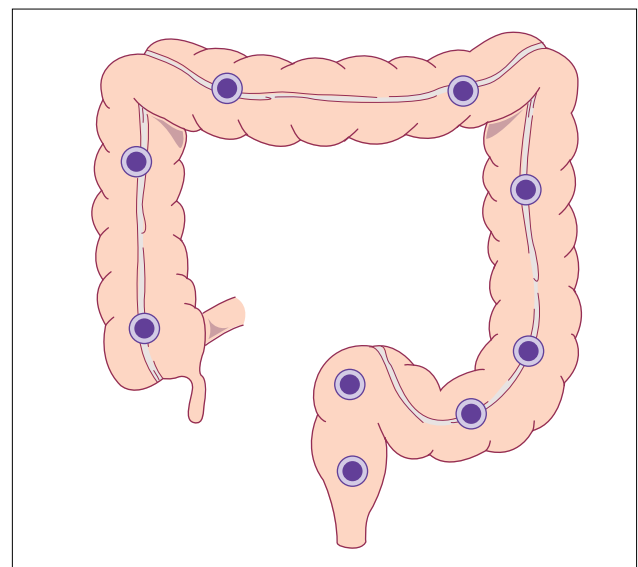


Fig. 27.8 Representative biopsy sites in surveillance for dysplasia and cancer in UC and Crohn’s disease. Nine sites with four biopsies per site. Landmarks are used rather than the “every 10 cm rule”.

forty random biopsies per surveillance examination, and in addition biopsies of lesions such as bumps or ulcers, give a good chance of finding dysplasia if present [24]. Targetting lesions and taking biopsies at predetermined places should rule out endoscopically visible and invisible dysplasia or carcinoma. The management of polyps in UC and Crohn's has attracted considerable attention and therefore is discussed in detail in the next section.

Lumps and bumps in ulcerative colitis and Crohn's disease

Biopsy surveillance in UC and Crohn's disease is directed to the finding of dysplasia. Dysplasia is graded as indefinite, low grade, and high grade.

What is dysplasia?

Dysplasia is a neoplastic change confined to the lining epithelial cells. If dysplastic cells break through into the lamina propria it is termed intramucosal cancer. An *adenoma* is dysplastic by definition. In some countries the term adenoma is used for flat dysplastic lesions as well. In North America at least, dysplasia in the absence of a visible bump is usually termed just "dysplasia," whereas a visible collection of dysplastic (synonymous with adenomatous) tissue is referred to as an "adenoma." Pathologists' interobserver agreement rate for low-grade or indefinite dysplasia is in the range of 70% or less and for high-grade dysplasia in the range of 85% or less [12].

When one considers surveillance biopsy for dysplasia in UC and Crohn's one of the "hottest" areas of discussion is the management of lumps and bumps. The concern is whether a given raised lesion in UC represents a carcinoma. The safest approach to polypoid lesions in IBD relies more on the common sense, experience, and knowledge of the endoscopist than most other disorders encountered in gastrointestinal endoscopy.

The dysplasia-associated lesion or mass (DALM) lesion

The coining of this term has served a very useful purpose for clinicians. It alerted them to the fact that a sessile lesion with any grade of dysplasia could represent a carcinoma complicating ulcerative colitis [25]. Invasive cancer was defined by whether the dysplastic lesion (low or high grade) penetrates the muscularis mucosae into the submucosa. The DALM was a way of getting across an important concept, that the sessile lesion of UC might be a carcinoma and not an ordinary sessile adenoma. The principle of DALM is the same as for all sessile adenomas in non-UC patients but served to put endoscopists on alert when a sessile lesion was encountered

and for pathologists to use the term to arouse the suspicion of the clinician.

The initial judgement that the endoscopist must make is whether a polypoid lesion in IBD is a "sporadic adenoma," also termed "adenoma-like mass" or ALM, depending upon where it occurs [26], versus the more dreaded mass lesion that may represent a cancer at the outset, the "dysplasia-associated lesion or mass," the DALM. In practice, if a sessile lesion is encountered during colonoscopy in ulcerative colitis and it has the typical appearance of a benign adenoma (the type commonly seen in a non-UC patient), it should be considered to be an adenoma and polypectomy may be performed in the usual fashion without further consequences providing that it meets the following endoscopic and histopathologic criteria: it can be totally removed; there is no invasive cancer (although it may or may not have high-grade dysplasia); biopsies of the surrounding tissue reveal no dysplasia (indicating the absence of a widespread "field defect"). Although the above described endoscopically resected lesion in ulcerative colitis would qualify as a "mass", and it has dysplasia (by definition, all adenomas have dysplasia) its total removal avoids the ominous implication of the term DALM, and it can be assumed to be an ALM (a sporadic adenoma) even if it were located within the area affected by colitis. If the sessile dysplastic lesion is in an area affected by colitis and cannot be totally removed endoscopically, it should be considered a DALM which requires surgical intervention.

Furthermore any grade of dysplasia ALM is a term that has been applied to sessile lesions that look like ordinary adenomas but occur within the colitis zone whereas sporadic adenoma-like polyps are those that look innocuous and occur proximal to the colitis zone [26]. For this discussion the conceptual focus will be on pedunculated adenomas, sporadic-type sessile adenomas that look benign, irrespective of whether they occur within or outside the colitis zone, and DALM lesions that are sessile, larger and may have other worrisome endoscopic appearances.

Excluded from this discussion is the consideration of giant (filiform) pseudopolyps, which have to be differentiated from a carcinoma when localized and confluent [27]. Giant filiform pseudopolyps often look like worms and may bridge the lumen, occur in groups as discrete lesions, or are confluent and frightening to those unfamiliar with them for the possibility of cancer.

Also excluded is the question of dysplasia (in either flat mucosa or bumps) in patients with ileoanal pouches. Dysplasia has been reported in endoscopically visible and invisible areas but overall appears to be rare [28]. However the few reports of ileoanal or anal region adenocarcinoma in pouches suggest we should do some kind of follow-up but there are no guidelines regarding when to do it and how.

Management and implications of lumps and bumps in UC and Crohn's

Pseudopolyps

Definition

There is nothing “pseudo” about pseudopolyps. They are visible bumps and as such are polyps, which actually represent “pseudoadenomatous” polyps. When these become confluent over several centimeters or more, it is difficult to reliably exclude cancer or DALMs. Pseudopolyps that look nearly transparent and pale are more reassuring. When pseudopolyps are confluent and extend over more than a few centimeters it is important to inform the patient that a relative blind zone (for surveillance) is now present and to consider whether surveillance as usual will continue or whether this should be used as one factor in the decision for colectomy. In surveillance biopsy of pseudopolyp clusters the aim is to look for lesions that stand out especially because of color or shape differences.

How many isolated totally benign-appearing pale pseudopolyps should be biopsied at the time of colonoscopic biopsy surveillance in colitis?

It is hard to resist biopsying a few, but if they are all isolated, pale or semitranslucent without any “shape-alerts” then one should focus on the flat mucosa nearby rather than these lesions themselves, in the hunt for dysplasia.

Pedunculated adenoma management

Typical “balloon-on-a-string” adenomatous polyps in colitis either inside or outside of the inflammation zone can be generally regarded as sporadic adenomas. It is worthwhile to biopsy the surrounding mucosa within a centimeter of the lesion, at four quadrants. The purpose is to be sure that this innocuous looking typical polyp is not occurring in a dysplastic soil. Pedunculated polyps in the setting of IBD should be distinguished from sessile tumors with pseudostalks that are thick and semimobile. These should be considered masses (see subsequent discussion below).

DALM lesion management

Because cancer may already be present in 40–50% of these patients [29], the idea has become ingrained that the only reliable way to exclude cancer is to remove the colon to see if the carcinoma is present.

DALM has been a catchy and highly effective term to get across the point that to exclude invasive cancer in a

sessile adenoma requires that it be removed completely to prove that the adenomatous (i.e. dysplastic) process does not extend into the submucosa. The same principle applies throughout the gut.

Colectomy has been the standard when DALM lesions were found, but recent evidence (see below) has demonstrated that lesions that look like adenomas, are dysplastic but can be removed endoscopically, act like adenomas on follow-up. The decision is normally clear cut for surgery when a lesion is ≥ 2 cm with irregular margins and a bumpy surface.

Some have done EMR on large DALM lesions rather than recommend colectomy. If this is done the area should be re-examined after 3 months to rebiopsy the site and near the site.

Inject the polypectomy site with a permanent marker

Any worrisome lesion that is to be removed should have the site injected with a permanent tattoo marker (see Chapter 36) so that the area can be identified at the next endoscopy.

Managing the smaller, smoother sessile adenoma

When sessile lesions are < 2 cm, and look completely benign, they can be removed with snare polypectomy, and the surrounding mucosa biopsied as for pedunculated polyps. The patient should have repeat endoscopic biopsy surveillance thereafter every year. Two studies have shown that a careful biopsy evaluation at the time of polypectomy and careful follow-up endoscopic biopsy surveillance is safe [30,31]. “Safe” refers to the fact that if no dysplasia is seen in mucosa adjacent to the polyp then one can assume that there is no field defect, and that the polyp is equivalent to a sporadic adenoma (see Chapter 33).

Some have advocated that the intensity of surveillance can be tailored according to whether the polyps occur in or outside of the colitis zone [26]. This may be true, but one cannot assume that the current colitis and non-colitis zones represent the true extent of disease. The presence or absence of histologic footprints (quiescent colitis) may not be reliable to decide where the disease is or has been. The reason is that the mucosa can return completely to normal from a previously inflamed state in ulcerative colitis.

Summary: polyps and commonsense in colitis

If invisible or flat dysplasia is found at any time in biopsies of adjacent mucosa, low grade or high grade in association with an apparent sporadic adenoma, colectomy should be advised. Those who prefer to continue heightened surveillance for low-grade dysplasia should

provide the patients with the data regarding cancer risk when low-grade dysplasia is found in colitis [32].

If any adenoma occurs in a very young patient (e.g. age 30), then it should be more suspect as a colitis-related adenoma than a sporadic one. If this younger patient keeps producing small benign adenomas the patient should be considered at higher risk for cancer. The same analogy holds for patients with primary sclerosing cholangitis [33]. If the patient has a family history of colon adenomas or cancer then the concern should also be heightened [34]. Future follow-up in these patients should be yearly, at least for several years of no further polyps.

Summary

I believe that those who understand how colonic mucosal biopsy can help in diagnosis and management and have modern pathologists to work with will do the best for their patients. I hope that the next generation of endoscopists will come to believe in the "joy of biopsy," will find great pathologists to partner with, and will be less timid when it comes to a procedure that is a high-powered extension of our eyes.

Acknowledgments

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Chapter 28

Cleaning and Disinfection

David A. Greenwald

Introduction

Colonoscopy is safe and effective. In the USA, estimates are that in excess of 10 million endoscopic procedures are performed annually [1]. The extremely low incidence of infection transmission is evidence that the procedure is safe. Effective cleaning and disinfection of the endoscope is an integral part of the procedure itself. Standards concerning infection control in endoscopy have been developed and disseminated widely since the late 1980s, helping to ensure continued safety in gastrointestinal endoscopy [2,3].

Colonoscopy reprocessing

Flexible gastrointestinal endoscopes are complex instruments with internal channels for air, water, and accessories. When endoscopes are used for diagnostic or therapeutic procedures, body fluids and contaminants may remain on and in the instrument. Both visible debris and invisible microorganisms are removed from the endoscope during reprocessing, which involves cleaning and high-level disinfection. In contrast to rigid endoscopes and some reusable accessories, flexible endoscopes are heat-labile and cannot be autoclaved, requiring meticulous attention to detail during the reprocessing of flexible endoscopic instruments.

Numerous professional organizations, including the American Society for Gastrointestinal Endoscopy (ASGE), the Society for Gastroenterology Nurses and Associates (SGNA), the World Congress of Gastroenterology, the Association for Professionals in Infection Control and Epidemiology (APIC), the American Society for Testing and Materials (ASTM), and the Association of Operating Room Nurses, have issued guidance documents for reprocessing gastrointestinal endoscopes [4–8]. These documents are intended to aid users of endoscopic equipment to achieve the accepted standard of high-level disinfection, defined as the destruction of all microorganisms with the exception of high levels of bacterial spores [9].

High-level disinfection vs. sterilization

High-level disinfection is the current standard for reprocessing of endoscopes [10]. This may be achieved by automated or manual reprocessing. High-level disinfection is defined as a process that results in the destruction of vegetative bacteria, viruses, fungi, and mycobacteria but not necessarily all bacterial spores. Sterilization is defined as a process in which all microbial life is destroyed. High-level disinfection in gastrointestinal endoscopy is usually achieved through the use of manual precleaning followed by exposure to a liquid chemical sterilant (LCS) [11].

An LCS is capable of sterilizing accessible and exposed surfaces under appropriate conditions (i.e. adequate precleaning) and with appropriate length of exposure (i.e. longer than that for high-level disinfection). Sterilization of an endoscope is possible through use of steam autoclaving (but it destroys the endoscope) and via ethylene oxide sterilization, although the latter is associated with a turnaround time of greater than 24 h, which is economically unacceptable in a busy endoscopy suite.

While sterilization of an endoscope sounds like an attractive goal, it has not been recommended for semi-critical devices (see Spaulding criteria below), such as an endoscope within the gastrointestinal tract, for several reasons.

- 1 There are no data to demonstrate that it is possible to reliably and consistently achieve and monitor sterilization of internal channels (e.g. the elevator mechanism in duodenoscopes is inaccessible).
- 2 There are no data proving decreased infections, improved safety, or improved outcomes when comparing sterilization with high-level disinfection.

Spaulding criteria

Criteria exist to categorize medical devices based on their risk of transmission of infection during use. This scheme is based on the Spaulding classification of medical devices [9]. Three categories of medical device are described.

1 Critical devices: those that enter sterile tissue or vascular spaces. These devices require sterilization, defined as complete elimination of all forms of microbial life. Examples of critical devices include biopsy forceps and papillotomes.

2 Semicritical devices: those that contact intact mucous membranes and do not ordinarily penetrate body surfaces. These devices require high-level disinfection, defined as the destruction of all microorganisms, including bacteria, mycobacteria, small or nonlipid viruses, but not some highly resistant spores. An example would be a colonoscope.

3 Noncritical devices: those that contact only intact skin. These devices do not need to be sterilized or high-level disinfected. Examples would include a stethoscope or blood pressure cuff.

Transmission of microorganisms during endoscopy

Transmission of infection at the time of gastrointestinal endoscopy is a rare event. At present, most cases of infection deemed related to an endoscopic procedure can be traced to failure to adhere to published guidelines for reprocessing [12]. These errors can be further divided into the following broad areas.

1 Procedural errors in the meticulous cleaning and disinfection of the endoscope, leading to retained microorganisms on the endoscope. These organisms may accumulate in the crevices and joints of the instrument.

2 Insufficient exposure time to liquid chemical germicides or use of inappropriate disinfectant solutions.

3 Improper use of automated endoscope reprocessing equipment.

4 Contaminated water bottles and irrigating solutions.

5 Inadequate drying and improper storage of endoscopes after reprocessing.

The reported frequency of transmission of infection in gastrointestinal endoscopy has been estimated to be 1 in 1.8 million [13]. Spach and colleagues [14] reviewed 281 infections related to gastrointestinal endoscopy as well as 96 felt to have been caused by bronchoscopy. Of the 281, all but 28 occurred prior to 1988, the year in which the importance of adequate manual cleaning as well as disinfection were stressed in guidelines published by the ASGE and the British Society of Gastroenterology (BSG) [15,16]. The ASGE Technology Committee reviewed Spach's data in 1993 and then estimated that 40 million gastrointestinal procedures had been done in the USA between 1988 and 1992. This meant that there had been 28 reported infections in approximately 40 million endoscopic procedures, an estimated rate of transmission of infection of 1 in 1.8 million, a rate that is frequently cited.

It is likely that the reported infection rate is an underestimate due to factors such as inadequate sur-

veillance, asymptomatic infections, and infections with long incubation periods [17,18]. Some authors have suggested that endoscopists do not capture all their complications because follow-up is too short; infectious complications might not be recognized as having been related to the procedure. These authors recommend 30-day follow-up of gastrointestinal procedures (as opposed to the "traditional" assessment of complications recognized during and immediately after the procedure) as a better measure for studying endoscopic complications [19].

Viruses

The blood-borne viruses that are of most concern include human immunodeficiency virus (HIV), hepatitis B virus (HBV), and hepatitis C virus (HCV). Gastrointestinal viruses, such as Norwalk virus, rotaviruses and enteroviruses, that would be contacted by an endoscope inside the gastrointestinal tract are also of concern, although these are effectively eliminated by standard reprocessing protocols.

Endoscopic transmission of HBV has been reported in only one patient [20]. In this case, standard reprocessing protocols were not followed, as the endoscope's air/water channel was not flushed with glutaraldehyde. Several prospective studies of patients harboring HBV have failed to demonstrate its transmission to subsequent patients during gastrointestinal endoscopy [21].

Patient-to-patient transmission of HCV during colonoscopy has been reported [22]. In this case, HCV was transmitted from an infected patient to two others who subsequently had colonoscopy in that unit; the HCV was confirmed to be the same by genotyping and nucleoside homology. Transmission of viral infection in this instance occurred because of (i) failure to adhere to proper manual cleaning of the endoscope after colonoscopy (the biopsy-suction channel was never cleaned with a brush) and (ii) a breach in proper protocol for sterilizing endoscopic accessories. HCV has also been reported to have been transmitted during colonoscopy via a multidose anesthetic vial using the same needle or syringe between patients [23]. Studies have failed to identify endoscopy as a risk factor for contracting HCV infection [24]. It has been demonstrated that use of current reprocessing guidelines adequately eliminates HCV from endoscopes [25,26].

HIV, much like the other viruses, is very sensitive to high-level disinfection or sterilization. No documented cases of HIV transmission have occurred after gastrointestinal endoscopy. Several studies have demonstrated that in endoscopes deliberately contaminated with HIV, the virus is easily eliminated in all cases using standardized manual cleaning and high-level disinfection techniques [27].

Table 28.1 Microorganisms transmitted by (or shown to contaminate) endoscopes. Major factor(s) involved in incident indicated by ✓. (Modified from Alvarado & Reichelderfer [6].)

	Infection (I) or contamination (C)	Cleaning procedure	Disinfection process	Rinsing process	Automated processor	Contaminated processing or water bottle
Before guidelines						
Gram-negative bacilli						
<i>Pseudomonas aeruginosa</i>	I	✓	✓	✓	✓	✓
<i>Klebsiella</i> sp.	I	✓	✓			
<i>Enterobacter</i> sp.	I	✓	✓			
<i>Serratia marcescens</i>	I	✓	✓			
<i>Salmonella</i> sp. including <i>S. typhi</i>	I	✓	✓			✓
<i>Helicobacter pylori</i>	I	✓	✓			✓
<i>Bacillus</i> sp.	C	✓	✓			
<i>Proteus</i> sp.	C	✓	✓			
Mycobacteria						
<i>Mycobacterium tuberculosis</i>	I	✓	✓			
Atypical mycobacteria	I	✓	✓			
Fungi						
<i>Trichosporon</i> sp.	C		✓		✓	✓
<i>Rhodotorula rubra</i>	C	✓			✓	✓
Parasites						
<i>Strongyloides</i>	I	✓	✓			
Viruses						
Hepatitis B	I	✓	✓			
After guidelines						
Gram-negative bacilli						
<i>P. aeruginosa</i>	I	✓	✓		✓	
Mycobacteria						
<i>M. tuberculosis</i>	I	✓	✓		✓	✓
Atypical mycobacteria	C				✓	
Viruses						
Hepatitis C	I	✓	✓			✓

Bacteria

Transmission of Gram-negative bacteria, especially *Salmonella* sp. and *Pseudomonas aeruginosa*, has been reported following gastrointestinal endoscopy (Table 28.1). Nine publications cited endoscopic transmission of salmonella in 84 patients [14]. All these infections predate the institution of standardized guidelines for endoscope reprocessing, and typically involved inadequate LCS. One report concluded that there was a “lack of scrupulous cleaning of equipment prior to soaking” [28]. Use of a recommended high-level disinfectant, with thorough mechanical cleaning prior to high-level disinfection, would have prevented all of these cases.

There have been 45 reported cases of endoscopic transmission of *Pseudomonas*, mostly in association with endoscopic retrograde cholangiopancreatography [14,29,30]. Infection with this organism generally occurs as a consequence of contamination of the water source (either an inadequately disinfected water bottle feeding the endoscope or contamination of an automated repro-

cessing machine). Use of an inadequate disinfectant (benzalkonium bromide and alcohol), as well as a breach in accepted cleaning and disinfection procedures, have also been reported [14,29]. Sterile or filtered water should be used in the water bottle feeding the endoscope; this water bottle should be cleaned and dried between uses [30].

Transmission of *Staphylococcus* [29], *Enterobacter* [31], and *Helicobacter pylori* [32] have also been reported. However, in each instance mechanical cleaning, disinfection, or storage techniques were found to have been inadequate. *Helicobacter pylori* has been isolated from used endoscopes and biopsy forceps [33]. Studies have reaffirmed that procedures following published reprocessing guidelines effectively eliminate bacteria and other microorganisms from endoscopes [34].

Although bacterial spores are the most resistant to liquid chemical germicides, there have been no well-documented cases of endoscopic transmission of infections with these organisms [6]. Studies have shown that *Clostridium difficile* spores can be completely inactivated by standard reprocessing techniques [35].

Mycobacteria

Mycobacteria also are difficult organisms to eradicate with chemical sterilants or disinfectants (the most difficult besides bacterial spores), but there have been no reported cases of mycobacterial transmission by gastrointestinal endoscopy. Glutaraldehyde, hydrogen peroxide, *o*-phthalaldehyde, and peracetic acid have all been demonstrated to adequately eradicate mycobacteria, both *Mycobacterium tuberculosis* and the atypical mycobacteria [9,36,37]. Mycobacteria have been detected in tap-water samples, which raises the specter of possible transmission of the agent if filtered or sterile water is not used for rinsing the endoscope following high-level disinfection [38].

Fungi, protozoa, and parasites

There have been no reported cases of transmission of fungi following gastrointestinal endoscopy, although contamination of an endoscope with *Trichosporon beigelii* has been documented [39]. One report exists of *Strongyloides* sp. esophagitis related to cross-infection from a single endoscope [40]. There have been reports of difficulties in inactivation of *Cryptosporidium parvum* oocysts [41,42]. However, such reports demonstrated marked diminution of *Cryptosporidium* oocyst infectivity when endoscopes were reprocessed using accepted protocols and air-dried for 90 min after reprocessing [41].

Prions

Concern has been raised over possible endoscopic transmission of prions and other transmissible spongiform encephalopathies (TSE), including Creutzfeldt–Jakob disease, kuru, and bovine spongiform encephalopathy [43]. There have been no reported cases of transmission of these agents by endoscopy. The World Health Organization recommends that decontamination of medical instruments should be guided by the infectivity level of the tissue contaminating the instrument. Prions infect central nervous system tissue. Saliva, gingival tissue, intestinal tissue, and blood are regarded as having no detectable infectivity and therefore, for the purposes of gastrointestinal endoscopy, are classified as noninfectious [44]. A draft statement on TSE and endoscopes from the US Centers for Disease Control concluded that current guidelines for cleaning and disinfection of instruments need not be changed [6,45].

Steps in endoscope reprocessing

Four steps have been described for the effective reprocessing of gastrointestinal endoscopes:

1 manual cleaning;

2 high-level disinfection;

3 rinsing;

4 air-drying/appropriate storage.

Effective reprocessing of gastrointestinal endoscopes is achievable through strict adherence to published guidelines. These standards include those published by the SGNA, ASTM, and APIC in the year 2000 and the ASGE in 1999 [3,5–7]. When transmission of infection via inadequately reprocessed endoscopes has occurred, it has been due to:

- inadequate manual cleaning;
- inadequate disinfectant or germicidal concentration;
- use of a final rinse with tap water or without adequate drying;
- poor compliance with reprocessing recommendations.

When reviewed critically, most cases of transmission of infection by gastrointestinal endoscopy have resulted from a failure or breakdown in the manual cleaning of the endoscope.

Mechanical cleaning

The initial step in endoscopic disinfection, mechanical cleaning, is the most critical [46]. Mechanical cleaning leads to removal of a significant amount of organisms, feces, and foreign material from the endoscope. It is completed immediately after withdrawal of the endoscope from the patient and is usually done with water, brushing and/or enzymatic detergents. Washing the exterior of the endoscope and washing/brushing the interior channels and valves prevents build-up of organic debris and decreases the bioburden (degree of microbial contamination) in gastrointestinal endoscopes by four orders of magnitude or 99.9% [34,46–49].

The critical nature of the manual cleaning step is widely acknowledged in all published guidelines. Indeed, the importance of manual cleaning cannot be overemphasized. Without adequate manual cleaning, retained biofilm on the surface or in the channel of the endoscope can prevent further adequate disinfection, regardless of the method employed [46]. All subsequent steps in the reprocessing of an endoscope first require meticulous cleaning of the internal and external surfaces. Disturbingly, a survey by Cheung and colleagues in 1999 [50] reported that 9.3% of reporting centers failed to brush the accessory or suction channel, brush the valves, or suction cleaning solution through the endoscope. Worse still, these results were largely unchanged from a similar survey done in 1995 [51].

Choice of disinfectant

LCSs used as high-level disinfectants have been approved by the Food and Drug Administration (FDA)

Table 28.2 Liquid chemical sterilants used for high-level disinfection in reprocessing of gastrointestinal endoscopes. (Modified from Rutula & Weber [11].)

Liquid chemical sterilant	Advantages	Disadvantages
Glutaraldehyde	Relatively inexpensive Compatible with endoscope materials Long history of use	Vapors cause respiratory irritation/sensitization Requires ventilation Can fix debris if inadequate cleaning
Hydrogen peroxide	Effective at room temperature No activation needed No odor	May be incompatible with some materials May cause eye damage if contacted Longer contact time
Peracetic acid	Single use Labeled for "sterilization" Rapidly sporicidal	Relatively expensive May be incompatible with some materials No demonstrated advantage to high-level disinfection
Peracetic acid + hydrogen peroxide	No activation required No odor	May be incompatible with some materials Limited clinical experience
<i>o</i> -Phthalaldehyde	Rapidly tuberculocidal No odor No activation Effective at room temperature	May require ventilation due to odors May cause staining of clothes Limited clinical experience

(Table 28.2) [11]. Such LCSs may be used in both manual and automated reprocessing techniques. Glutaraldehyde ($\geq 2.4\%$ concentration) remains the most commonly used LCS. Other commonly used LCSs include hydrogen peroxide 7.5%, peracetic acid 0.2%, *o*-phthalaldehyde 0.55%, and peracetic acid 0.08%/hydrogen peroxide 1.0% [11,52]. Previously used disinfecting solutions such as hypochlorite solutions, alcohol, quarternary ammonium compounds, phenolics, and iodophors may not be efficacious; their use is discouraged.

Use of *o*-phthalaldehyde has been increasing because it has several potential advantages over glutaraldehyde, including that it is odorless, nonirritating to the eyes, requires no activation or mixing, and has a 12-min high-level disinfection claim [11]. Hydrogen peroxide 7.5% and peracetic acid 0.08%/hydrogen peroxide 1%, while both FDA cleared as high-level disinfectants, have been linked to cosmetic and functional damage to the endoscope, and some endoscope manufacturers have reported that their instruments are incompatible with these products [11].

Peracetic acid is used as part of an FDA-cleared liquid chemical sterilization processor for medical devices. The liquid sterilant, 35% peracetic acid, is diluted and mixed in the processor to its final concentration of 0.2% peracetic acid with a neutral pH; it is sporicidal at 50 °C. At this concentration and temperature, it is rapidly active against all microorganisms including bacterial spores, and is effective in the presence of organic matter [52]. This LCS is available for use in conjunction with the automated Steris System 1. Studies have shown similar clinical outcomes for medical devices reprocessed using the peracetic acid reprocessor compared with those

treated by 2% glutaraldehyde high-level disinfection [53]. However, use of the peracetic acid reprocessor has been associated with markedly increased costs per reprocessing cycle and an increased rate of endoscope repairs compared with high-level disinfection [53].

Disinfection

High-level disinfection is the current standard for reprocessing of endoscopes. This may be achieved by automated reprocessors or manual reprocessing. High-level disinfection requires complete immersion of the endoscope in the disinfecting solution under specified conditions. The use of endoscopes that cannot be fully immersed is unacceptable.

Many standards recommend that after an endoscope has been mechanically cleaned, high-level disinfection may be achieved by immersion in 2.4% glutaraldehyde for at least 20 min at 20 °C [54]. This is in conflict with the product labeling. In 1993, the FDA assumed jurisdiction over the regulation of clinical germicides, and at that time required manufacturers of 2.4% glutaraldehyde (as part of the 510[k] clearance process for medical devices) to label their product recommending 45 min of exposure to glutaraldehyde at 25 °C. This recommendation was based on the length of time and temperature needed for glutaraldehyde to kill 100% of *M. tuberculosis* without any manual precleaning [55]. Recognizing the crucial role of mechanical cleaning, subsequent guidelines have suggested that once recommended precleaning has been done, 20 min of glutaraldehyde immersion at room temperature is sufficient to achieve high-level disinfection. Current ASGE/SGNA/ASTM/APIC guidelines reflect

this thinking. Glutaraldehyde is currently used in 67% of units at 2.4% concentration; 3.4% glutaraldehyde is used in another 13% of units. Currently, 84% of reporting centers use a “20-min soak time,” while only 24% of centers heat their glutaraldehyde solution [56].

Potency testing is critical to the successful use of liquid chemical germicides. Standards for infection control mandate that when liquid chemical germicides are used, their concentration is monitored regularly. As LCSs are reused, dilution occurs that can decrease their microbicidal activity. Product-specific test strips should be used to monitor that solutions remain above their minimum effective concentration. Unfortunately, in a 1999 survey, 16% of sites did not perform potency testing at all [50].

Automated endoscope reprocessors

Many endoscopy units now use automated endoscope reprocessors as part of their disinfection procedure. These devices are not “washing machines”; the use of an automated endoscope reprocessor does not eliminate the need for manual cleaning [56,57]. Despite the popularity of automated reprocessors, studies have not shown a clear advantage for them over manual high-level disinfection [58]. Automated reprocessors offer potential advantages such as decreased exposure of personnel to liquid chemical germicides, standardization of the disinfection process, and a reduction in manual labor for the staff. Disadvantages include higher cost, inability to disinfect narrow channels (elevator in duodenoscopes), and possibly increased reprocessing time [59]. There has been a significant increase in the use of automated reprocessors when comparing 1999 to 1995 (69.9% vs. 41.5%) [55]. Of note, one-third of respondents reported problems with automated reprocessors, including breakdowns, leaks, and damage to endoscopes [55].

Rinsing

Rinsing the endoscope thoroughly after reprocessing with an LCS is critical to prevent residual germicide from contacting the gastrointestinal mucosa of subsequent patients. The channels and the endoscope’s external surface should be rinsed with copious amounts of water [7]. Glutaraldehyde colitis is a well-recognized phenomenon, and may occur rapidly after exposure of a patient to glutaraldehyde [60]. Exposure of the colonic mucosa to hydrogen peroxide leads to a characteristic “snow-white” sign [61]. Recommendations for rinsing suggest that it is done with filtered (through 0.2- μm pores) or sterile water to decrease the risk of microorganisms being reintroduced into the endoscope after high-level disinfection has been completed. Tap

water may contain *Pseudomonas*, mycobacteria, or other microorganisms [62].

Drying/storage

The final step in the reprocessing procedure is forced air-drying (with or without a final 70% isopropyl alcohol rinse to facilitate drying). This step eliminates residual water that may be trapped in the channels of the endoscope, where such standing water might provide a suitable environment for the multiplication of microorganisms. Endoscopes should be stored without coiling (again to prevent possible pooling of residual water) in a well-ventilated closet [7].

Current standards

Guidelines for the reprocessing of endoscopes were first widely published in 1988 [15,16], revised and updated through the 1990s, and again in 2000 [5]. Guidelines are now available from the ASGE, ASTM, SGNA, APIC, Association of Perioperative Nurses, and the BSG [3,5–8]. Gastroenterologists must be aware of these guidelines as well as the current reprocessing protocols in their local practice situation.

Compliance

Strict adherence to published endoscope disinfection guidelines cannot be overemphasized. Adequate staff training, as well as dedicated staff with dedicated “backup,” is critical to the success of any program of endoscope reprocessing. This job must not be relegated to a part-time or temporary worker. Attention to adequate staffing levels in order to provide knowledgeable and trained staff for this task in any individual office or endoscopy suite is crucial. Similarly, care must be taken in the scheduling of trained personnel so as to avoid situations where the only personnel available has limited or no expertise in reprocessing of endoscopes [7].

Proper manual cleaning of the endoscope prior to disinfection must be emphasized. Automated reprocessors are not “washing machines”; they do not perform the manual cleaning. Without the manual-cleaning part of reprocessing, all other steps are rendered ineffective. Testing of glutaraldehyde and other liquid chemical germicides for sustained potency must be done uniformly and regularly. Finally, practitioners must be aware of the specifics of reprocessing in their own situation and correct deficiencies.

Endoscope design

Flexible gastrointestinal endoscopes are complicated instruments by nature of their design. They have chan-

nels and ports that may acquire cracks and nicks over time, as well as movable parts (such as the elevator on a duodenoscope) where debris and possibly microorganisms may become lodged. These areas may be relatively inaccessible to contact with liquid chemical germicides [9].

Endoscopes are heat-sensitive instruments; they cannot be heat-sterilized without destruction of the instrument. Therefore, it is apparent from the design characteristics of heat-labile gastrointestinal endoscopes that sterilization or even high-level disinfection cannot be absolutely guaranteed. Destructive testing of model endoscopes after contamination and then reprocessing would be needed to assess the level of disinfection/sterilization. Thus, while the available evidence suggests that the rate of transmission of infection via gastrointestinal endoscopy is extremely low, one must accept the possibility that under rare circumstances transmission of an infection could occur. Manufacturers have been encouraged to redesign endoscopes to allow disassembly and verification of the cleaning/disinfection process.

Summary

Despite concerns about safety with regard to reprocessing of endoscopes, the reported rate of transmission of infection in gastrointestinal endoscopy is exceedingly low. Reprocessing of endoscopes is effective when published standards are followed. However, *strict* adherence to published guidelines is critical to avoid the transmission of infectious agents, particularly as endoscopic units become busier and the number of procedures increases. Certain points warrant emphasis.

1 Close adherence to thorough manual cleaning of the endoscope *prior* to disinfection is essential. There is no substitute for meticulous cleaning. Automated reproprocessors are not “washing machines”; they do not do the precleaning.

2 Testing for maintained potency of glutaraldehyde or the chosen LCS must be done appropriately and regularly to assure the intended efficacy of the disinfectant. Current guidelines suggest that potency testing be done at least daily, or more frequently as dictated by a high number of endoscopes being reprocessed or as directed by the manufacturer of the germicide.

3 Only well-trained personnel should perform manual cleaning and disinfection. A quality-assurance program to assure consistent procedures and adequate outcomes should be established in all offices and gastrointestinal endoscopic units.

4 Many practitioners remain ignorant of some or all of the details of reprocessing in their local situation. Practitioners are advised to be aware of the specifics of reprocessing in their own office or gastrointestinal unit, and to monitor regularly for updated recommendations.

Further progress in this field will come with modifications of endoscope design that allow the instrument to be more completely disassembled for easy cleaning and disinfection, and with improvements in sterilization technologies appropriate for the materials and design of an endoscope.

Infections are rare in gastrointestinal endoscopy. HCV, HBV, and HIV, as well as bacteria and other microorganisms, are easily eradicated if guidelines are followed. Attention to meticulous cleaning and adherence to established standards are crucial.

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Chapter 29

Insertion Technique

Christopher B. Williams

Introduction

There are numerous ways of managing colonoscopy, determined by local circumstances and endoscopist preferences as well as by the choice of equipment or medication (from no sedation to use of general anesthesia). The account given here covers the general principles involved.

Preprocedure checks

Equipment, accessories, and the functions of the endoscope should be checked before starting. Ensure that insufflation is satisfactory, with vigorous bubbling when the tip is under water. Suboptimal insufflation is difficult to spot once the endoscope is inserted if a connection is loose, the air/water valve misplaced, or the air outlet partially obstructed. The lens must be clean and (for videoscopes) the color corrected by “white balance.”

Patient position

Most endoscopists place the patient in the left lateral position for the whole procedure, although the supine position is common in some countries, especially if anesthesia is used. Changes of position can help when there is technical difficulty.

Inserting into the anus

Start with a digital examination to prelubricate the anal canal and relax the sphincters. Lubricate about 10 cm of the instrument tip and then insert while supporting the bending section with the forefinger and pressing in obliquely (Fig. 29.1). Alternatively, the instrument may be introduced directly end-on while holding the shaft about 10 cm from the end.

Rectum

The initial view of the rectum may be a “red-out” if the lens has pressed against the rectal mucosa. Insufflating and pulling back will reestablish vision. Angulating and rotating the endoscope will help to find the lumen. Aspirate fluid or residue from the rectum at this stage to

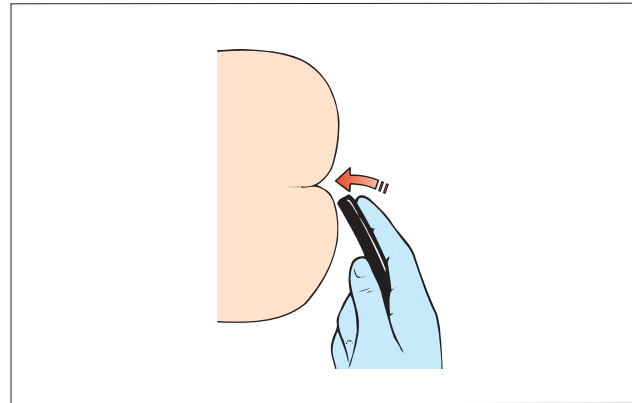


Fig. 29.1 Colonoscope insertion, with finger support of the bending section.

avoid leakage; this is partly to reassure the unседated or lightly sedated patient, since the lubricated shaft, warmed by body heat, gives a distressing illusion of incontinence whenever it is pulled back through the anus.

Pass into the proximal rectum and beyond only when an adequate view has been obtained. Torque-steering is the economic way of steering at this stage, when the shaft is relatively straight, using the thumb to angulate the tip up or down and the right hand for shaft-twist. Corkscrew around the rectal valves of Houston and the haustrations and bends of the sigmoid, alternately twisting clockwise and counterclockwise. This avoids use of the lateral angulation control and makes insertion easy and fluent.

Retroversion can be important. The distal rectum is a potential blind spot that needs careful inspection at some stage of the procedure (usually on withdrawal). The rectal ampulla will usually (but not always) allow tip retroversion. Choose the widest part, angulate both controls fully and push gently inward with a twisting movement to invert the tip toward the anal verge (Fig. 29.2). “Video proctoscopy” involves insertion of a rigid rectoscope that allows passage of a video endoscope to illuminate and view the hemorrhoidal area, with the opportunity to take prints or record on videotape.

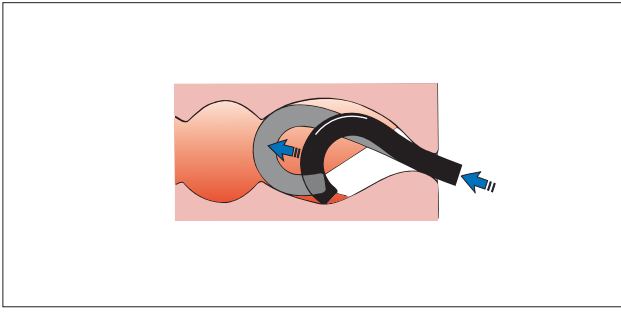


Fig. 29.2 Angulate maximally with both angulation controls, then push in to retrovert in the rectum.

Handling

Single-handed, two-handed, or two-person approach?

The one-person, single-handed approach to colonoscope control is used by most skilled endoscopists (Fig. 29.3), although a few still work successfully with the two-person method, using an assistant to manipulate the shaft, as was the original design intention for (gastro)scope handling.

In true single-handed colonoscopy, the left hand manages the angulation controls alone (Fig. 29.4). Using two fingers (the third and little finger) to grip the control body allows the thumb to rest on the up/down angulation control for immediate responses and leaves the middle finger free to assume a “helper” role to the

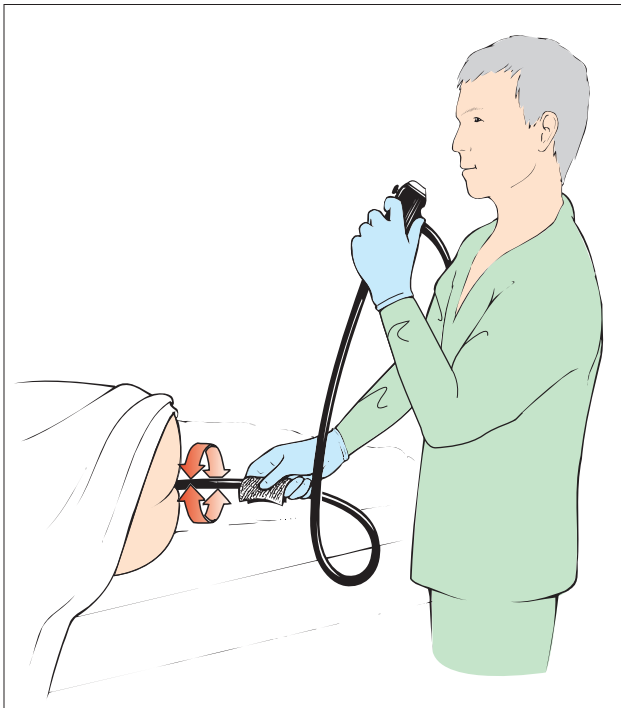


Fig. 29.3 Single-handed colonoscopy.

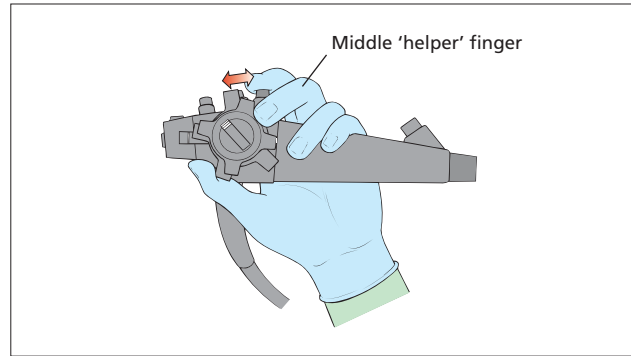


Fig. 29.4 Single-handed control: the forefinger alone activates the air/water and suction valves; the middle finger acts as “helper” to the thumb for angulation.

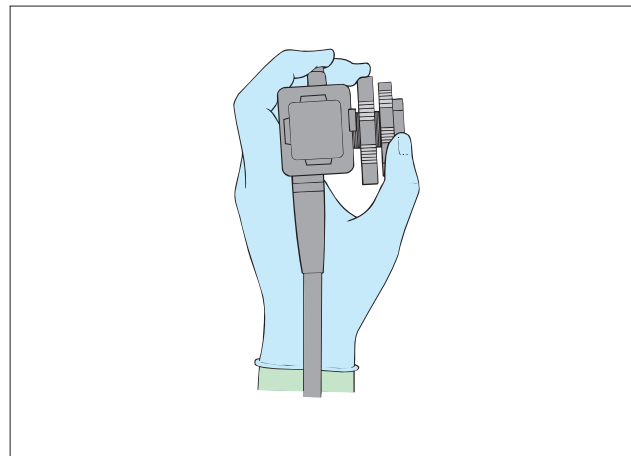


Fig. 29.5 The thumb can reach the lateral angulation control if the hand is correctly positioned.

thumb when needed. It is most efficient if the first finger *alone* operates the air/water or suction valves. For those with reasonably large hands it is practicable for the left thumb to reach both the up/down and the lateral angulation controls (Fig. 29.5). Many with smaller hands use the right hand on the lateral angulation control from time to time, but for a fluent examination this should be avoided except when absolutely necessary.

The right hand holds the shaft 25–30 cm away from the anus, using a towel or gauze for hygiene and friction-grip. This avoids the frequent hand changes and jerky insertion that results from holding it closer to the anus. The right hand also feels whether the shaft moves easily (is straight) or there is resistance (due to looping). The shaft (insertion tube) of a colonoscope is made to be “torque-stable,” meaning that twisting force applied at one end is faithfully transmitted to the other end. Feel and precise torque control are both helped by holding the shaft by the fingers (Fig. 29.6) and not more clumsily in the fist.

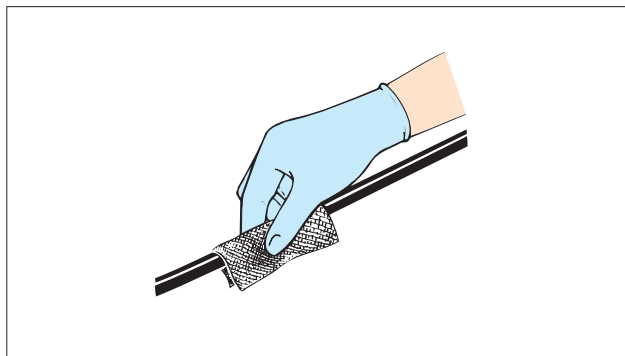


Fig. 29.6 The instrument shaft should, whenever possible, be held delicately between the thumb and fingers.

Two-person colonoscopy, with an assistant controlling the shaft, allows the endoscopist two-handed management of the angulation controls, while the assistant performs the role ascribed to the right hand of the single-handed endoscopist, pushing and pulling according to spoken instructions. Experience has shown that an assistant tends to push excessively, causing unnecessary loops, and rarely torques appropriately. Except with an unusually skilled assistant, two-person colonoscopy tends to be as clumsy as would be expected. However in occasional difficult situations, for instance passing an awkward angulation or snaring a difficult polyp, all endoscopists justifiably use the assistant briefly to control the shaft.

As coordination develops between right and left hands (or between endoscopist and assistant in the two-person technique), colonoscopy, from slow deliberate beginnings, becomes rapid and fluent. Attention to small practical details is part of this process.

Pointers for handling the colonoscope

1 Twisting (torquing) the shaft only affects the tip when the shaft is straight. If a loop is present, twisting only affects the loop. When the shaft is straight,

twist or “torque-steering” of the angulated tip is highly effective.

2 Torque-steering is affected by the direction in which the tip is angulated. With the tip angulated upward, clockwise torque moves the tip to the right, but it moves to the left if angulation is down (Fig. 29.7).

3 Torque-steering involves first angulating up or down, then torquing (twisting, rotating) the shaft clockwise or counterclockwise. This rotation should corkscrew the tip around laterally, precisely and quickly, usually making use of the lateral angulation control unnecessary. Tip angulation is important because rotating a completely straight instrument does not result in position change of the tip.

4 Torque (as a maintained twist) can also be used to control spiral loops, but lateral steering may then have to be done with the angulation controls. It is essential to realize that if torque is being applied to control a loop but is released or reversed in order to steer, the loop will reform again.

5 Coordinate left-hand and right-hand activities: each hand is disciplined to fulfill only its appropriate tasks.

6 Use the lateral angulation control as little as possible. It is the least effective of the available angulating or steering actions (whether by the left thumb or right hand).

7 If maximal up/down angulation has already been applied, lateral angulation adds only a small degree of increased tip deflection. This additional angulation may assist in locating the lumen in a tortuous sigmoid colon. Aggressive application (two-handed) of both angulation controls is rarely helpful (but can damage the angulation wires).

8 A fully angulated tip will not slide through the colon, the “walking-stick handle” phenomenon (Fig. 29.8).

9 If the tip is impacted or fixed by adhesions, it cannot be steered: on attempted angulation the shaft moves instead (Fig. 29.9). This is an unavoidable limitation of flexible endoscopes, apparent in fixed diverticular disease or tight strictures. Torque-steering is less affected in such situations.

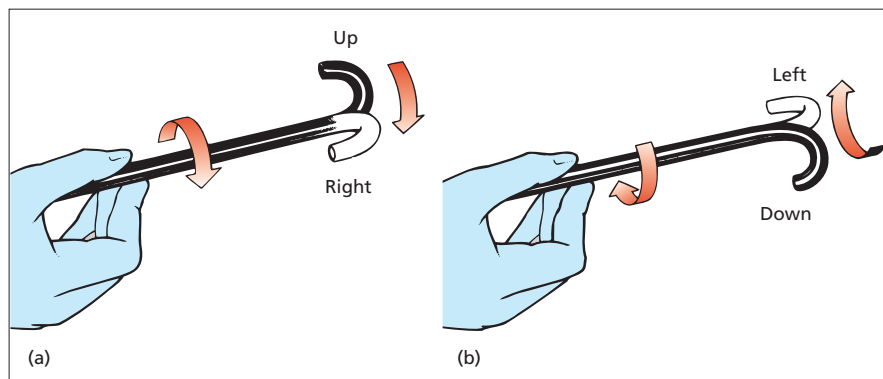


Fig. 29.7 With clockwise shaft twist: (a) an up-angled tip moves to the right; (b) a down-angled tip moves to the left.

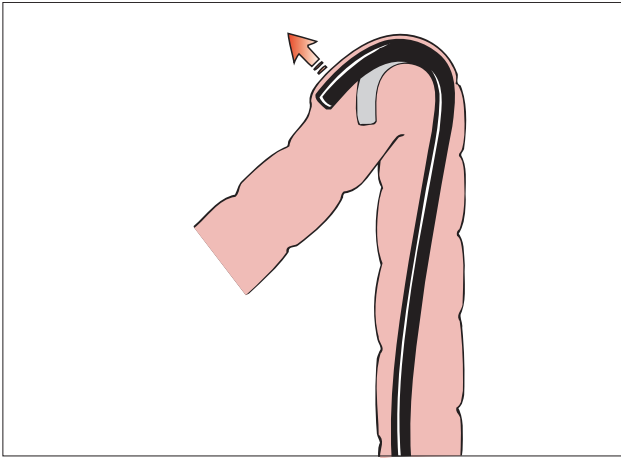


Fig. 29.8 Do not overangulate when pushing around flexures: the “walking-stick handle” effect.

Insertion and steering

Principles

Insertion to the cecum should be as quick as reasonably possible, because the insertion phase is the most uncomfortable and stressful for the patient. However, trying to hurry insertion by using force usually results in looping, leading to a slower, traumatic, or failed insertion. The sigmoid colon is an elastic tube (Fig. 29.10a). When inflated it becomes long and tortuous; deflated it is significantly shorter. When stretched by a colonoscope, especially if overinflated as well, the bowel forms loops and acute bends (Fig. 29.10b). If shortened (by pulling back) and deflated, the colon can be telescoped into a few convoluted centimeters (Fig. 29.10c).

Pointers for insertion and steering of the colonoscope

1 *Insufflate as little as possible.* Gentle insufflation may be

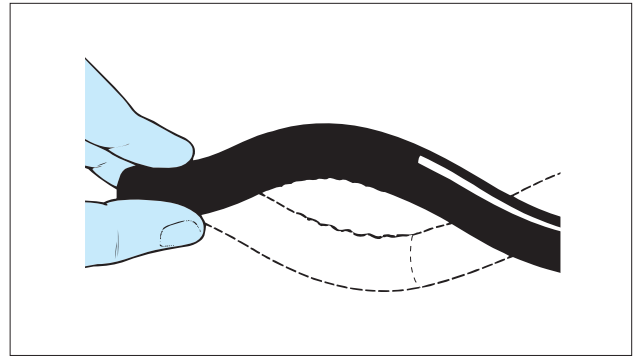


Fig. 29.9 If the tip is fixed, it cannot be steered (the shaft moves instead).

needed throughout the examination in order to maintain vision, but it is counterproductive to overinflate. Bubbles caused by insufflating underwater can be avoided by first angling above the fluid as far as possible. Remember that the colonoscope air outlet is below and to the left of the lens view (and the suction/instrumentation channel below and to the right) (Fig. 29.11). If preparation and residual bile salts result in excessive bubbles, introducing antibubble silicone emulsion will remove them, as during gastroscopy.

2 *Suction air frequently.* A perfect view is not necessary. Whenever fully distended, it takes only a second or two to suction excess air from the colon until it starts to wrinkle and collapse slightly, becoming shorter and easier to manipulate.

3 *Suction fluid infrequently.* Having evacuated fluid from the rectum, only aspirate fluid during the rest of the insertion phase when absolutely necessary to maintain vision. Aspirating each pool of retained fluid wastes time, loses the view, and requires reinflation. It is often quickest to steer over the fluid levels, leaving aspiration of any fluid or residue until withdrawal. When suctioning, orientate accurately above the surface of the fluid so

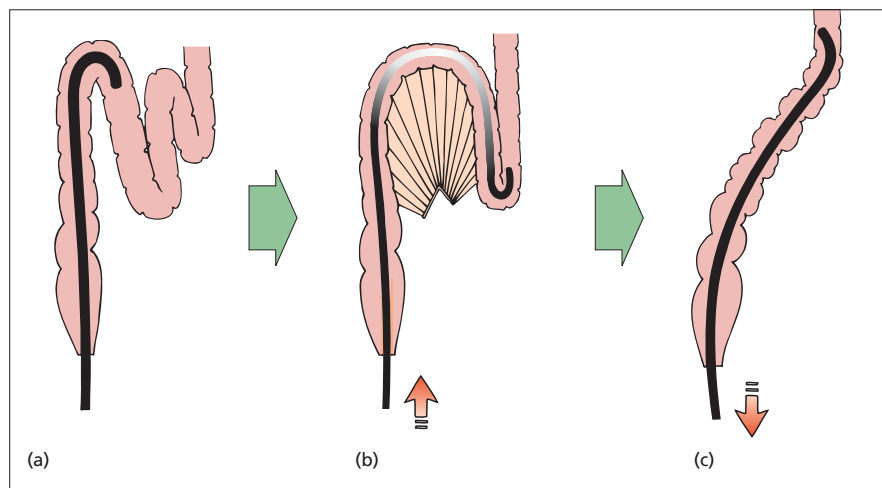


Fig. 29.10 (a) The sigmoid colon is an elastic tube: (b) pushing causes loops, but (c) pulling back shortens and straightens the colon.

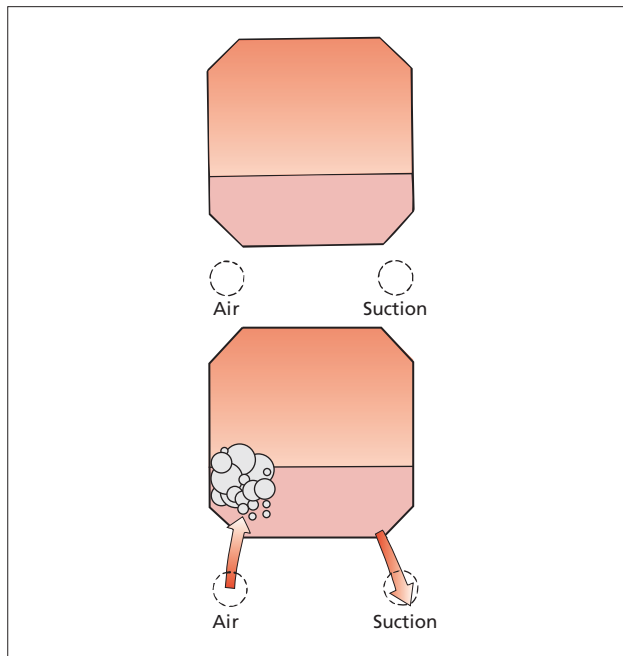


Fig. 29.11 The colonoscope air outlet is at bottom left of the view and suction channel opening at bottom right: orientate correctly before use.

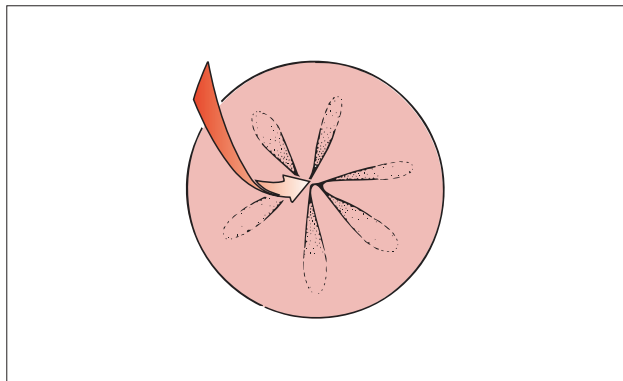


Fig. 29.12 Aim at the convergence of folds.

that the channel dips in precisely (Fig. 29.11), which avoids time-wasting air evacuation or mucosal suction “blebs.”

4 Use all visual clues. The direction of the colonic lumen should be ascertained *before* pushing in. The lumen when deflated or in spasm is at the center of converging folds (Fig. 29.12). Aim toward the darkest area, worst illuminated because it is furthest from the instrument and nearest the lumen (Fig. 29.13). Lumen direction is at the center of any convex arcs, formed by visible wrinkling of the circular muscles, haustral folds, or the highlights reflected from the mucosa over them. The slight inward bulge of one of the underlying longitudinal muscle bundles (teniae coli) is another, occasionally useful, clue (Fig. 29.14).

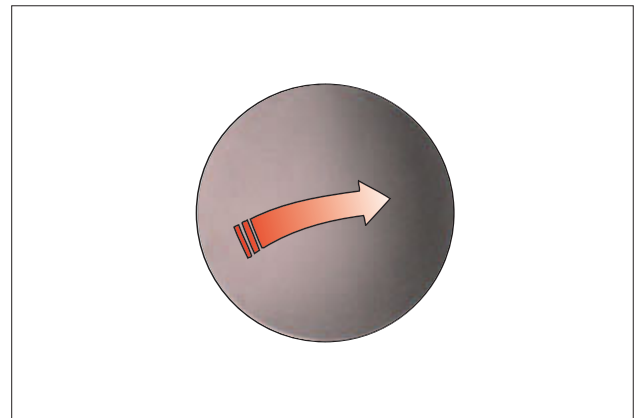


Fig. 29.13 Aim at the darkest area.

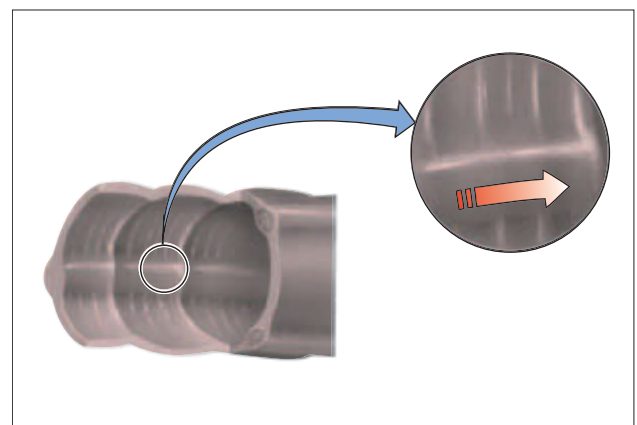


Fig. 29.14 Aim at the center of the arc formed by folds, muscle fibers, or reflected highlights.

5 Steering direction is predictable from the view. Because endoscopes are made torque-stable, angulating “up” always moves the tip toward the top of the monitor view (and similarly for other directions). Seen in close-up, however, the surface will appear to move in the opposite direction; thus to angulate successfully “up” the surface vessel pattern must move down.

6 Steer slowly and exactly (rather than jerkily and erratically). A rapid steering movement in the wrong direction can simply lose the view altogether, quite unnecessarily. Each individual movement should be slow and purposive.

7 Consider the proper steering actions before engaging the colonoscope in an acutely angled portion of the colon. Colonic bends can be acute and it is easy to become unsighted when angling around them.

8 “Prepare” bends so that steering around them is easier. An acute bend is most easily passed if its axis is upward or downward (for easy thumb steering). Optimize mechanical efficiency by having the colonoscope shaft straight (for better push) and the bending section not overangled (to help it slide around).

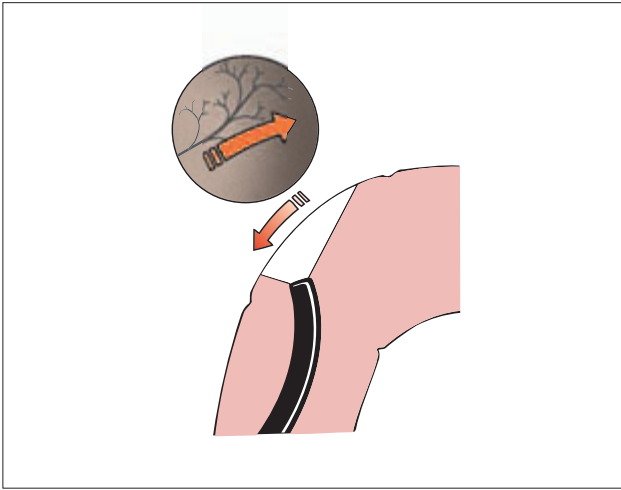


Fig. 29.15 Pull back when lost: the mucosa slides away in the direction of the lumen.

9 *If there is no view, pull back at once.* If lost for even a few seconds, keep the angulation controls still or let go of them, insufflate and gently withdraw the instrument. The mucosa will then slip slowly past the lens in a proximal direction (Fig. 29.15). Follow the direction of this slippage by angulating the controls or twisting the shaft and the lumen of the colon will come back into view. Pushing blindly, especially if there is a “red-out” and total loss of view, is usually a pointless waste of time and potentially a cause of perforation.

10 *Position change* may help if the view is poor, especially when there is excess fluid. Let gravity reposition fluid and gas (and the colon also, often beneficially).

11 *Keep the colonoscope as straight as possible* in order to transmit inward shaft push to the tip.

Sigmoid colon

Endoscopic anatomy

The sigmoid colon is 40–70 cm long when stretched but will crumple to 30–35 cm once the instrument is straightened. This crumpling is why inspection is also important during insertion, because small lesions can be missed during the withdrawal phase. The sigmoid mesentery is very variable in length and may be affected by adhesions from previous inflammatory disease or surgery. After hysterectomy the sigmoid tends to be angulated and fixed into the area previously occupied by the uterus.

Colonoscope insertion may stretch the bowel to the limits of its attachments or the confines of the abdominal cavity (larger loops can occur in a protuberant belly). The shape of the pelvis, with its curved sacral hollow and forward-projecting sacral promontory, causes the

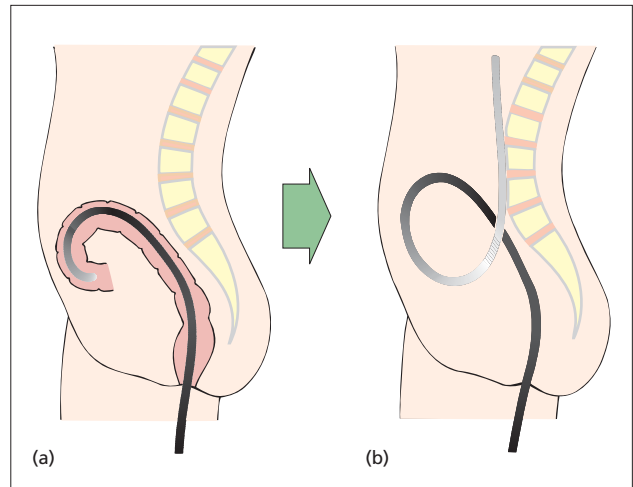


Fig. 29.16 The sigmoid colon loops anteriorly (a) and then passes up into the left paravertebral gutter (b).

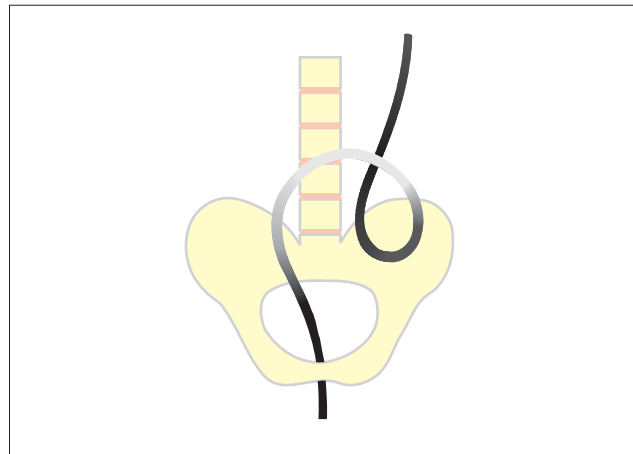


Fig. 29.17 Sigmoid loop: anterior view (clockwise spiral).

colonoscope to pass anteriorly (Fig. 29.16a). The shaft often loops near the anterior abdominal wall before it passes posteriorly to the descending colon (Fig. 29.16b). The resulting anteroposterior loop usually (80%) forms a clockwise spiral loop (Fig. 29.17). When a sigmoid colonoscope loop runs anteriorly against the abdominal wall, it may be possible to affect it by hand pressure (Fig. 29.18).

The descending colon is normally fixed retroperitoneally in the left paravertebral gutter. Ideally, the descending colon runs straight to the splenic flexure, but colonoscope stretch usually creates an acute bend at the junction with the sigmoid colon. A particularly acute “hairpin bend” results when the sigmoid is long enough to make a large upward loop (Fig. 29.19).

Mesenteric variations and mobility, occurring in at least 15% of subjects, can result in varying degrees

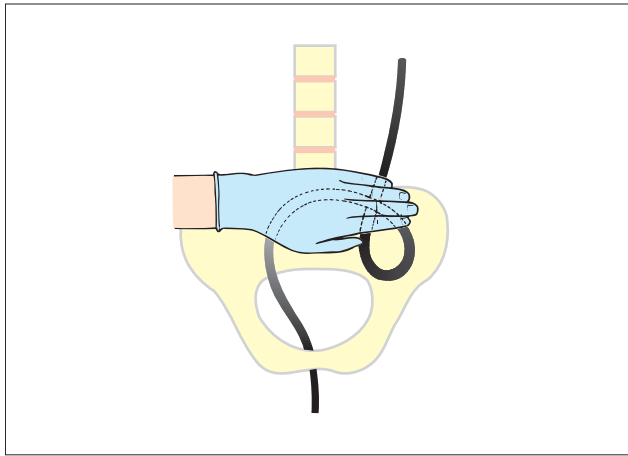


Fig. 29.18 Hand pressure may restrict looping of the sigmoid.

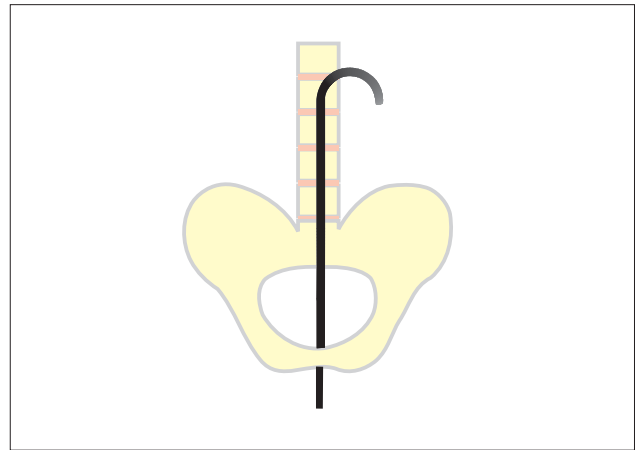


Fig. 29.20 The endoscope may push a fully mobile distal colon up the midline.



Fig. 29.19 Acute (iatrogenic) hairpin bend at the sigmoid–descending junction.

of descending mesocolon displacement rather than the usual retroperitoneal fixation. For instance, the descending colon can run up the midline (Fig. 29.20) or allow atypical (counterclockwise spiral) “reversed alpha” looping.

Avoiding or minimizing sigmoid loops

Sigmoid looping of some degree is unavoidable as the colonoscope pushes inward. It helps to warn the patient that “stretch pain” or “wind pain” may be felt during this brief (20–30 s) push around the apex of the sigmoid loop.

Hand pressure on the abdomen may help modestly during sigmoid insertion, opposing any spiral loop that passes anteriorly, close to the abdominal wall. The assistant compresses nonspecifically over the lower abdomen, hoping to buffer the sigmoid loop, which often reduces stretch pain and helps the colonoscope slide around more easily (because the loop is smaller). Assistant hand

pressure is only relevant during the 20–30 s of inward push. More prolonged muscular effort is pointless, especially as in around 50% of patients the sigmoid loop is nowhere near the abdominal surface.

It helps to push little and slowly, and pull often and fast. The challenge is to progress the instrument tip through the sigmoid without repeatedly losing the view, and to minimize colon and colonoscope looping as far as possible. Pushing movements should therefore start slowly and gently, giving time for accurate torque-steering and allowing the colonoscope to slide in (rather than just buckle upward toward the diaphragm, as tends to happen with a rapid push). In contrast, pull-back movements must be frequent and vigorous in order to straighten out loops effectively.

Navigating through the sigmoid

Torque-steering single-handedly is an efficient way of passing the multiple bends of the sigmoid, whereas coordination with an assistant can be difficult. Each of the succession of serpentine bends requires a conscious steering decision. Consider the best combination of angling and rotation to steer correctly into the axis of the bend and perform the combination of advance, torque, and tip deflection as the tip engages the angulated bowel (Fig. 29.21). This ensures the tip will subsequently slide around with minimal push pressure even though close to the surface and occasionally relatively blind but always in the predetermined direction of the lumen. Using torque-steering, most of the sigmoid can be traversed with little or no use of the lateral angulation control, the angled tip corkscrewing by twisting the shaft first one way and then the other round the succession of bends.

Acute and mobile bends are a particular problem in the sigmoid. Having angled around an acute bend, if

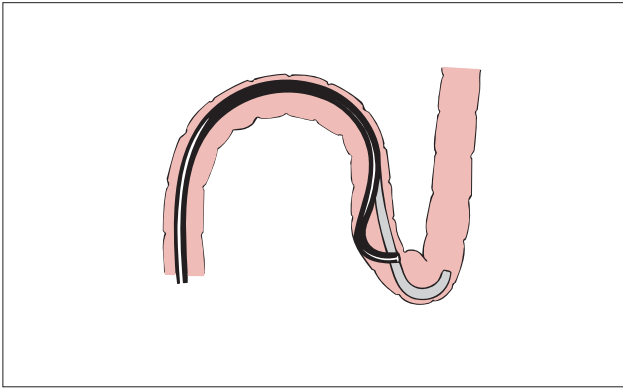


Fig. 29.21 Pre-steer before pushing into an acute bend.

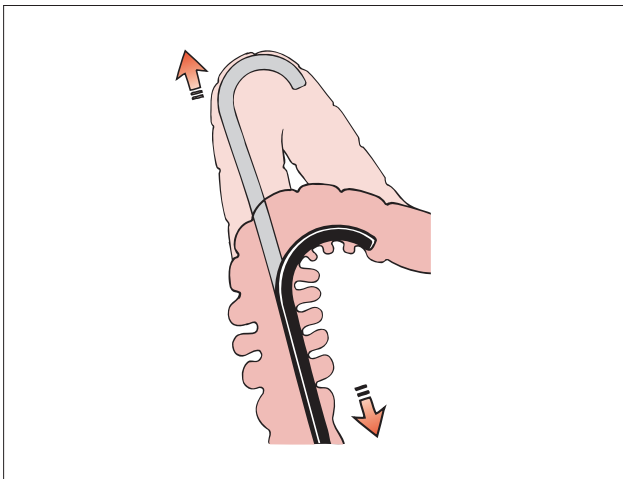


Fig. 29.22 Pulling back flattens out an acute bend and improves the view.

the view is poor, gently pull back the angled/hooked tip, which should simultaneously reduce the angle, shorten the bowel distally, straighten it proximally, and disimpact the tip to improve the view (Fig. 29.22). Maneuvering around a bend may cause a mobile colon to swing around on its attachments, seen in close-up as a rotation of the visible vessel pattern, indicating which direction to follow (Fig. 29.23).

Sigmoid loops

Pushing through a long sigmoid and into and up the descending colon is occasionally easy and may prove to be the best option (Fig. 29.24) (see also section on alpha loop). However, pushing through any loop is unacceptable if force is required or pain results. Pain indicates potential for damage to the bowel or mesentery. Similarly, pushing blindly around any bend should be limited to a few centimeters and only if “slide-by” of the mucosal vascular pattern view continues smoothly and only toward the predetermined direction of the lumen.

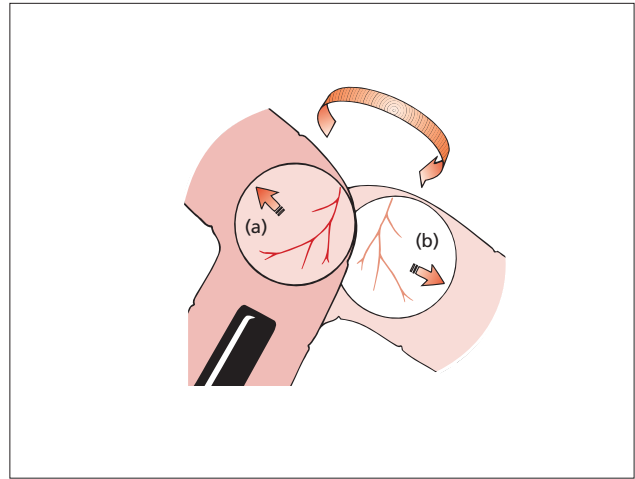


Fig. 29.23 Rotation of vessel pattern (from a to b) indicates rotation of the colon, so the endoscopist needs to change steering direction correspondingly.

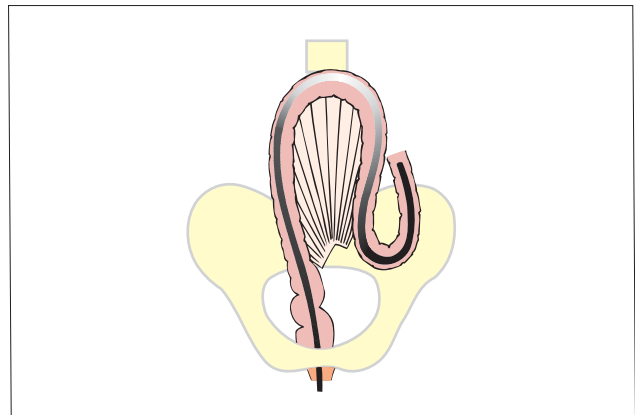


Fig. 29.24 A very long sigmoid may allow the scope to push through without a hairpin bend.

Stop if the mucosa blanches (indicating excessive local pressure) or the patient experiences pain (indicating undue stress on the bowel or mesentery); perforation is a possibility if excessive or unrelenting force is used. Patients with short sigmoid loops tend to experience more pain, since their shorter mesenteric attachments are more aggressively stretched. Long colons, with longer mesenteries, simply stretch upward and adapt to let the colonoscope pass relatively easily into the descending colon without an acute hairpin bend (Fig. 29.24). Inward push should be applied gradually, avoiding sudden shoves and limited to a tolerable duration, no more than 20–30 s. The “wind pain” of loop stretch stops immediately when the instrument is withdrawn slightly.

“N” or spiral sigmoid looping

Looping of the sigmoid into the so-called N-loop (Fig. 29.25) occurs in a wide variety of presentations,

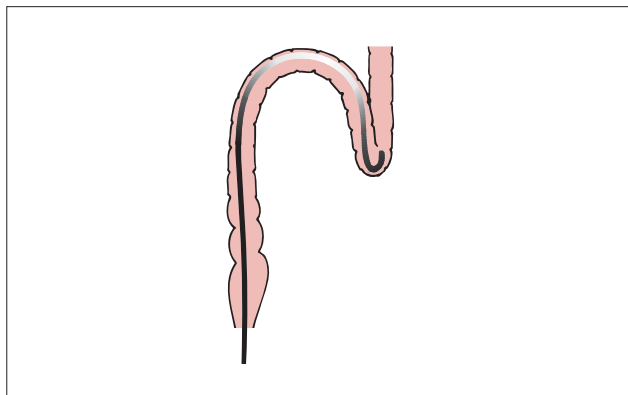


Fig. 29.25 Spiral N-loop in the sigmoid.

ranging from a minor upward deviation (Fig. 29.25) to a huge loop reaching to the diaphragm. The three-dimensional imaging system (see Chapter 24) shows exactly what is happening. Some (10%) sigmoid loops are flat but most have a three-dimensional spiral component. Clockwise spiral loops predominate, whether the N type (80%) or the longer alpha type (10%).

Removal of the sigmoid loop is essential. Most of the pain or difficulty experienced while passing the proximal colon (splenic flexure, transverse colon, and hepatic flexure) stems from recurrent or persistent N-looping in the sigmoid. It is for this reason that, both initially and when inserting through the proximal colon, repeated “pull-back” straightening of the sigmoid colon is so important. With a longer colon, complete removal of

the N-loop may be difficult until the instrument tip has reached well up the descending and nearly to (or around) the splenic flexure, giving adequate purchase for vigorous withdrawal.

Sigmoid spiral loop straightening involves a degree of vigorous shaft torque (usually clockwise) as the loop is pulled straight (Fig. 29.26). The feel of the shaft should indicate whether torque is being applied in the correct direction to straighten the spiral; twist in the wrong direction worsens the loop, so worsening the feel of shaft and controls (Fig. 29.27).

Alpha loop and maneuver

An alpha loop is a blessing, since its shape (Fig. 29.28) means that there is no acute bend between the sigmoid and descending colon, and the splenic flexure can be reached rapidly and relatively painlessly. If the instrument appears to be inserting a long way through the sigmoid without problems or acute angulations, an alpha loop may have formed. If so (especially if confirmed on fluoroscopy or the three-dimensional magnetic imager) carry on pushing to the proximal descending colon or splenic flexure at 90 cm (sometimes even around the splenic flexure into the transverse colon) before trying any withdrawal/straightening maneuver. Even though the patient has mild stretch pain or the view in the descending colon is poor because of fluid, push on inwards (Fig. 29.29). Applying normal sigmoid straightening maneuvers halfway round an alpha loop is a potential mistake, since this may lose the beneficial alpha shape and convert it to an N-loop configuration with a hairpin

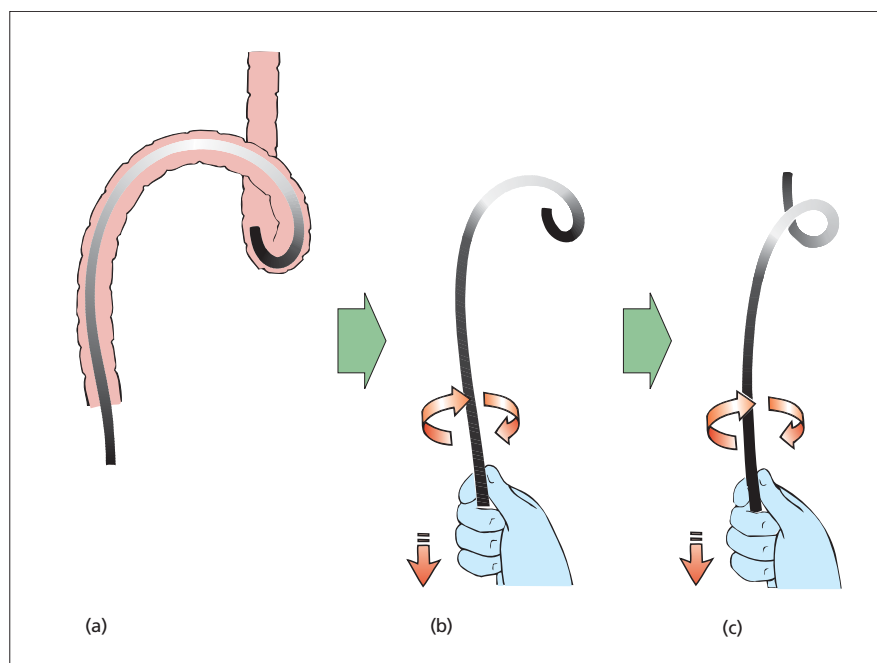


Fig. 29.26 (a) An N-loop with the tip at the sigmoid–descending junction: (b) twist clockwise and withdraw; (c) keep twisting and find the lumen of the descending colon.

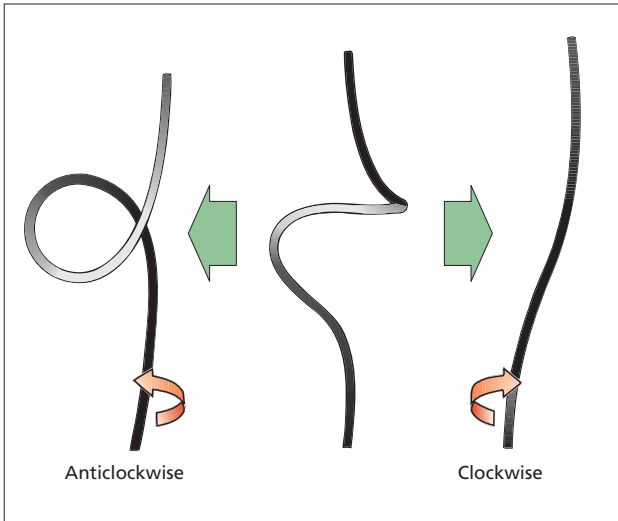


Fig. 29.27 A clockwise spiral is straightened by clockwise twist. A counterclockwise twist worsens it.

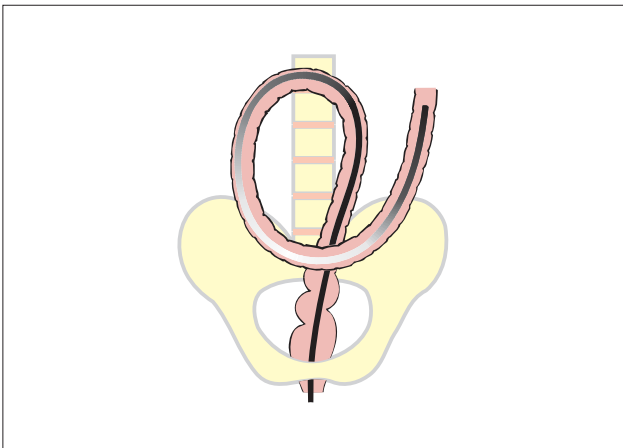


Fig. 29.28 An alpha loop.

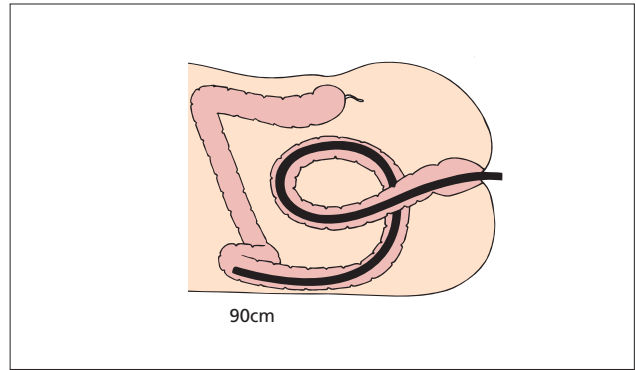


Fig. 29.29 In an alpha loop, the colonoscope runs through the fluid-filled descending colon to the splenic flexure at 90 cm.

bend, which causes much greater difficulty in reaching the descending colon.

The *alpha maneuver* describes the intentional formation of an alpha loop, first performed in the 1970s using fluoroscopy but now likely to return to favor with the introduction of three-dimensional magnetic imaging. The principle of the alpha maneuver is to twist the sigmoid colon around into the partial volvulus of an alpha loop (Fig. 29.30). Using the three-dimensional imager the screen view allows the endoscopist either (i) to realize that an alpha loop is forming, thus warning against pulling back and risk losing the beneficial configuration, or (ii) to maneuver further to encourage the alpha shape when passing a generous-sized sigmoid. However, it is not always possible to maneuver successfully into an alpha loop, probably due to adhesions or quirks of mesenteric mobility.

Straightening an alpha loop

Alpha loop straightening is performed by combined withdrawal and strong clockwise derotation. Withdrawing

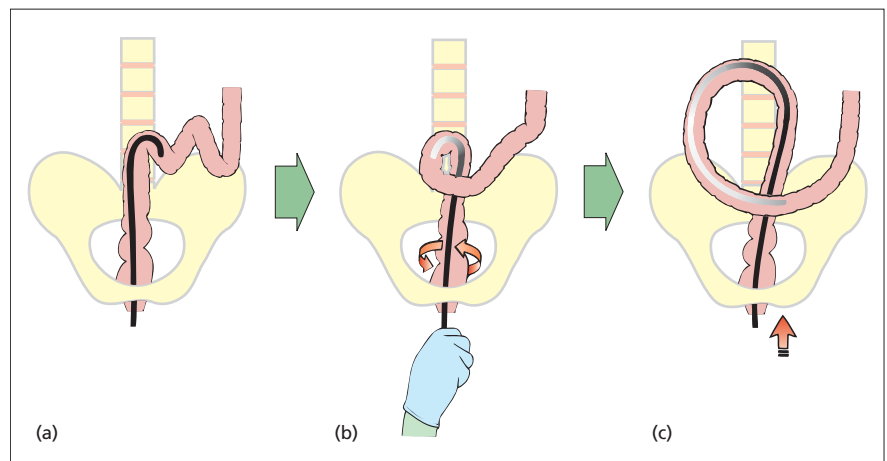


Fig. 29.30 (a) Alpha maneuver (with three-dimensional imager): manipulate the sigmoid by (b) rotating the loop counterclockwise to pass toward the cecum, then (c) down into an alpha and easily on up into the descending colon.

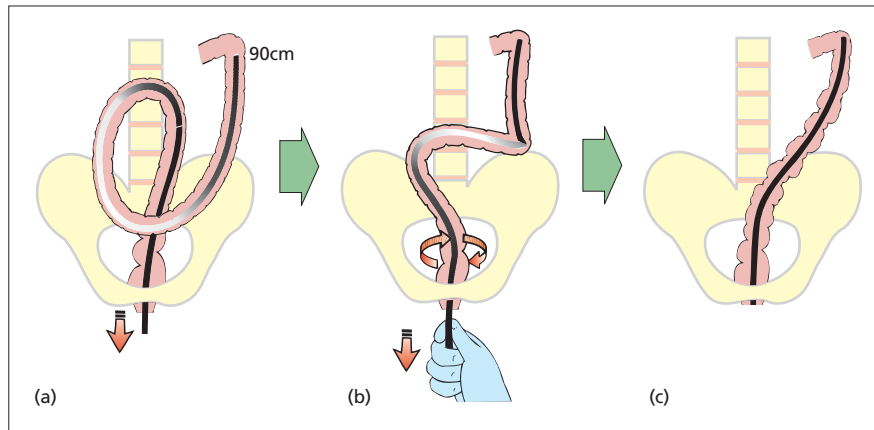


Fig. 29.31 To remove an alpha loop (a), pull back and twist clockwise (b) to straighten completely (c).

the shaft initially reduces the size of the loop, which makes derotation easier (Fig. 29.31). Most colonoscopists prefer to straighten the alpha loop as soon as the upper descending colon is safely reached (at 90 cm) and then to pass the splenic flexure with a straightened instrument. Occasionally it is better to pass into the proximal transverse colon with the alpha loop in position before straightening. If straightening the loop proves difficult or the patient has more than the slightest discomfort, the situation should be reassessed. Adhesions can make derotation difficult and occasionally impossible. *Do not use force*. The sigmoid loop may not be a true alpha loop but a reversed alpha (see below), which needs counterclockwise derotation.

Atypical sigmoid loops and the reversed alpha

Atypical spiral loops can form when the colon attachments are unusually mobile, particularly when the descending colon is not fixed. Normally, retroperitoneal fixation of the descending colon forces the advancing colonoscope shaft into its characteristic clockwise spiral as it traverses the sigmoid colon. However, a fully mobile colon can permit the colonoscope to assume a counterclockwise spiral or even a complex mix of clockwise and counterclockwise loops. Although a counterclockwise reversed alpha loop (Fig. 29.32) may allow the colonoscope tip to slide up into the descending colon nearly as easily as a conventional alpha loop, with no obvious clue that there is anything odd or unusual, in order to withdraw and straighten it, counterclockwise twist is required. Since almost 90% of sigmoid loops spiral clockwise, the unsuspecting endoscopist can waste time and make things worse by trying to derotate an atypical loop in the wrong direction.

Instrument shaft loops external to the patient

Rotating the colonoscope in the process of straightening one or more sigmoid loops and also in making torquing

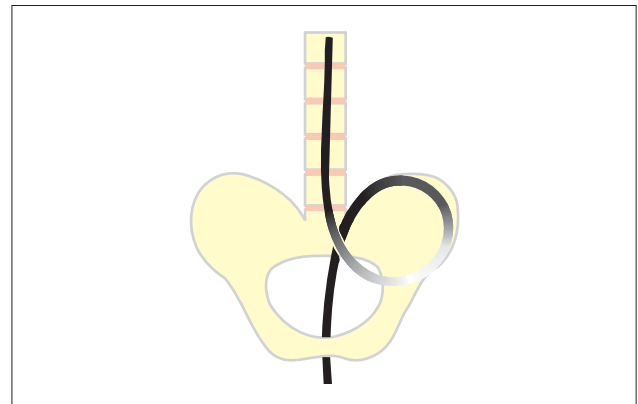


Fig. 29.32 Reversed alpha loop (counterclockwise spiral) is due to a persistent descending mesocolon.

movements may result in a loop forming in the shaft external to the patient. Such a loop makes instrument handling awkward, inhibiting torque-steering and causing unnecessary control-wire friction, and is best removed by rotating the control body to transfer this loop from the shaft to the umbilical (Fig. 29.33). Alternatively, a dexterous endoscopist can, if the instrument is straight, torque the external shaft loop out while steering up the lumen so that the colonoscope rotates on its axis within the colon.

Diverticular disease

In severe diverticular disease, there can be a narrowed lumen, pericolic adhesions, and problems in choosing the correct direction. A close-up view of a diverticulum means that the tip must be at right angles to the lumen and major reorientation is required (Fig. 29.34). The perfectly round shape of a diverticulum contrasts with the narrowed lumen of pronounced diverticular disease, often quite difficult to locate and never circular. Once the instrument has passed through, however, the “splinting” effect of the abnormally muscular diverticular

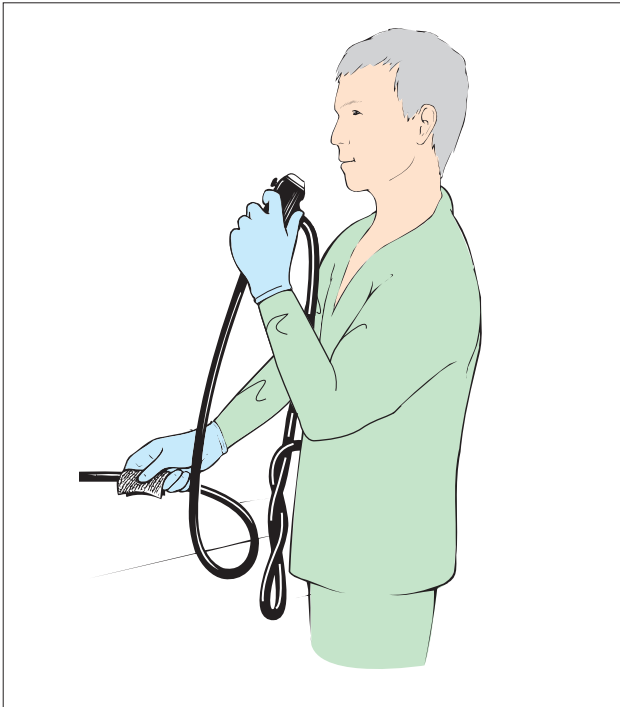


Fig. 29.33 Shaft loops external to the patient can be transferred to the umbilical by rotating the control body.

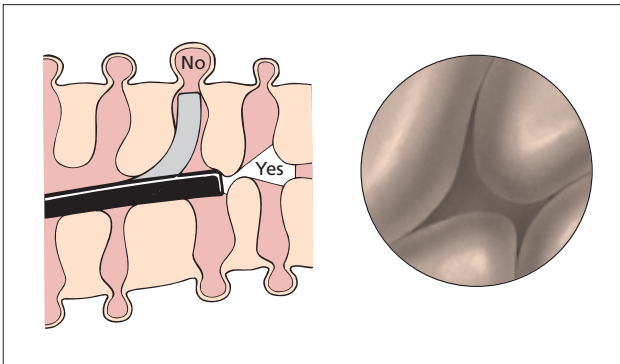


Fig. 29.34 In diverticulosis the lumen is often difficult to locate.

segment usually prevents any sigmoid looping problems for the rest of the examination. The secret in passing significant diverticular disease is extreme patience in visualization and steering, with particular use of withdrawal, rotational, or corkscrewing movements. Using a thinner and more flexible pediatric colonoscope or gastroscope may make an apparently impassable narrow, fixed, or angulated sigmoid colon relatively easy to examine, which sometimes also saves the patient from surgery. Severe angulated sigmoid diverticular disease and a proximal colon that proves to be long and mobile is the ultimate endoscopic nightmare.

“Underwater” colonoscopy, using a 50-mL syringe to instill water, may help passage in some patients with

very hypertrophic musculature and redundant mucosal folds in diverticular disease, in whom it can sometimes be difficult to obtain an adequate air view.

Be prepared to abandon if postoperative or peridiverticular adhesions have fixed the pelvic colon so as to make passage impossible or dangerous. If there is difficulty, the instrument tip feels fixed and cannot be moved by angling (Fig. 29.9) or twisting, and the patient complains of pain during attempts at insertion, there is a danger of perforation or instrument damage.

Sigmoid–descending colon junction

The junction between the sigmoid and descending colon can be so acute as to appear to be a blind ending. In a capacious colon there may be a longitudinal fold pointing toward the correct direction of the lumen, caused by the muscle bulk of a tenia coli (Fig. 29.35); follow the longitudinal fold closely to pass the bend. Inexperienced endoscopists frequently, and even experts occasionally, have trouble in passing into the descending colon. An overaggressive endoscopist will probably have stretched into a large sigmoid (iatrogenic) spiral N-loop (Fig. 29.9) and created unnecessary difficulty. The measures described below will be rewarded by easier passage from sigmoid to descending colon.

Reaching the sigmoid–descending colon junction, usually a retroperitoneally fixed point, gives the endoscopist a chance of obtaining leverage control of the sigmoid loop. Even when the colonoscope tip is just at the start of the junction, it is worthwhile trying a pull-back-and-shortening move.

Clockwise shaft twist tends to be effective at this point because of the clockwise spiral of most sigmoid colons, so a “pull and clockwise twist” is worth trying. With luck this will simultaneously shorten (pleat/accordion) the sigmoid over the colonoscope shaft and also slide the tip forward into the fixed descending colon, without force or pain.



Fig. 29.35 At acute bends, a longitudinal bulge (tenia coli) shows the axis to follow.

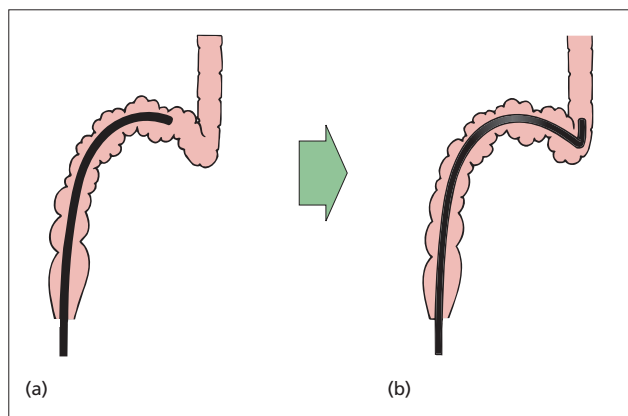


Fig. 29.36 Pull back and deflate to keep the sigmoid short (a), which may allow direct passage to the descending colon (b).

Position change can help if things are going badly or the view is poor. Changing from left lateral to supine has some effect on both colon and fluid; the right lateral position may improve things further still.

Pointers for traversing from the sigmoid to the descending colon

Direct passage to the descending colon is the ideal, trying to wriggle the tip around the junction without forcing up the sigmoid loop. The steps listed below should be followed.

1 Straighten the shaft by withdrawal to reduce the sigmoid loop and create a more favorable angle of approach to the junction (Fig. 29.36).

2 Apply abdominal pressure, the assistant pushing on the left lower abdomen to compress the loop or reduce the abdominal space within which it can form.

3 Deflate the colon (without losing the view) to shorten it and make it as pliable as possible.

4 Angulate the controls and use torque simultaneously in approaching the bend, so the tip is coaxed into the axis of the descending colon just *before* the bend and so is likely to slide around more easily (see Fig. 29.21).

5 Try shaft twist (clockwise) in case the configuration allows this corkscrewing force applied to the tip to swing it around the bend, with no inward push pressure required (Fig. 29.37).

6 Change of patient position can improve visualization of the sigmoid–descending junction (air rises, water falls). Gravity sometimes also causes the descending colon to drop down into a more favorable configuration for passage.

7 Pushing through the loop should, as always, be the option of last resort. Warn the patient to expect discomfort, then a few seconds of careful “persuasive” pressure may slide the instrument tip successfully around the bend and up the descending colon, before pulling back and straightening again (to 45–50 cm). In some patients a large spiral or alpha loop may have formed, resulting in easy passage, despite looping, while in others a long colon allows push-through into the descending colon without difficulty (see Fig. 29.24). Without fluoroscopy or the three-dimensional imager the endoscopist is usually unsure what has happened. Providing the patient has no pain, the exact configuration does not matter as long as the loop (whichever it is) is then rapidly and fully removed.

Clockwise twist-and-withdrawal maneuver

Once the tip is hooked around the bend toward the descending colon, the sigmoid loop is pulled straight

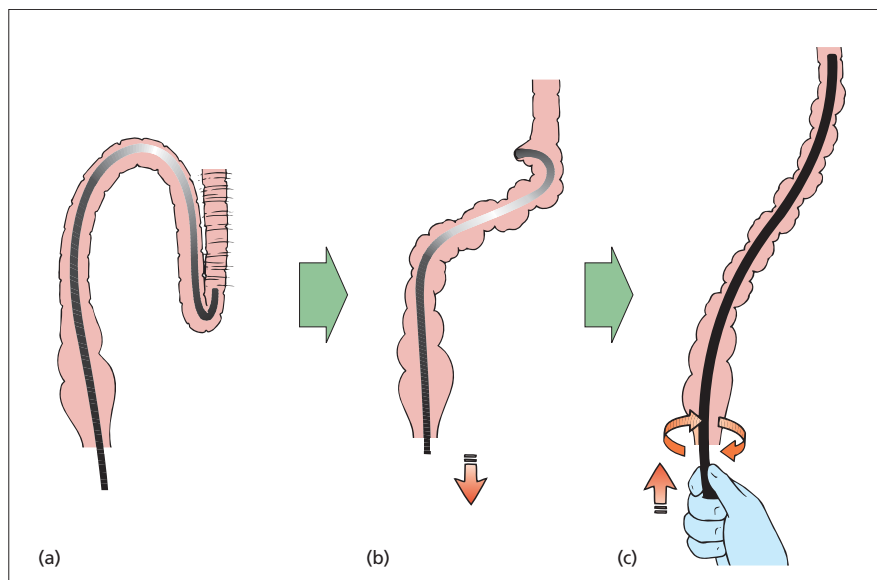


Fig. 29.37 (a) The tip is hooked into the retroperitoneal descending colon, then pulled back. (b) When the endoscope is maximally straightened the tip is redirected and (c) the endoscope pushed, with clockwise twist, into the descending colon.

to help the colonoscope slip up the descending colon (Fig. 29.37a). Simply pulling back unavoidably causes the hooked tip to impact the mucosa (Fig. 29.37b), so it is essential at the same time to steer toward the lumen of the descending colon (Fig. 29.37c). A wrong move at this point will lose tip-hold in the retroperitoneal fixation and the instrument can fall back into the sigmoid. Careful close-up view, minimal insufflation, twist, delicate steering movements, and patience are all needed to pass straight up into the descending colon without relooping.

Descending colon

The conventional descending colon, which characteristically has a horizontal fluid level, is normally traversed in a few seconds with a short “straight” advance (Fig. 29.38). If fluid makes steering difficult, it may be quicker, rather than wasting time suctioning and re-inflating, to turn the patient onto the back or right side in order to fill the descending colon with air. Sometimes the descending colon is far from straight and the endoscopist, having struggled through a number of bends and fluid-filled sumps, believes the tip to have reached the proximal colon when the colonoscope is only at the splenic flexure.

Distal colon mobility and “reversed” looping

In the absence of fixation of the descending colon, all sense of anatomy can disappear. At the most extreme, the colonoscope may run through the “sigmoid” and “descending” distal colon straight up the midline (see Fig. 29.20), resulting inevitably in a “reversed” splenic flexure (see later) and consequent mechanical problems later in the examination. When counterclockwise rotation seems to help insertion at the sigmoid–descending junction, the endoscopist is alerted to the probability that there is atypical mobility. This mobility may mean that an unconventional counterclockwise spiral or reversed alpha loop has formed (see Fig. 29.32), in the presence of a descending mesocolon, allowing the descending

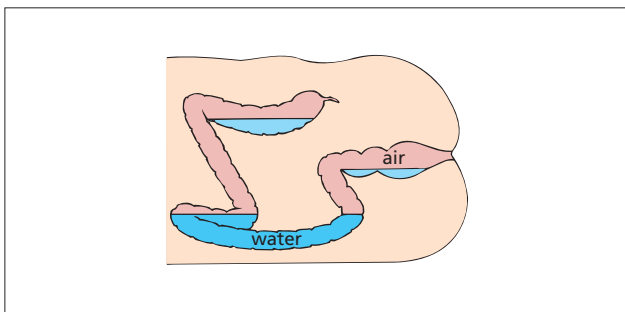


Fig. 29.38 Fluid levels in the left lateral position.

colon to deviate medially (descending colon is usually fixed retroperitoneally, and so is not mobile). If possible, the endoscopist tries to use counterclockwise twist and the springiness of the colonoscope shaft to push the mobile descending colon laterally, regaining conventional configuration. The instrument will then pass from lateral to medial around the splenic flexure (rather than in reverse) and adopts the favorable “question-mark” shape for pushing around to the cecum.

Splenic flexure

Insertion

The splenic flexure is the halfway point during colonoscopy insertion and an excellent place to ensure that the instrument is straightened (to 50 cm) before tackling the proximal colon. A common reason for problems in the proximal colon is inadequate straightening of distal loops, so making the rest of the procedure progressively more difficult or even impossible. Anyone who frequently finds the proximal colon or hepatic flexure difficult to traverse should apply the “50-cm rule” at the splenic flexure, and is likely to find most of the problem solved.

The splenic flexure is conventionally a fixed point because of the phrenicocolic ligament (Fig. 29.39). Passage around the apex of the splenic flexure is usually obvious, because the instrument emerges from fluid into the air-filled, often triangular, transverse colon. However, while the flexible and angled-tip section of the colonoscope passes around without effort, the stiffer shaft may not follow so easily.

Pointers to pass the splenic flexure

To pass the splenic flexure without force or relooping follow the steps listed below.

1 Straighten the colonoscope, pulling back with the tip hooked around the flexure until the instrument is

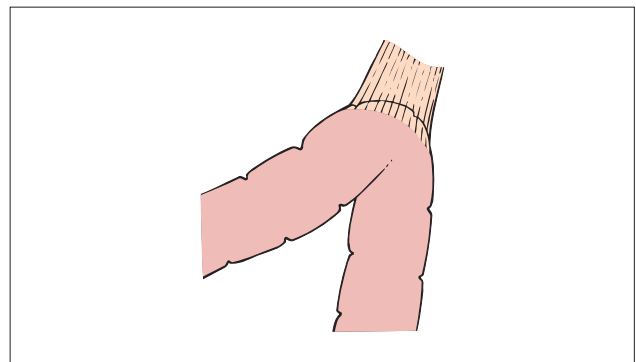


Fig. 29.39 Phrenicocolic ligament.

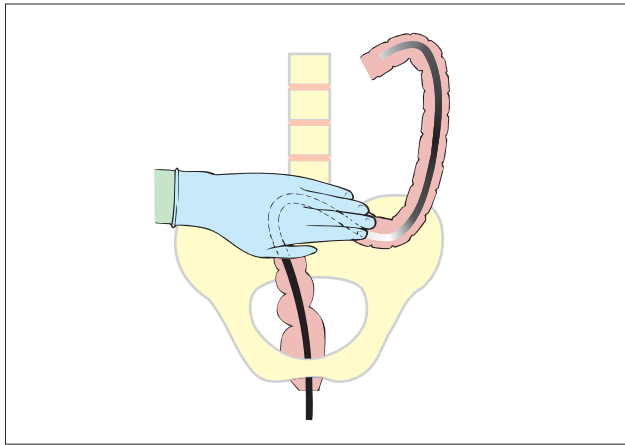


Fig. 29.40 Control sigmoid looping by hand pressure to help pass the splenic flexure.

40–50 cm from the anus (splenic avulsions or capsular tears have been reported, so do this *gently*).

2 Avoid overangulation of the tip (“walking-stick handle” effect), which causes impaction in the flexure and impeding insertion. Consciously deangulate a little so that the instrument runs around the outside of the bend (see Fig. 29.8), even if the view is worsened.

3 Deflate the colon slightly to shorten the flexure and make it more flexible.

4 Apply assistant hand pressure to the left lower abdomen to resist looping of the sigmoid colon (Fig. 29.40).

5 Use clockwise torque on the shaft to counteract any spiral looping tendency in the sigmoid colon while pushing in (Fig. 29.41). Because the tip is angulated,

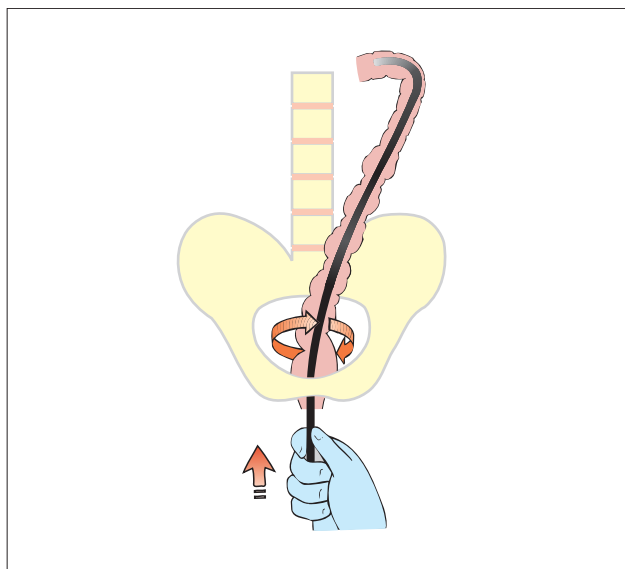


Fig. 29.41 Twist the shaft clockwise while advancing to hold the sigmoid straight.

applying such clockwise shaft torque may affect the luminal view, so readjustment of the angulation controls may be needed to compensate and maintain vision.

6 Push in *slowly*. Pressure is needed to slide around the flexure but aggressive push will simply reform the sigmoid loop. While pushing in, if possible deflate again and, if necessary, resteer with the angulation controls to wiggle the bending section around the curve.

7 If the combination does not work, pull back and start again. Run through all the above actions again, and push in once more. It can take two or three attempts to achieve success.

8 Finally, change patient position and try again.

Position change

Patient position change is the single most effective trick if the splenic flexure is hard to pass. The left lateral position, used by most endoscopists, has the undesirable effect of causing the transverse colon to flop down (Fig. 29.42a), making the splenic flexure acutely angled. In the right lateral position, the transverse colon sags under gravity, pulling the splenic flexure into a smooth curve (Fig. 29.42b). Supine position has an intermediate effect and is an easier move to make, so first try rotating the patient onto the back.

“Reversed” splenic flexure

In 5% of patients with a long and mobile colon, three-dimensional imaging shows the instrument to pass from medial to lateral around the splenic flexure, because the descending colon has moved centrally on a mesocolon (Fig. 29.43). This has the disadvantage that the transverse colon is positioned into a deep loop and the resulting angulation makes it more difficult to steer. The deep transverse colon loop creates an unusually acute angle when approaching the hepatic flexure, which also makes it difficult to reach the cecum and virtually impossible to steer into the ileocecal valve.

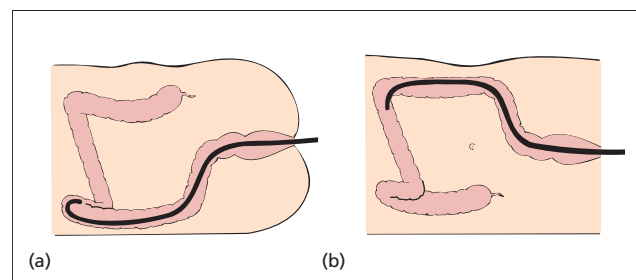


Fig. 29.42 (a) In left lateral position the transverse colon flops down, making the splenic flexure acute. (b) In right lateral position gravity rounds off the splenic flexure, making it easy to pass.

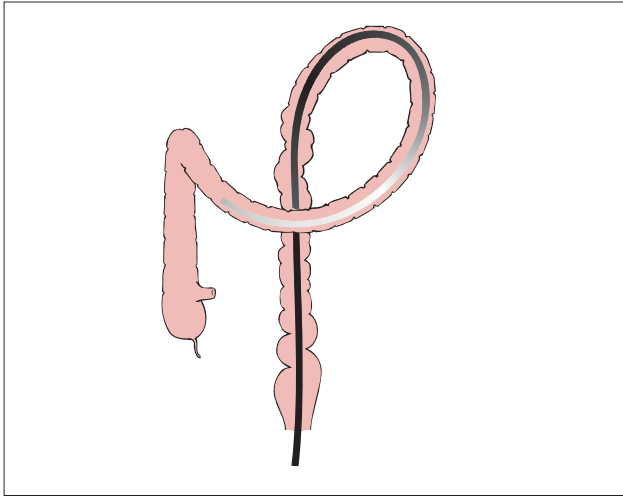


Fig. 29.43 “Reversed” splenic flexure will result in a deep transverse loop.

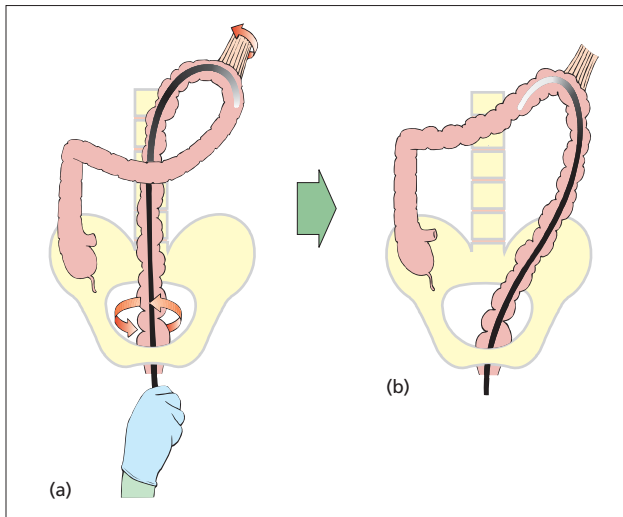


Fig. 29.44 Counterclockwise rotation (a) swings a mobile colon back to a normal position (b).

Derotation of a reversed splenic flexure loop is sometimes possible, but usually only after withdrawing the tip toward the splenic flexure and then twisting the shaft strongly counterclockwise (Fig. 29.44a). Counterclockwise derotation makes the tip pivot around the phrenicocolic suspensory ligament. Maintaining this counterclockwise torque while pushing in causes the instrument to pass the transverse colon in the “question-mark” configuration because the descending colon is forced laterally against the abdominal wall (Fig. 29.44b).

Although easier under three-dimensional imaging, this counterclockwise straightening maneuver is also quite feasible by feel alone. Try these guidelines (and a little imagination) whenever atypical looping is suspected in the proximal colon, since a reversed splenic

flexure/mobile descending colon is the most frequent reason for an unexpectedly difficult adult or pediatric colonoscopy. However, if straightening does not work, it may be better simply to push through harder than usual (if necessary with extra sedation) and to abandon the procedure when a reasonable view of the right colon has been obtained.

Transverse colon

Problems in the transverse colon are often due to the sigmoid colon forming into an N-loop, thus reducing effective transmission of inward push pressure to the colonoscope tip. The transverse colon can also be pushed downward by the advancing colonoscope into a deep loop, with greater resistance and force needed to advance the tip; this often results in sigmoid looping as well. A clue is given that the transverse is long, and likely to be problematic, when a tenia coli indents the colon, acting as a useful pointer to follow—rather like the white line down the center of a road (Fig. 29.45). At acute angulations, such as the mid-transverse, the tenia coli can be followed blindly to steer or push round the bend and see the lumen beyond (Fig. 29.46).

After the midpoint of the transverse, it may be slow and difficult to “climb the hill” up the proximal limb of the looped transverse colon (Fig. 29.47a). Pull back repeatedly, using the hooked tip to lift up and straighten the transverse (Fig. 29.47b). The tip often advances as the shaft is withdrawn, the phenomenon known as *paradoxical movement* (i.e. when a loop with proximal and distal limbs is removed by pulling on one end, the other limb will move in the opposite direction as the loop decreases). Hand pressure can be helpful, whether over the sigmoid colon during inward push or in the left hypochondrium or central abdomen to lift up the transverse loop. Deflation of the colon, torquing movements, and even change of position (usually to the left lateral

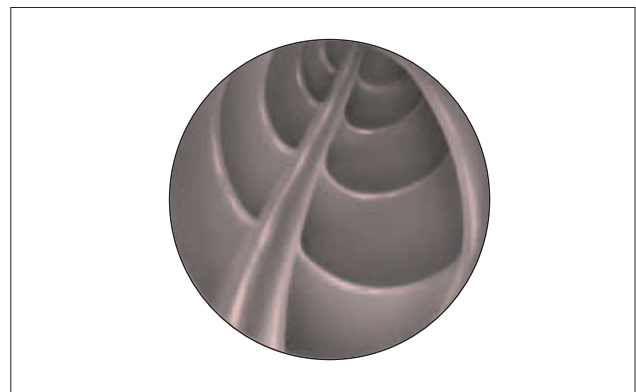


Fig. 29.45 The longitudinal bulge of a tenia coli shows the axis of the colon.

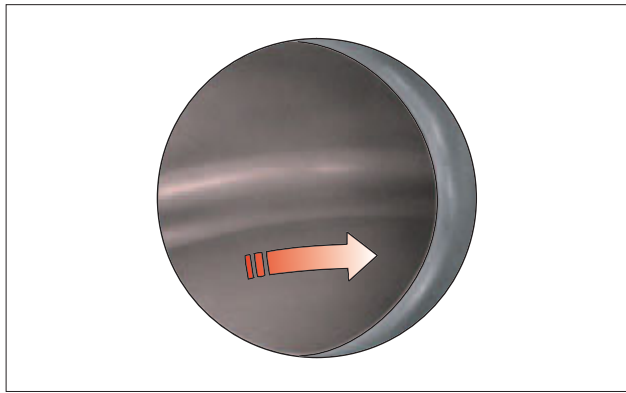


Fig. 29.46 Follow the longitudinal bulge (tenia coli) round an acute bend.

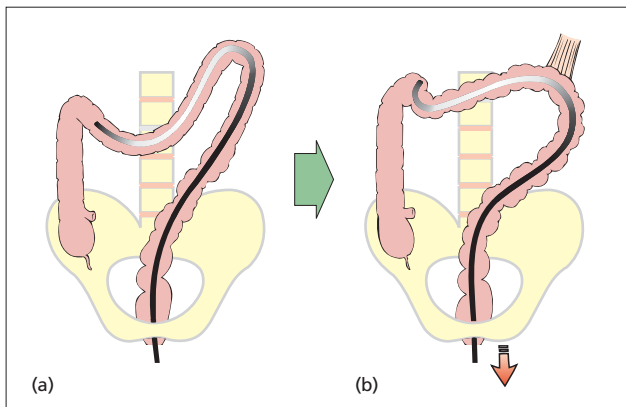


Fig. 29.47 (a) If passage up the proximal transverse is difficult, (b) pull back to lift and shorten.

position, sometimes to supine, right lateral or even prone position) can also help. Counterclockwise torque often helps advance the last few centimeters towards the hepatic flexure, providing that the shaft has been straightened enough (so that torsional force transmits proximally).

Effect of a mobile splenic flexure

The “lift” maneuvers in the transverse colon depend on the fulcrum or cantilever effect made possible by the phrenicocolic ligament fixing the splenic flexure. In some patients this attachment is lax, allowing the splenic flexure to be pulled back to 40 cm (rather than the usual 50 cm) (Fig. 29.48a). The colon is then found to be hypermobile, the shaft inserting or withdrawing massively with little of the usual cantilever effect, so that the tip remains unresponsive to any of the normally effective push-pull or twist forces (Fig. 29.48b). However, whereas in a mobile colon the use of force is relatively ineffectual, deflation, hand pressure, position change

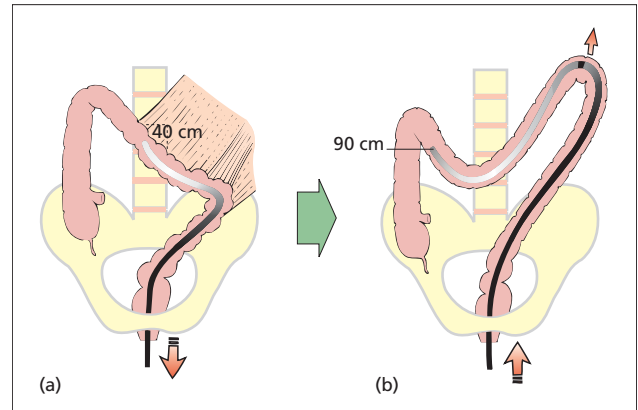


Fig. 29.48 (a) If the phrenicocolic ligament is lax, withdrawal maneuvers are ineffective; (b) pushing in simply reforms the loop.

(usually to the right lateral position), and gentle perseverance eventually coax the tip up to the hepatic flexure. Simple aggression and force usually only worsens the looping.

Gamma looping of the transverse colon

A gamma loop (1% of examinations) forms when the transverse colon and its mesocolon (Fig. 29.49a) is so long that colonoscope pressure pushes it across the abdomen into a large drooping loop, a “volvulus” analogous to alpha loop formation (Fig. 29.49b). A gamma loop is rarely removable, both because of its size (which conflicts with the small intestine and other organs during attempted derotation) and because colon mobility makes it difficult to find any fixation point on which to angulate and stop the tip falling back during withdrawal. The cecum can be reached with a gamma loop in position, but control-wire friction makes it difficult to enter the ileocecal valve.

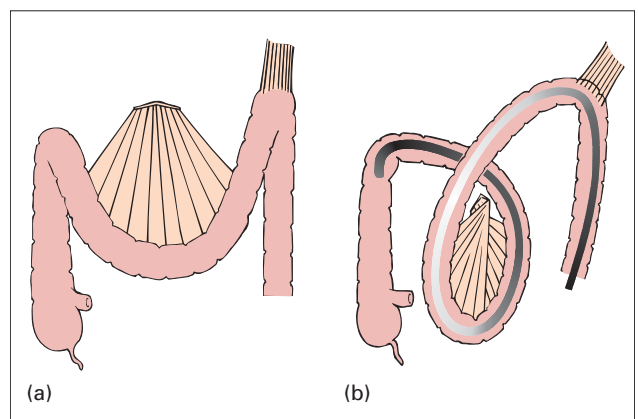


Fig. 29.49 (a) Transverse mesocolon; (b) gamma loop.

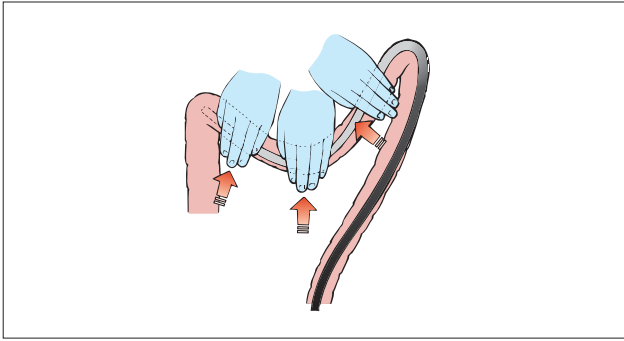


Fig. 29.50 “Specific” hand pressure may elevate the transverse colon.

Hand pressure in the transverse colon

The use of hand pressure to attempt control of the looping sigmoid colon has been described (see Fig. 29.18). The tendency of the sigmoid to reloop at all stages of insertion means pressure over it is worthwhile whenever the instrument is looping, described as *nonspecific* hand pressure.

Other loops can also be reduced or resisted by appropriate hand pressure, notably a drooping transverse colon. Once a transverse loop has been pulled up and shortened as far as possible, *specific* hand pressure may help push the colonoscope tip further inwards (Fig. 29.50). Try pushing empirically (to see if the tip can be advanced) in:

- 1 left hypochondrium (to lift the loop and the tip across the abdomen toward the hepatic flexure);
- 2 mid-abdomen (to counteract the sagging transverse colon);
- 3 right hypochondrium (to impact directly on the hepatic flexure).

Hepatic flexure

A common problem in the transverse colon is to be able

to see the hepatic flexure but not to be able to reach it without relooping and falling back. If the flexure is only 2–3 cm away, with a reasonably straight colonoscope (70–80 cm), hand pressure has already been tried and perhaps anticlockwise torque also, a final combination of small actions (listed below) should ensure rapid passage around the hepatic flexure.

Pointers to pass the hepatic flexure

- 1 Assess from a distance the correct eventual steering direction around the flexure.
- 2 Aspirate air carefully from the inflated hepatic flexure in order to collapse it toward the tip.
- 3 Ask the patient to breathe in (and hold the breath), which lowers the diaphragm and often the flexure too.
- 4 It may be possible to push the scope tip toward the hepatic flexure by finding a specific pressure point on the abdomen, often requiring only one finger. The intention is to push the wall (which is further away from the colonoscope) toward the tip. This may cause the view of the flexure to be lost. As the assistant presses, perform the next maneuver.
- 5 Angulate the tip blindly in the previously determined direction around the flexure. The hepatic flexure is very acute, often a 180° hairpin bend, so it takes some confidence to angulate around with partial view (Fig. 29.51a). Use both angulation controls simultaneously for full angulation (using both hands makes this major angulation easier). Adding clockwise torque may also help.
- 6 Withdraw the instrument substantially (up to 30–50 cm) to lift up the transverse and straighten the colonoscope (Fig. 29.51b) for passage into the ascending colon.
- 7 Aspirate air again once the ascending colon is seen, which shortens the colon and drops the tip down toward the cecum (Fig. 29.51c).
- 8 If actions 1–7 are ineffective, position change to right lateral or even prone (compressing a particularly bulging abdomen) may help coax the colonoscope tip into and around the hepatic flexure. Forceful pushing rarely

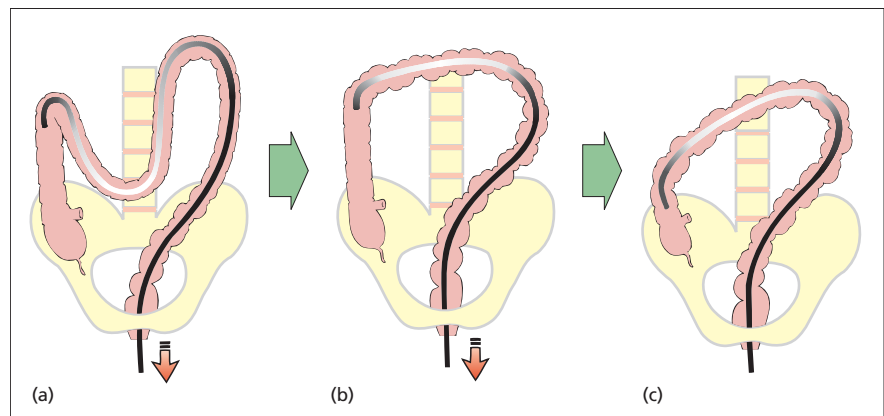


Fig. 29.51 When around the hepatic flexure and viewing the ascending colon (a), pull back to straighten (b), and aspirate to collapse the colon and pass toward the cecum (c).

pays off, since looping in the sigmoid and transverse colon can use up most of the length of the colonoscope shaft. With the instrument really straightened at the hepatic flexure, only about 70 cm of the shaft should remain in the patient, and it is at this point that the subtleties described above are likely to work.

9 Be realistic. If things are not working out at the hepatic flexure after applying these various tricks, the colonoscope may actually still be in the splenic flexure. In a long and mobile colon it is easy to be overoptimistic and become hopelessly lost. The clue to this is often that the hepatic flexure (in left lateral position) is dry or air-filled, whereas the splenic flexure is likely to be fluid-filled.

Ascending colon and ileocecal region

The temptation to push in to the ascending colon from around the hepatic flexure should be resisted, as it usually only results in the transverse loop reforming and the tip sliding back. The secret is to deflate; the resulting collapse of the capacious hepatic flexure and ascending colon will drop the tip downward toward the cecum (see Fig. 29.51c). Deflation also lowers the hepatic flexure, a mechanical advantage, so that pushing inwards is more effective. Repeated aspirations, steering carefully down the center of the lumen (with torque if it helps), then pushing for the last few centimeters, should reach the cecum. If the last few centimeters to the cecal pole are difficult, position change to prone (even a partial position change of 20–30° may help) or to supine should do the trick.

Total colonoscopy or *completion* requires identification of the ileocecal valve, with the slit or curve of the appendix, sometimes at the “crows foot” or “Mercedes-Benz” sign (Fig. 29.52) where the teniae join. Right iliac fossa transillumination or finger palpation indenting the cecal region are less exact, but do show that the tip has reached proximally.



Fig. 29.52 Caecal pole: “Mercedes-Benz” sign of teniae fusing at the appendix.

The cecum can be voluminous and confusing to examine. It is also possible to be mistaken; the ileocecal valve fold can be in spasm, being mistaken by the unwary for the appendix orifice or cecal pole. Insufflation, antispasmodics, or pushing in a few centimeters further reveals the cavernous cecal pole beyond.

Entering the ileocecal valve

The “appendix trick” or “bow-and-arrow” sign is an ingenious (and usually successful) way of both finding and entering the valve.

- 1** Find the appendix orifice. This is usually crescentic and shaped like a bow.
- 2** Imagine an arrow in that bow. It will point in the direction of the ileocecal valve (Fig. 29.53a).
- 3** Angulate in that direction and withdraw so the tip (still angled) slides back about 3–4 cm.
- 4** Watch for the proximal lip of the ileocecal valve to start to ride up over the lens (Fig. 29.53b).
- 5** When it does, stop, insufflate and angulate gently into the ileum.

The trick works, as it does more often than not, only when the angulated appendix lies bent in the direction of the center of the abdomen, from which direction the ileum enters the cecum. The crescentic fold created

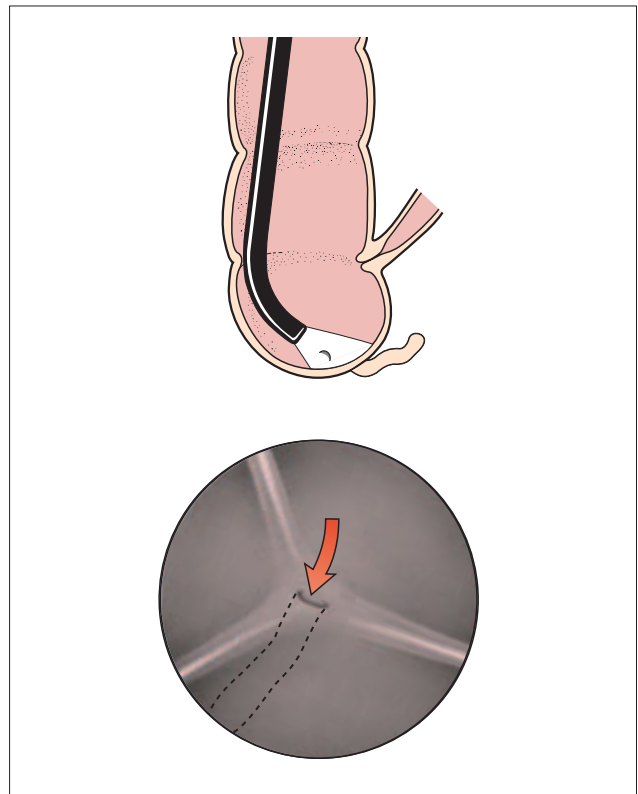


Fig. 29.53 The “bow” of the appendix opening shows the direction of the appendix—and usually the ileum too.

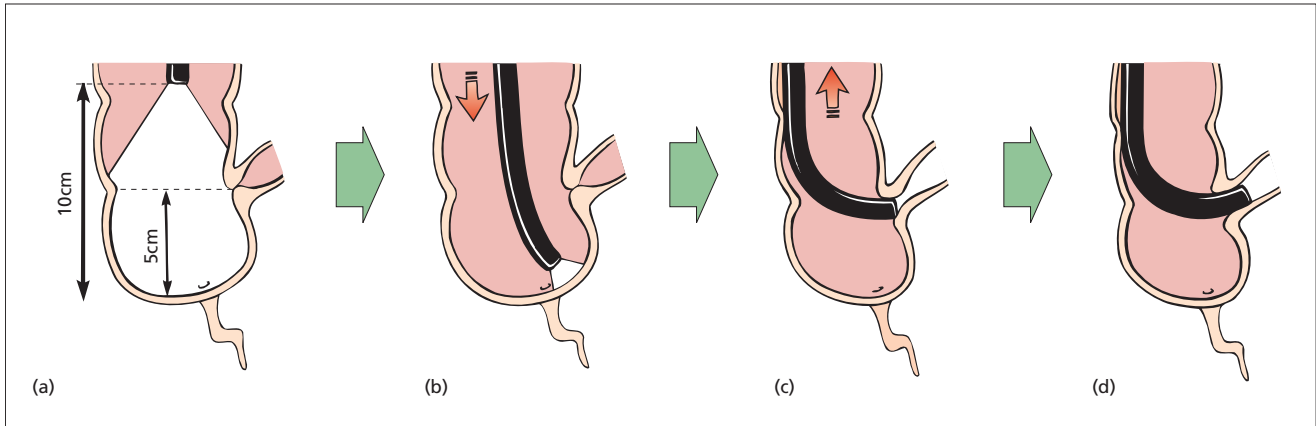


Fig. 29.54 Locate the ileocecal valve (preferably at 6 o'clock) (a), pass in and angulate and deflate slightly (b), pull back until "red-out" is seen (c), and insufflate to open the valve (d).

by the angulation of the appendix acts as a directional indicator, much as an airport windsock indicates wind direction for a pilot. After appendicectomy or when the cecum is mobile and the appendix is straight-on, there is no such indication.

Finding the valve otherwise requires the endoscopist to pull back about 8–10 cm from the cecal pole and identify the first prominent circular haustral fold, around 5 cm back from the pole. On this "ileocecal" fold will be the tell-tale thickening or bulge of the valve. From the side, the valve may look flattened, may bulge in (especially on deflation, when it can bubble), can show a characteristic "buttock-like" double bulge or, less commonly, have obvious protuberant lips or a "volcano" appearance. The best the endoscopist can usually achieve is a partial, close-up and tangential view, often only after careful maneuvering. Change of patient position may be helpful if the initial view is poor or entry proves difficult.

Entering the ileocecal valve, other than by the "appendix trick" described above, is by one of three methods.

Direct entry into the ileum

Direct entry into the ileum is almost always possible but often takes some patience.

1 Rehearse at a distance (10 cm back from the cecal pole) the easiest movements for entry. If possible, rotate the endoscope so that the valve lies at the top or bottom of the visual field, which allows entry with an easy downward angulation movement (lateral or oblique movements are awkward single-handedly) (Fig. 29.54a).

2 Pass the colonoscope tip in over the ileocecal valve fold (aspiration alone may do this) and angle toward the valve (Fig. 29.54b). Overshoot a little so that the action

of angulation directs the tip into the opening, not short of it.

3 Deflate the cecum partially to make the valve supple (Fig. 29.54b).

4 Pull back the colonoscope, angling toward the valve until the tip catches in its soft lips, resulting in a "red-out" of transilluminated tissue (Fig. 29.54c), typically with dappled reflections or granular appearance of the villi in close-up (as opposed to the pale shine of colonic mucosa).

5 On appearance of the "red-out," freeze all movement, insufflate air to open the lips (Fig. 29.54d), gently twisting or angling the endoscope a few millimeters to find the ileal lumen.

6 Multiple attempts may be needed to succeed in locating the valve and entering the ileum. Change of position may also help.

Entry using biopsy forceps

Entry using the biopsy forceps is helpful only if a distant, partial, or uncertain view can be obtained of the ileal bulge or opening. The biopsy forceps is used to locate and then pass into the opening of the valve, either to obtain a blind biopsy or to act as an "anchor" (Fig. 29.55).

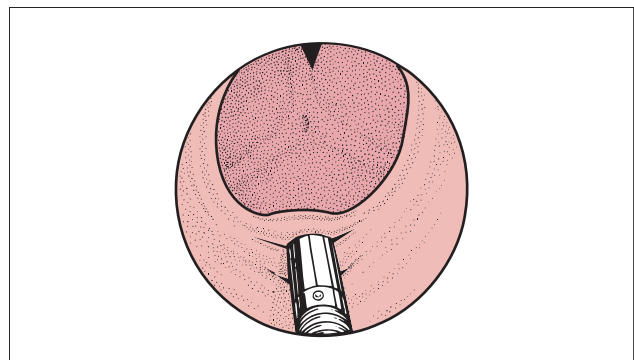


Fig. 29.55 Biopsy forceps can be used to locate and pass into the ileocecal valve.

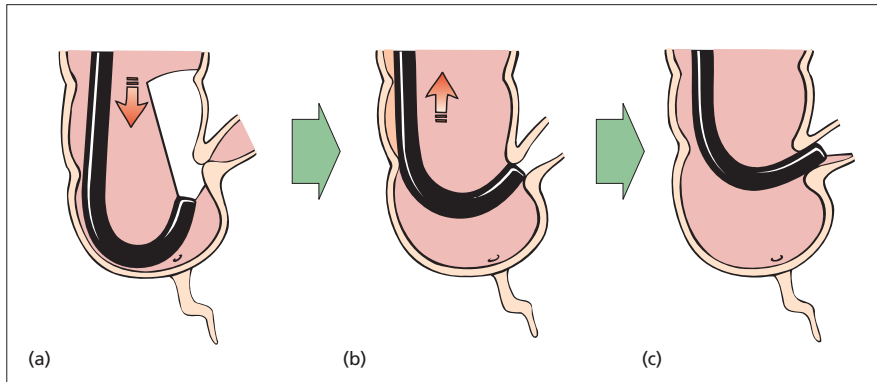


Fig. 29.56 If necessary (a) retrovert to see the valve, (b) pull back to impact, and (c) insufflate and deangulate to enter the ileum.

Aspiration then deflates the colon and usually allows the tip to slide into the valve.

Entry in retroversion

Entry in retroversion is useful if the ileocecal valve is slit-like and invisible from above, and the colon is capacious enough. Retroversion is also a useful way of checking for possible blind spots in the ascending colon or in snaring awkwardly placed polyps in the proximal colon. However, with video endoscopes the extra length of the bending section (even if retroversion is possible) may preclude any view of the valve. If retroversion works and the valve slit is visible (Fig. 29.56a), pull back to impact the tip within it (Fig. 29.56b), then insufflate to open the lips and deangulate and pull back further to enter the ileum, with or without use of the forceps (Fig. 29.56c).

Problems in finding or entering the ileocecal valve

Problems in finding or entering the ileocecal valve occur for a number of reasons. The endoscope may be in the hepatic flexure not the cecum. The opening may be unclear; some valve openings are flat and slit-like, effectively invisible on the reverse side of the fold. In Crohn's disease the valve can be narrowed and impassable, although a limited view may be possible and biopsies may be taken through it.

Terminal ileum

The surface characteristics of the terminal ileum are variable. The ileal surface looks granular or matt in air, but

under water the villi are seen projecting. In younger patients it is often studded with raised lymphoid follicles resembling small polyps, or these can be aggregated into plaque-like Peyer's patches. Sometimes the ileum is surprisingly colon-like, with a pale shiny surface and visible submucosal vascular pattern. After colon resection the difference between colon and ileum may be imperceptible because of villous atrophy, although dye-spray will discriminate between the granular or "sandpaper" appearance of the ileal mucosa and the circumferential "innominate grooves" of the colonic surface.

Once the colonoscope tip is in the ileum, it can often be passed for up to 30–50 cm with care and patience, although this length of intestine may be convoluted onto only about 20 cm of instrument. Air distension in the small intestine should be kept to a minimum since it is particularly uncomfortable and slow to clear after the procedure.

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Chapter 30

Missed Neoplasms and Optimal Colonoscopic Withdrawal Technique

Douglas K. Rex

Introduction

In the development and investigation of colonoscopic technique, the withdrawal phase of colonoscopy has received limited attention. For example, in five previous textbooks of colonoscopy, the number of pages devoted to instrument insertion was 20, 38, 34, 27, and 8, and the number devoted to the withdrawal phase of colonoscopy was 0.5, 1, 1, 1.5, and 0.5 [1–5]. Certainly, the most technically challenging aspects of diagnostic colonoscopy involve the insertion phase. However, with improvements in instruments and the performance of colonoscopy in high volumes, experts have consistently reported intubation rates in more than 90% of patients in general [6] and more than 95% of screening patients [7–9]. Simultaneously, evidence that colonoscopy is associated with failed detections of both cancers [10] and adenomas [11,12] and that there is variation between examiners [11–13] has increased interest in the withdrawal phase of colonoscopy. Most but not all colonoscopists perform their detailed examination for colonic neoplasia during the withdrawal phase. Since high sensitivity for neoplasia is an important positive outcome for colonoscopy, the withdrawal phase is then a critical aspect of the procedure. Optimal withdrawal technique and the optimal time that withdrawal should take are issues that are not yet fully clarified. This chapter reviews available evidence on the phenomenon of missed lesions at colonoscopy and the association of these lesions with withdrawal technique and withdrawal time.

Adverse consequences of missed neoplasms at colonoscopy

Poor patient outcomes

The most serious adverse consequence of missing lesions is the appearance of colorectal cancer in the interval shortly after (within a few years of) a colonoscopy that apparently cleared the colon of neoplasia. Whether the occurrence of a surgically curable incident cancer after clearing colonoscopy should be deemed a failure of colonoscopy is subject to interpretation. However,

the occurrence of late-stage cancers [14,15] is clearly an adverse outcome for the patient.

Available data suggests that in many centers colonoscopy and polypectomy are highly protective against the development of colorectal cancer. For example, in the two studies constituting the strongest evidence that colonoscopy and polypectomy reduce the incidence of colorectal cancer, the estimated reduction in the incidence rate of colorectal cancer during the postadenoma resection surveillance interval was 76–90% [16] and 80% [17]. In these studies, the reduction in incidence was calculated by comparison to the expected rate of incident colorectal cancers in reference populations. In the National Polyp Study [16] where five cancers were found on follow-up examination, all were early cancers, being stage I or II lesions. In another study, Norwegian investigators performed a prospective randomized trial in 800 patients (the “Telemark Polyp Study”) in which screening by flexible sigmoidoscopy with colonoscopy for any polyp detected was compared to no screening [18]. During 13 years of follow-up, the incidence of colorectal cancer in the treatment group was reduced by 80% compared to the control group. Thus, three studies have demonstrated a substantial reduction in incidence of colorectal cancer via colonoscopy and polypectomy, although the observed reduction was not complete. Similarly, review of previous observational studies in which adenoma-bearing cohorts have been followed after clearing colonoscopy demonstrates a consistent low rate of appearance of incident colorectal cancers in the postpolypectomy surveillance interval, and very early stages among those incident cancers that did occur [19].

The extent to which missing cancers or advanced adenomas at the baseline colonoscopy contributed to the incident cancers observed in the above cited studies is uncertain. Alternative explanations are based on variable biological behavior of tumors which results in rapid growth in some adenomas and cancers. For example, it is known that tumors passing through the microsatellite instability genetic pathway of colorectal cancer are capable of passing through the adenoma–carcinoma sequence faster than occurs typically in the chromosomal instability pathway [14,15,20,21]. Indeed, this is the

rationale for the performance of colonoscopy at 1- to 2-year intervals in patients with hereditary nonpolyposis colorectal cancer. However, 10–15% of sporadic colorectal cancers and 20% of all right-sided colon cancers demonstrate microsatellite instability [22,23]. Therefore, even in the setting of sporadic colorectal cancers, the occurrence of mismatch repair gene inactivation is a potential mechanism for the rapid appearance of a cancer after clearing colonoscopy. Similarly, poorly differentiated cancers might in some instances grow at a relatively rapid rate. Another potential contributor to incident lesions is the occurrence of flat or depressed lesions, which may be difficult to detect with even optimal western colonoscopic technique. Whether western colonoscopists should utilize Japanese colonoscopic techniques (chromoscopy with or without high magnification) is a matter of continuing debate that is discussed elsewhere in this book. There are, however, plausible biologic explanations for the appearance of cancers at short intervals following a colonoscopy that was considered to have cleared the colon of neoplasia. It is the relative contributions from missed lesions versus variable biologic behavior that is unclear.

Although the mechanisms accounting for incident cancers in the studies cited above are unclear, it is also the case that the occurrence of incident cancers [24,25] has been as much as fourfold higher than in the above cited studies [16–18]. This large variation in observed incidence rates of colorectal cancer after clearing colonoscopy suggests that post colonoscopy incident cancers must be at least partly accounted for in these studies [24,25] by lesions that were missed at previous colonoscopies. The only alternative explanation would be that any biologic factors that contribute to incident cancers after clearing colonoscopy vary substantially between study populations. This seems unlikely, given that all the above mentioned studies [16–18,24,25] were performed in the USA and Europe, and therefore presumably included populations with similar biologic mechanisms for cancer development.

Medical-legal risk

A second adverse consequence of incident cancers after clearing colonoscopy is medical-legal risk for physicians. The allegation is generally that a lesion was missed because of negligent technique. This issue is likely more pertinent in the USA. Appropriate steps to reduce medical-legal risk have been reported elsewhere [26], and some of these risk-avoidance maneuvers are: the cecum should be documented by notation of landmark identification, in particular the ileocecal valve orifice and the appendiceal orifice. Photodocumentation is advisable, with the most convincing still photograph usually being a photograph taken from just distal to the ileocecal



Fig. 30.1 The most convincing still photograph for documenting cecal intubation is taken from just distal to the ileocecal valve. This view shows the valve, which may or may not appear notched or lipomatous.



Fig. 30.2 The medial wall of the cecum is best photographed from a sufficient distance so that both the appendiceal orifice and the surrounding "crow's foot" appearance is visible.

valve (Fig. 30.1). A photograph of the medial wall of the cecal caput including the appendiceal orifice is also advisable (Fig. 30.2). Anecdotally, failure to document visualization of key cecal landmarks and/or obtain photographs of the cecum has led to the allegation that either

the cecum or even the right colon was never intubated. Adequate bowel preparation to conduct an effective examination on withdrawal is one in which the prep allows identification of polyps greater than 5 mm in size. If there are only one or two areas of retained solid stool, it is better and more cost-effective to rotate the patient from one side to the other, in order to expose mucosa obscured in one position. The bowel preparation should generally be described as “excellent,” “good,” or “ideal.” Use of the terms “poor” or “suboptimal” is discouraged unless the patient is to be scheduled for an earlier follow-up than would be indicated by the presence of polyps, cancer, or other factors (such as a family history of colorectal cancer) that affect follow-up intervals. Surprisingly, incident cancers often appear in the rectum. Documentation of a digital rectal exam prior to colonoscopy insertion as well as performance of rectal retroflexion (unless the rectum is narrow), accompanied by a photograph of the retroflexed appearance, is useful in documenting careful technique. Because there is clear evidence that overlooking adenomas occurs even in the most careful hands, the informed consent statement should list “missed lesion” as a risk of colonoscopy.

Overuse of surveillance

A final adverse outcome of missing lesions is that awareness of missed lesions contributes to the overuse of colonoscopy through performance of surveillance at intervals that are less than currently recommended. Anecdotal events involving the occurrence of incident cancers after clearing colonoscopy can affect the surveillance practice not only of the colonoscopist who performed the original clearing colonoscopy, but also of their partners and other endoscopists who become aware of the event. Currently, postpolypectomy surveillance accounts for about 25% of all colonoscopies performed in the USA [27], even though the yield in general is lower than all colonoscopy indications except for ulcerative colitis surveillance [19]. There is increasing consensus that shifting resources away from surveillance and toward screening would have a greater impact on colorectal cancer mortality. Fear of missing and a resultant tendency to repeat examinations at too close intervals reduces the capacity of the endoscopy delivery system to provide screening colonoscopy.

Evidence for missing neoplasms at colonoscopy

Every study that has explored colonoscopy sensitivity has identified missed lesions. The most direct evidence for overlooked lesions comes from so-called “tandem” or “back-to-back” colonoscopies, in which patients undergo two colonoscopic examinations in the same

Table 30.1 Miss rates in tandem colonoscopy studies.

Reference	Miss rates by polyp size		
	1–5 mm	6–9 mm	≥ 1 cm
28	15%	12%	0%
11	27%	13%	6%

day. The first of these studies to be reported involved two experienced examiners and 90 patients [28]. Significant miss rates for small polyps were identified in this study (Table 30.1), though one of the examiners averaged 51 min per colonoscopy. The largest tandem colonoscopy study involved 183 patients and 26 experienced examiners [11] (Table 30.1). A study of tandem flexible sigmoidoscopy involving gastroenterologists and nurses demonstrated comparable adenoma miss rates of about 20% for both groups [29]. Studies in which two or more colonoscopies are performed at short intervals in time have also been used to calculate miss rates [30]. The most recent of these studies evaluated colonoscopies performed in the same patients at a mean interval of 47 days (range 1–119 days) and estimated a miss rate for adenomas of 11–17% [30].

The National Polyp Study can be considered as a miss rate study [31]. Thus, a group of patients who had undergone clearing colonoscopy were randomized to undergo a colonoscopy at 1 and 3 years versus 3 years. At the 3-year time point, one group had undergone two surveillance colonoscopies and the other group only one. The cumulative incidence of adenomas greater than 1 cm in size at 3 years was 3% in both groups but the overall incidence of adenomas was 42% in the two-colonoscopy arm and 32% in the one-colonoscopy arm. Thus, two colonoscopies increased the number of patients with at least one adenoma identified by nearly one-third [31].

Studies of colorectal cancer sensitivity have identified evidence that colonoscopy misses colorectal cancers. A study performed in 20 hospitals in central Indiana (18 community, two university) examined medical records of 2193 consecutive colorectal cancer diagnoses over a 5-year interval [10]. Chart reviews to identify all procedures performed identified 943 cases in which the initial diagnostic procedure within 3 years of the diagnosis of colorectal cancer was a colonoscopy. The overall sensitivity of colonoscopy for colorectal cancer was 95%. A similar but smaller study in Hamilton, Ontario, demonstrated a sensitivity of colonoscopy for cancer of 85% [32]. Both studies counted cases as misses if the colonoscopy failed to reach a cancer because it was not inserted into the cecum.

Detailed examination of the above studies demonstrates the following additional observations regarding

missed lesions. Tandem colonoscopy studies demonstrate that miss rates are inversely proportional to polyp size [11,28]. Altering the patient's position on the examining table for a second examination did not affect the miss rate in one tandem colonoscopy study [11]. Missed cancers are more common in the proximal colon [33]. Evaluation of individual missed cases often shows inadequate identification of cecal landmarks, raising the possibility that for some apparently missed proximal colon cancers the area was never reached [33], though this remains unproven. Pathologic features of missed cancers in general tend to be similar to those of detected cancers [33], and such evaluations have failed to identify biologic differences that would account for rapid growth patterns in most cases of missed cancer. To the author's knowledge, studies of microsatellite instability have not been performed on incident cancers after clearing colonoscopy.

Evidence for variation in colonoscopic miss rates between examiners

In the above-mentioned study of sensitivity of colonoscopy in 20 hospitals in Indiana, the sensitivity of colonoscopy for colorectal cancer among gastroenterologists was 97% and for nongastroenterologists was 87% (odds ratio for missed cancer by a nongastroenterologist 5.36, 95% CI 2.94–9.77) [10]. Among gastroenterologists, a private group at one large hospital accounted for 316 of the total 943 cases evaluated. The sensitivity for colorectal cancer among this private group of gastroenterologists was 95%, which was lower than the 99% sensitivity by all gastroenterologists at the other 19 hospitals evaluated ($P = 0.001$) [33].

In the largest tandem colonoscopy study, the range of sensitivities for adenoma detection among 26 examiners was 17–48% [11]. The two examiners at the extreme ends of sensitivity had each performed more than 10 000 colonoscopies prior to initiation of the study. In order to investigate whether differences in technical performance of withdrawal were associated with the miss rates observed by these two examiners, each examiner agreed to have their withdrawal technique videotaped for 10

consecutive examinations [13]. In each of the 20 cases, it was the examiner who turned on the videotape after cecal intubation and turned it off after withdrawal from the anus. The videotapes were then shown in random order to four independent expert colonoscopists who judged them by four criteria (Table 30.2). On each videotape, each of seven different sections of the colon was scored on a rating of 1–5 (Table 30.2). The examiner with the lower miss rate was judged by the independent experts to have superior colonoscopic withdrawal technique for each of the examination criteria and by each of the independent experts. In addition, the mean withdrawal time for the examiner with the low miss rate was 8 min 55 s, which was longer than that of the examiner with the high miss rate (6 min, 41 s; $P = 0.02$).

A multicentre study of single time flexible sigmoidoscopy in persons age 55–64 is being conducted in the UK [12]. An initial report demonstrated variable prevalence of adenomas between study centres, with a range of prevalence being 9% and 15% ($P < 0.001$). Initial investigation of factors associated with variable miss rates identified only the time taken to perform the flexible sigmoidoscopy, which was directly related to the prevalence of adenomas [12].

A retrospective evaluation of colonoscopy at the Mayo Clinic Rochester identified variation in adenoma prevalence rates between endoscopists [34]. Among a total of 4285 colonoscopies performed by attending physicians in intact colons, the mean procedure time for negative examinations was 21.4 min. The mean number of polyps per examination ($P = 0.019$) and the detection of multiple polyps ($P = 0.014$) were both related to the median procedure time of individual endoscopists in normal examinations. The association between nondiminutive lesions and median procedure time approached significance ($P = 0.051$) [34].

A Norwegian group evaluated the quality of screening flexible sigmoidoscopies in 8840 cases performed by eight different endoscopists. Five of the endoscopists were highly experienced (had performed > 5000 colonoscopies) before the trial began, and three had been recently trained (had performed 100 colonoscopies each before beginning the trial). The adenoma detection rate

Criterion	Colonoscopist #1†	Colonoscopist #2	P
Looking on the proximal sides of folds, valves, etc.	31.5	19.6	< 0.001
Adequacy of cleaning	33.1	21.9	< 0.001
Adequacy of distention	33.5	24.0	< 0.001
Adequacy of time spent viewing	32.4	21.0	< 0.001

* Scores are the means for all colonoscopies and for all four judges. The highest score possible is 35.

† Colonoscopist number 1 had the lower miss rate.

Table 30.2 Quality scores for colonoscopic withdrawal by two colonoscopists with known differences in miss rates.* (Adapted from Rex [13].)

varied from 12% to 22% between the endoscopists ($P < 0.001$ for variability between endoscopists) and did not correlate with the endoscopist's experience [35].

The EPAGE Study is a multicentre European observational study involving 20 European centers and one Canadian center, focussed on variation in technical performance and quality of colonoscopy [36]. Among 5291 patients evaluated, the rate of polypectomy varied from 14% to 35%. The mean time to perform withdrawal varied from 5.7 to 17.2 min, but the investigators did not report the correlation with the polypectomy rate or the adenoma prevalence rate [36]. In a matter related to withdrawal technique, satisfactory colon cleansing varied from 51% to 90% [36].

In summary, variation in sensitivity has been demonstrated for colorectal cancer between gastroenterologists and nongastroenterologists and among gastroenterologists. Variation in adenoma sensitivity has been found between gastroenterologists. The quality of withdrawal technique, as measured by evaluating the proximal sites of folds and flexures, adequate distention, and adequate cleaning, has been associated with adenoma detection rate, and the time taken to perform both the withdrawal phase of examination and the complete examination has been associated with adenoma detection. All reports in the literature that refer to the quality of and time taken to perform the examination mention that both factors influence the detection of adenomas.

Optimal withdrawal technique

In this section, the author gives his perception of optimal colonoscopic withdrawal technique, based on both available evidence and the author's experience. Clearly, optimal detection of lesions requires spending an adequate amount of time. The mean time spent on withdrawal by examiners with known low miss rates suggests that mean examination time during withdrawal in normal persons with intact colons should average at least 6–10 min [37]. To document this, it is best to record the time of colonoscope insertion into the anus, the moment of cecal intubation, and the moment of colonoscope withdrawal. At our hospital nurses record this data on the nursing record. Because experienced colonoscopists insert the colonoscope in many cases in only a few minutes, this means that total examination time can in some cases of adequate performance be as little as 8–14 min. Furthermore, colons in which cecal intubation is very fast (1–2 min) may be relatively short and less redundant so that adequate examination can be performed at the lower range of the recommended 6- to 10-min intervals. This can contribute to the occasional occurrence of normal colonoscopies where the total duration could be less than 10 min and withdrawal technique was adequate. The optimal duration of examina-

tion is not yet settled and the recommendation that mean times should average 6–10 min is based on available evidence [37]. However, no study has directly addressed the issue of what the optimal length of withdrawal should be.

Second, withdrawal technique fundamentally involves methodology to carefully and meticulously examine the proximal sides of the ileocecal valve, all flexures, all haustral folds, and the rectal valves. Thus, a "straight pullback" technique, in which the examiner slowly pulls the colonoscope back with the tip in the center of the lumen, is suboptimal. Rather, as each fold, flexure, and turn is passed, an assessment must be made of how far that fold projects into the lumen and therefore how much the projection obscures mucosa on the proximal side of that structure. In general, good technique involves constant use of torque on the examining shaft with the right hand, essentially prying apart the space between haustral folds. During withdrawal, the experienced examiner can sense whether the next haustral fold will appear in the up, down, right, or left endoscopic fields by knowing whether the colonoscope tip is flexed up or down via the position of the left thumb on the up/down wheel and by the feel of the instrument shaft with the right hand. Thus, when the scope tip is flexed up and the right hand senses some resistance to withdrawal as the scope pulls on a fold protruding downward from the 12 o'clock position, the examiner can anticipate that the next fold will appear in the up direction (Fig. 30.3). By continuing or further exaggerating upward deflection, the examiner can see the mucosa on the proximal aspect of that fold. Whenever a fold or flexure is passed at a rate that does not allow careful examination of the proximal aspect of a fold, reinsertion to a point proximal to that fold, flexion in the direction of the fold, and rewithdrawal is necessary. In some cases, slight deflation of the lumen will allow the examiner to maintain the colonoscope tip on the proximal aspect of a fold or flexure for an adequate period of time to achieve inspection. My own preference is to rely on instrument torque with the right hand to achieve adequate right/left movement and to use the thumb to control up/down movement from the angulation control. Some examiners use their left thumb to also control the right/left movement, using the lateral angulation control, but I find that maneuver to be ergonomically stressful. Slow withdrawal and careful attention to the hidden portions of mucosa is the essential ingredient of careful withdrawal technique.

Occasionally, particularly in the sigmoid, an angulation is so sharp that a "redout" occurs during withdrawal and the examiner has the sense that substantial portion of the mucosa proximal to the sharp curve cannot be seen. In this case the entire turn can generally be visualized by reinsertion and viewing during insertion. The bend in the instrument shaft that develops during

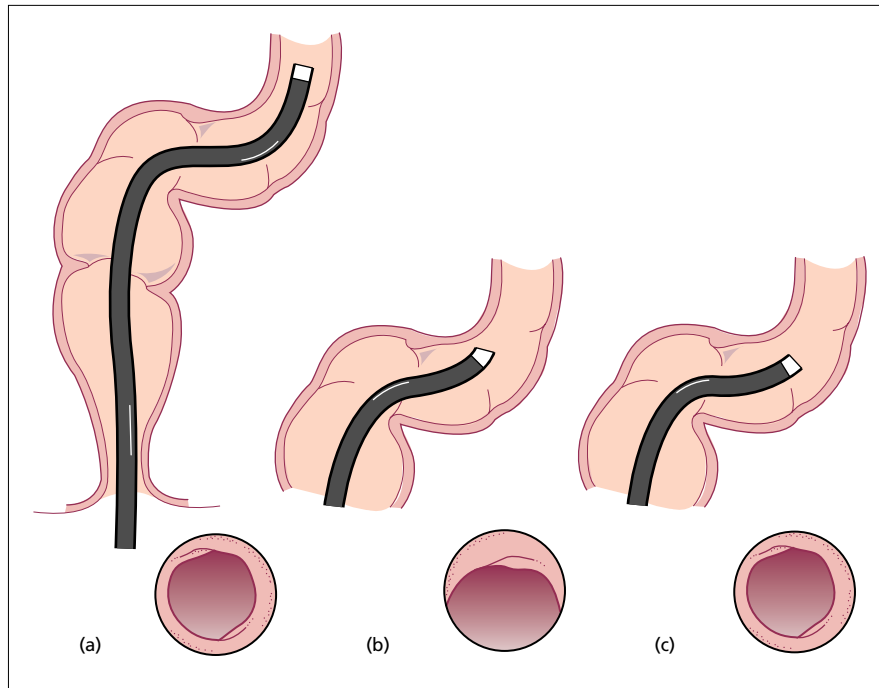


Fig. 30.3 In (a), the endoscope tip is deflected in the up direction during withdrawal. The examiner can anticipate therefore that the next fold will appear in the upper aspect of the visual field (b). This anticipation facilitates rapid downward deflection to maintain the lumen in the center of the visual field (c).

insertion usually changes the contour of the colon and exposes the lumen of the angulated colon.

The issue of distention is also important. Some experts have advocated suctioning air as withdrawal is performed. However, if examinations are performed primarily during withdrawal, then suctioning air in order to improve patient comfort can interfere with adequate examination. When colonic mucosa collapses onto another section of mucosa because of deflation, the opposing portions of mucosa can hide lesions. Therefore, adequate distention is critical. My own practice is to maintain luminal distention by air insufflation as necessary during withdrawal. If a section of colon is difficult to distend on withdrawal, it usually means that it is dependent (or down in relation to gravity), and rolling the patient even slightly into a different position may allow distention of that section. After withdrawal, I typically palpate the abdomen and if it seems distended, will quickly run the colonoscope back up to the proximal colon and then deflate and withdraw rapidly, with continuous deflation. The use of carbon dioxide for insufflation obviates the need to reinsert the scope for deflation and allows the examiner to distend adequately, without fear of postprocedural pain and distention [38].

All pools of fluid material should be suctioned. Adding water to the lumen, followed by suctioning, is appropriate when semisolid debris occludes the view. The experienced examiner develops a sense of when adherent mucus is sufficiently tenacious that it cannot be washed clear, even with repeated washing, and when it

can be readily washed free and removed. Appropriate preprocedure attention to patient instructions regarding preparation is recognized by the experienced examiner as an essential element of efficient and accurate colonoscopic examination. If areas are insufficiently prepped to allow adequate examination, photo documentation assists in the justification of a repeat procedure. In areas where solid stool is present, rolling the patient from one side to another can expose the underlying mucosa and is a reasonable undertaking if the areas of retained solid debris are isolated to small areas.

During appropriate insertion technique, the colon often becomes telescoped over the instrument shaft. Overly rapid withdrawal can be associated with slippage of a section of colon off the tip of the instrument at a rate that does not allow adequate examination. In this instance, reinsertion and reexamination is essential. During withdrawal, slight deflation and/or jiggling of the instrument with the right hand can facilitate more gradual unpleating of the colon off the colonoscope tip and ensure an adequate view of the bowel wall.

In some instances, retroflexion in the colon may be appropriate to achieve adequate examination. Retroflexion in the rectum is performed by most experts routinely (Fig. 30.4). My own practice is to first examine the entire rectum, in the forward view. The proximal sides of rectal valves are often reexamined a second time (Fig. 30.5). After examining the entire rectum adequately in the forward view, the retroflexion maneuver is performed. The instrument shaft is positioned with most or



Fig. 30.4 Typical endoscopic appearance of the retroflexed rectum.

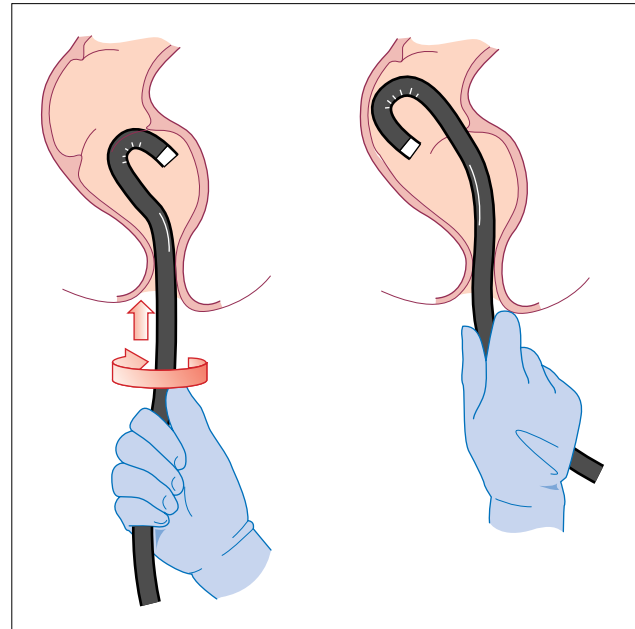


Fig. 30.6 Technique for retroflexion. With the tip deflected in the maximum up and left direction, advance and apply counterclockwise torque (left panel), resulting in a retroflexed view of the anus (right panel).

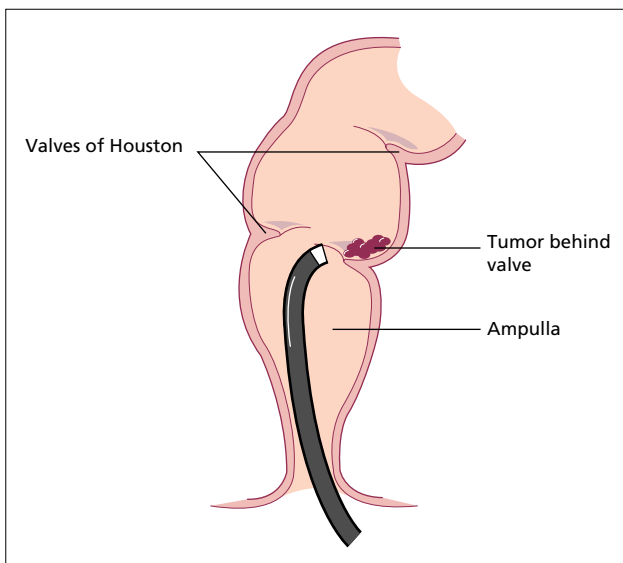


Fig. 30.5 The careful examiner looks behind haustral folds and rectal valves (as shown here).

all of the bending section just inside the anus. The instrument tip will achieve maximum retroflexion by flexing in both an up or down direction and a right or left direction simultaneously. My own practice is to flex the instrument up and to the left maximally. The right hand is then placed under the instrument shaft with the palm facing up, and the instrument is torqued to the left or in a counterclockwise direction and inserted (Fig. 30.6).

The instrument tip should not be deflected when resistance to tip deflection is apparent or when resistance to advancement and torque is felt. If the rectal lumen is very narrow (such as often occurs in chronic ulcerative colitis), retroflexion (particularly with standard scopes) may not be feasible. The utility of rectal retroflexion has been both substantiated [39] and questioned [40]. Retroflexion is facilitated by the use of upper endoscopes, which have a shorter and more compact turning radius when maximally deflected in the up and left or right direction. Thin upper endoscopes will usually allow retroflexion within the sigmoid colon and can be used to perform retroflexion in the proximal colon, though in some instances they have insufficient length to reach the cecum [41]. Retroflexion in the right colon can be readily achieved using pediatric or standard colonoscopes (Fig. 30.7) and is sometimes achievable within the cecum, allowing a retroflexed view of the ileocecal valve (Fig. 30.8). The author has experience with an Olympus prototype pediatric colonoscope with a shortened bending section (Fig. 30.9), which allows retroflexion in the cecal tip in nearly all patients [42]. Neither the safety or any benefit of routine right colon retroflexion has been demonstrated, and routine use of the maneuver cannot be recommended.

Examination of difficult to access areas has also been achieved with prototype oblique viewing instruments [43] and anecdotally has been achieved with side-viewing instruments.

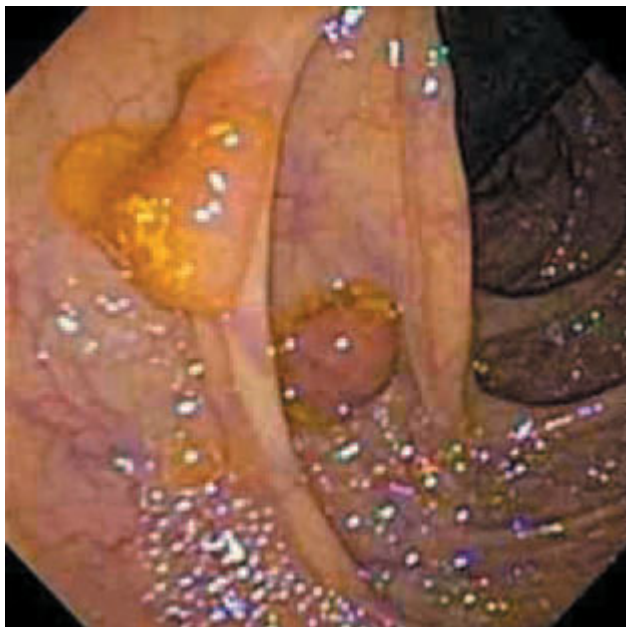


Fig. 30.7 Typical appearance of the right colon during retroflexion, demonstrating two polyps on the proximal side of a haustral fold. Only the tip of one polyp had been visible on forward view.



Fig. 30.8 Retroflexed view of the ileocecal valve, obtained with the prototype pediatric instrument shown in Figure 30.9. The instrument has a short bending section which facilitates retroflexion.

Investigational technologies to increase mucosal visualization

One method to improve colonoscopy sensitivity is to institute quality standards and continuous quality improvement programs. The US Multi-Society Task Force on colorectal cancer has published continuous quality improvement targets regarding withdrawal [37] (Table 30.3). These targets can be incorporated into continuous quality improvement programs with a goal of standardizing withdrawal technique at a minimal level that appears associated with higher detection rates.

Even with careful technique, the use of currently available commercial colonoscopes is associated with inherent miss rates, as noted above. Therefore, technical improvements in colonoscopic methodology may be needed to reduce this inherent miss rate. One such technique that has been evaluated in a small Japanese study is “cap-fitted” colonoscopy. In this technique, a clear plastic cap is placed on the end of the colonoscope (Fig. 30.10). The use of the cap does not impair cecal intubation in routine cases and may actually facilitate intubation of the terminal ileum [44]. The cap is used during withdrawal to flatten haustral folds and expose the mucosa proximal to them by flexing the cap against the haustral fold. In a study of 24 patients with polyps on barium enema, patients underwent two colonoscopies, one with the cap fitted to the colonoscope and another without. Patients were randomized to have the cap-fitted colonoscopy first or second. The miss rate for



Fig. 30.9 Photographs of a standard “adult” Olympus colonoscope (left), a pediatric colonoscope (center), and an Olympus prototype pediatric colonoscope with short bending section (right), all displayed in full retroflexion. Note the narrow diameter of the bending section with the retroflexed prototype.

adenomas without the cap was 15% and with the cap was 0%. Thus, in a single study, cap-fitted colonoscopy was demonstrated to eliminate polyp miss rates. Corroboration by additional studies and determination of the acceptability of cap-fitted colonoscopy are next important steps in the evaluation of this technique.

A second technique for potential reduction of miss rates is the use of wide-angle colonoscopy (Fig. 30.11). In

Table 30.3 Continuous quality improvement targets for colonoscopy withdrawal. (Adapted from Rex *et al.* [37].)

1 Mean examination times (during duration of withdrawal phase) Goal: withdrawal times should average <i>at least</i> 6–10 min
2 Adenoma prevalence rates detected during colonoscopy in persons undergoing first-time examination Goal: $\geq 25\%$ in men age ≥ 50 years and $\geq 15\%$ in women age ≥ 50 years
3 Documentation of quality bowel preparation Goal: 100%



Fig. 30.10 An EMRC cap on the tip of a pediatric colonoscope. The tip is flexed against haustral folds, flattening the fold and exposing the mucosa on the proximal side.

a tandem colonoscopy study in Indiana, a prototype Olympus scope with a 210-degree angle of view did not eliminate miss rates for adenomas [45]. In fact, adenoma detection rates were no different with the wide-angle colonoscope, compared to the standard colonoscope. The overall miss rate for polyps larger than 5 mm was decreased from 30% to 20% ($P = 0.046$) with the use of a wide-angle colonoscope. The wide-angle colonoscope appeared to improve detection of polyps in the periphery of the endoscopic field but was associated



Fig. 30.11 Tip of a prototype Olympus colonoscope with variable angle of view (160–210 degrees). The convex lens protrudes from the colonoscope tip.

with a reduction in sensitivity for adenomas located more centrally in the endoscopic field [45]. This reduction in sensitivity is presumably the result of reduced resolution associated with a wide-angle lens. An unanticipated observation was that wide-angle colonoscopy allowed faster withdrawal, presumably because it allows easier inspection of the proximal sides of folds, flexures, and valves. An additional potential advantage of a wide-angle colonoscope would be that no additional attachments to the endoscope are necessary, which could improve the acceptability to endoscopists. However, based on available evidence, it appears less effective in reducing miss rates than cap-fitted colonoscopy.

A third technical change in colonoscopic performance that could affect miss rates is the use of systematic dye-spraying. Uncontrolled studies of dye-spraying in western populations have demonstrated a high prevalence of flat adenomas and suggested that such lesions could not be detected without dye-spraying [46,47]. However, the definition of flat adenomas was very inclusive, in that any lesions that were more than twice as wide as they

were high were considered flat. However, some of these lesions had up to 5 mm of height. Controlled studies suggest that the principle advantage of systematic chromoscopy lies in the detection of diminutive (< 5 mm) adenomas. This was demonstrated in a randomized trial of 259 patients in the UK, in which 124 underwent systematic dye-spraying and 135 were controls [48]. The number of patients with at least one adenoma in the dye-spraying group (33%) was not different from the control group (25%; $P = 0.17$). However, the number of patients with at least one adenoma < 5 mm increased from 19% to 29% ($P = 0.056$), and the total number of adenomas < 5 mm increased from 37 to 89 ($P = 0.026$). The total number of adenomas increased from 49 in the control group to 125 in the dye-spray group and approached significance ($P = 0.06$). The actual time of examination was increased by a median of about 4 min by the use of systematic dye spraying with a spray catheter and 0.1% indigo carmine. In a study performed in the USA, 211 American patients underwent selective dye-spraying of the colon proximal to the splenic flexure and systematic dye-spraying of the left colon [49]. Two hundred age- and gender-matched controls colonoscoped by another endoscopist without dye-spraying served as controls. Examination time in the study group again increased by a mean of 4.2 min. The number of patients with adenomas ≤ 5 mm increased from 19 in the control group to 75 in the study group ($P < 0.001$), and the number of adenomas ≥ 5 mm actually decreased from 41 in the control group to 28 in the study group (a difference that was not significant). In neither of the above studies was there a difference between study and control group in detection of lesions with severe dysplasia or cancer.

Other techniques that could enhance adenoma detection and reduce miss rates are light-induced autofluorescence (see Chapter 44) and the recently described technique of molecular beacons [50]. Molecular beacons are injected compounds that are taken up specifically by dysplastic tissue and fluoresce after metabolism. Although this technique has been reported in a mouse model [50], it could potentially be adapted to endoscopic or tomographic diagnosis in humans.

At this time, it is not clear which, if any, of the above techniques will enter routine clinical practice. Wide-angle colonoscopy might be the most acceptable to endoscopists in the short run, since it does not require additional attachments to the endoscope or the use of time-consuming dye-spraying. Cap-fitted colonoscopy and wide-angle endoscopy, if they improve the detection rate of small adenomas, might be reasonably expected to also increase the detection rate of large adenomas in some hands, since they would appear to work inherently by exposing more colonic mucosa. Dye-spraying, on the other hand, does not expose more colonic mucosa but rather makes small surface defects in the mucosa more

readily apparent to the endoscopist. Thus, the potential of systematic dye-spraying to improve the detection of larger neoplasms, which are more clinically significant, remains uncertain. In the USA, techniques that decrease the efficiency of endoscopic procedures or increase the associated costs are generally not incorporated into routine clinical endoscopic practice. Thus, there will need to be clear evidence of the benefits of dye-spraying, and probably reimbursement for dye-spraying, before it can be routinely incorporated.

Summary and conclusions

Missing lesions is one of the most important adverse outcomes of colonoscopy. Detection of lesions is enhanced by spending adequate time during withdrawal and by colonoscopic technique that emphasizes careful evaluation of the proximal aspects of folds, flexures, and valves, as well as adequate distention and cleaning of fecal debris. Colonoscopists should obtain informed consent for the possibility of overlooking lesions, document their withdrawal time, document cecal landmarks in the colonoscopy report, and obtain photo documentation of cecal intubation. Because there is an inherent miss rate for colonoscopy, even with optimal performance, methods that reduce miss rates could have a significant impact on the effectiveness and cost-effectiveness of colonoscopy.

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Chapter 31

Polyp Biology

C. Richard Boland

Introduction

This chapter reviews the genetics, molecular biology, and familial aspects of adenomatous polyp development in the colon. Readers will be directed to other chapters for reviews of the epidemiology, pathology, prevalence and incidence rates, and growth characteristics of colonic polyps. The term “polyp” always refers to the adenoma, as this is clinically the most important lesion in the colon. Nonneoplastic polyps, including juvenile polyps, inflammatory polyps, and hamartomas, do not confer an increased risk for cancer unless adenomatous (neoplastic) tissue evolves within these lesions. Moreover, many of the paradigms developed for tumor development in general have been understood in the context of colorectal neoplasia, making this a cornerstone for understanding tumor biology.

Tumor genetics

Neoplasia is altered growth mediated by mutated genes. Nearly all the mutations that mediate tumor development are acquired *somatic* mutations. Somatic mutations are found within the tumor but are not present in the underlying mucosa from which the neoplasm has arisen. *Germline* mutations are present in every cell of an organism, and can be involved in conferring an increased risk for cancer. Germline mutations have been important in understanding carcinogenesis but are not commonly present in the general population of patients who develop colorectal neoplasms.

How many mutations?

The number of mutations in a tumor is highly variable. Because of “genomic instability,” some tumors may have several thousand, and perhaps tens of thousands, of unique mutations [1–3]. However, most of these mutations are not necessary for tumor development but rather reflect the hypermutability underlying the tumor [4]. One estimate of the number of mutations present in a tumor based upon direct sequencing of the DNA suggests that there were approximately 6000 point mutations in the tumor [5]. The number of muta-

tions that are essential for the development of most sporadic tumors may be relatively small, perhaps fewer than 10.

Clonality

Neoplasia is best understood in the context of clonality. Colonic epithelial cells have the same genes found in every other cell of the body. However, only a portion of these are expressed in colonic cells, giving rise to the differentiated phenotype of the epithelium. In fact, it is nearly impossible to grow colonic epithelial cells in culture because of the expression of genes that inhibit cell growth after terminal differentiation. A neoplasm begins rather inconspicuously when a genetic alteration occurs that permits a single cell to ignore the constraints on growth and to continue to replicate after it has migrated into the differentiated zone of colonic epithelium, in the upper portion of the crypt. Once cells develop selective growth advantages, they can overgrow neighboring cells and undergo clonal expansion. Unless additional genetic alterations occur, clonal expansion might be of no clinical importance to the host. However, if additional mutations occur which permit behaviors such as invasion or the complex features involved in tumor metastasis, the tumor can spread and kill the host.

Genes involved in carcinogenesis

Genes are encoded in less than 2% of the entire human genome, and most cells express only a proportion of the 30 000–40 000 genes. A minority of expressed genes are involved in regulating cell growth. Alterations in most genes will be of no benefit to the growth of a cell. Mutated genes that are critical for tumor development can be placed into two broad conceptual classes: oncogenes and tumor-suppressor genes.

Oncogenes are altered versions of normal genes (protooncogenes) that encode proteins which participate in the regulation of cell growth. Specific mutations in protooncogenes typically lead to the overexpression, or excessive enzymatic activity, of the protein, which accelerates cell growth. The best example of an oncogene in the context of colorectal neoplasia is the *K-ras*

protooncogene. This gene ordinarily serves in a signal transduction pathway required for ordinary cell proliferation. The *ras* oncogene family encodes proteins that are homologous to G proteins, which bind guanosine triphosphate (GTP) and catalyze its hydrolysis to guanosine diphosphate (GDP). *Ras* is active when bound to GTP, and specific mutations in the *ras* gene alter the ability of the *ras* protein to hydrolyze the GTP, which results in an unremitting stimulus for proliferation. This alteration leads to a cascade of events that accelerates cell growth and proliferation. Mutations in *K-ras* can be found in approximately half of all colorectal cancers; they are rarely found in tiny adenomatous polyps but mutations are detectable in proportion to the size of the adenoma [6,7]. Other oncogenes may be mutated in colorectal polyps, but none has been studied as extensively as *ras*.

A more important set of genes regulating cellular growth are the *tumor-suppressor genes* (TSGs), whose expression leads to the restraint of cell proliferation. These genes are typically silent in stem-cell populations and are expressed during terminal differentiation. The best example of a TSG in the context of the colorectal adenoma is the adenomatous polyposis coli (*APC*) gene, which is not expressed in the proliferative zone of the colonic crypt but is uniformly expressed in the upper portion of the colonic crypt. Mutational inactivation of *APC* permits colonic epithelial cells to grow and ignore signals to stop growing.

Oncogenes are activated typically by point mutations or by other rearrangements that lead to their overexpression. On the other hand, TSGs participate in carcinogenesis by inactivation. Since we have two copies of every somatic gene, biallelic inactivation of a TSG is required. In fact, inactivation of only one copy of a TSG usually has no effect on cell behavior. Inactivation of a TSG therefore requires “two hits” and, usually, the mechanisms involved in the inactivation of the two alleles are different. The requirement to inactivate both alleles of a TSG tends to make tumor development a relatively uncommon event during the lifetime of a host.

Causes of mutation

A number of different mechanisms can cause mutation; in fact, there is homeostatic balance between mutational damage to DNA and its repair. The balance can be pushed toward a higher number of mutations by either increasing the mutational rate or reducing the rate of repair. Examples of both mechanisms can be found in animal models of cancer. For example, by administering overwhelming doses of a chemical carcinogen to a rodent, one can develop a model in which colon cancer develops in nearly every animal. Likewise, by

inactivation of certain DNA repair mechanisms, one can achieve a similar outcome. The human disease xeroderma pigmentosum (XP) is an example where excessive tumor development occurs in response to a failed repair mechanism. Patients with XP lack nucleotide excision repair (NER) activity and cannot repair the damage to DNA caused by sunlight. As a result, after exposure to sunlight, patients with XP develop excessive skin injury and most will have multiple skin cancers by their early teenage years. XP is a recessive disease caused by homozygous inactivation of one of the NER genes, so every cell in the body is incapable of repairing specific types of DNA damage. The skin is the target of tumors because of sunlight.

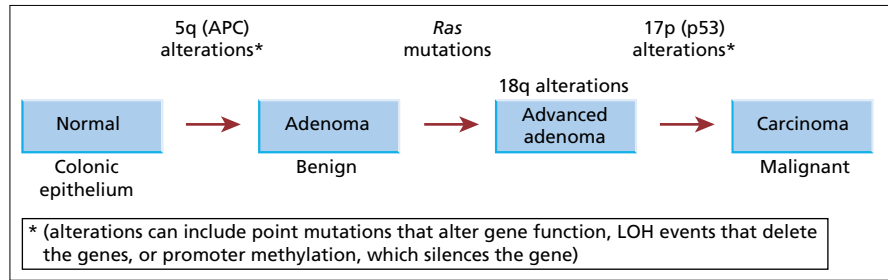
Similarly, Lynch syndrome or hereditary nonpolyposis colorectal cancer (HNPCC) is an inherited disease in which one allele of a DNA mismatch repair (MMR) gene is inactivated by mutation. However, each cell in the body still has one functioning allele and therefore intact DNA MMR activity. A second, somatic mutation to the wild-type (i.e. normal) allele will lead to loss of the DNA MMR activity in a cell and permit a very large number of mutations to occur at specific genetic sequences, and the colon is at very high risk for cancer.

Types of mutation

There are several classes of mutations that can be found in tumors. One common variety is point mutation, in which one nucleotide (i.e. T, A, C, or G) is converted to another. This can be caused by several different mechanisms, including ordinary decay of DNA, as well as chemical carcinogenesis caused by some constituents of the diet. The DNA encodes for amino acids based on a triplet code of three consecutive bases. As there are four bases, there are 64 possible triplet combinations. Since there are only 20 amino acids encoded by the triplet code, there is redundancy; several different triplets can therefore encode the same amino acids. Thus not all mutations will necessarily change the amino acid encoded, and there can be silent sequence variations without functional importance. However, many point mutations will alter the coding sequence and encode another amino acid (missense mutation), which may or may not alter the function of the protein depending on the nature of the coding alteration and its effect on protein folding and the ability of the protein to interact with other constituents in the cell. The most severe type of mutation is one that results in a premature “stop” codon, which terminates protein synthesis mRNA.

Another class of mutations that occurs particularly at repetitive sequences are those involving insertion or deletion. This results in a frameshift of the triplet reading sequence, which almost always produces a nonsense codon downstream.

Fig. 31.1 Chromosomal instability pathway was initially advanced by Fearon and Vogelstein [26], who proposed that sequential alterations in genes mediated tumor progression in the colon. This pathway identified the *APC* gene as the “gatekeeper” for adenoma formation and later the *p53* gene as the “gatekeeper” for malignant conversion. (Adapted from Boland [11].)



Chromosomal instability

One of the most common aberrations seen in colorectal cancers is aneuploidy, in which the integrity of chromosomal replication is altered. This can result in duplicated chromosomes, deleted chromosomes, and chromosomal rearrangements. This type of global nuclear aberration is referred to as chromosomal instability (CIN). Chromosomal deletions and rearrangements can lead to loss of TSGs, which is referred to as loss of heterozygosity (LOH) [8]. The mechanism for this is unknown, although it has been proposed that infection with JC virus (a DNA virus that encodes a transforming gene called T antigen) is capable of inducing CIN [9]. JC virus can be found in the majority of normal gastrointestinal tissues [10] and in nearly all colon cancers [9]. This pathway is illustrated in Fig. 31.1.

Silencing gene expression by promoter methylation

Another mechanism for loss of TSGs is their silencing by promoter methylation. About half of human genes have clusters of cytosine–guanine (CpG) sequences in their promoters. An enzyme called DNA methyltransferase can covalently transfer methyl groups to the cytosine residues. When a critical number of cytosines in the CpG “island” of a promoter are methylated, the gene is per-

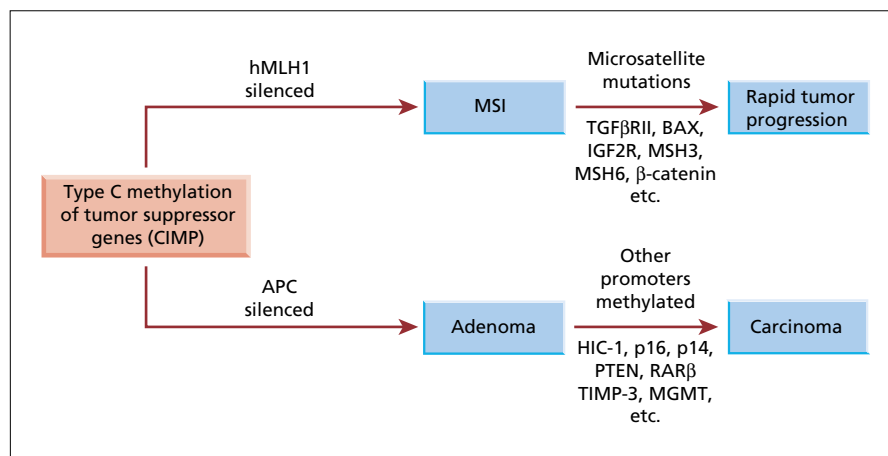
manently silenced. The methylation of cytosines is stably passed on to subsequent generations of that cell. In certain tumors, there is excessive widespread methylation of gene promoters. Such tumors are said to have the CpG island methylator phenotype (CIMP) [12] (Fig. 31.2). The mechanism for this is unknown. It is not yet clear what proportion of tumors develop via the CIMP pathway, but it may be common.

Mutational signatures

Colorectal neoplasia is the result of a heterogeneous collection of genetic abnormalities that leads to abnormal cell growth. One can characterize neoplasms based upon the predominant form of mutation found in the tumor, the “mutational signature.” Tumors with CIN are typically aneuploid, with a wide variety of chromosomal abnormalities. Some tumors show minimal degrees of CIN but are characterized by either promoter methylation (CIMP) or a large number of point mutations and insertions/deletions at short repetitive sequences called microsatellites [1]. Tumors with the latter form of mutational signature have microsatellite instability (MSI), which is caused by inactivation of the DNA MMR system.

It remains to be seen how knowledge of the mutational signatures in a neoplasm can be used to direct

Fig. 31.2 CpG island methylator phenotype (CIMP) pathway proposes that genome-wide methylation of tumor suppressor gene promoters silences these genes, which leads to tumor formation. The pathway bifurcates, depending on whether the *hMLH1* gene is silenced, in which case microsatellite instability (MSI) develops. Alternatively, tumors in the CIMP pathway will not have MSI but develop entirely on the basis of promoter methylation. (Adapted from Boland [11].)



treatment strategies to patients with polyps. However, it appears that some patients whose tumors have the CIMP phenotype have suffered inactivation of one of the DNA MMR genes (*hMLH1*) via promoter methylation, which then leads to MSI [13]. Thus, there can be overlap between the types of genomic instability. Although additional evidence is required to confirm this, it appears that neoplasms with MSI develop more rapidly and may convert from tiny adenomas to carcinomas in a time-frame of a few months, rather than several years.

Familial colon cancer

Although familial colon cancer accounts for less than 5% of all colorectal neoplasms, it plays an important role in identifying elevated risks for cancer, and these diseases have been particularly helpful in gaining an understanding of polyp biology [14].

Familial adenomatous polyposis

Familial adenomatous polyposis (FAP) is caused by a germline mutation in the *APC* gene, which predisposes the carrier to develop a very large number of adenomas at a young age. The *APC* gene has been termed a “gatekeeper gene” [15]. Inactivation of *APC* appears to be sufficient to permit the colonic epithelial cell to ignore signals from its environment to stop proliferating, which leads to clonal expansion. Ongoing proliferation of colonic epithelial cells at the top of the colonic crypt is the essence of the adenomatous polyp, as an early adenoma is a collection of colonic epithelial cells that do not properly differentiate and do not stop growing. If nothing more were to occur in these cells, they might be nothing more than trivial colonic excrescences which would occasionally become so large that they would obstruct the gut. However, because a very large number of adenomatous polyps develop in FAP, and because additional mutations may accrue in this expanding clone, these patients eventually develop cancer. The gatekeeper concept implies that loss of the *APC* gene opens the gate for ongoing proliferation. Adenomatous polyps occurring in FAP are fundamentally the same as adenomas that develop in the sporadic situation. In both instances, individual genetic lesions occur in both *APC* alleles, and these occur sequentially in time. Patients with FAP are born with one inactivated *APC* allele in every colorectal epithelial cell, which increases the likelihood of adenoma developing at an early age. Of interest, spontaneous regression of (small) colorectal adenomas has been observed in FAP, and the use of nonsteroidal antiinflammatory drugs (NSAIDs) such as sulindac and celecoxib can induce regression of adenomas in this disease [16]. It is not yet clear how these drugs can be used in patients with sporadic adenomatous polyps, but there

is very strong evidence that even casual use of aspirin and other NSAIDs can reduce mortality due to colorectal cancer [17,18].

Lynch syndrome

HNPCC is caused by a germline mutation in one of the DNA MMR genes, usually *hMSH2*, *hMLH1*, or *hMSH6* [19]. The DNA MMR system plays a “caretaker” function [15]. The presence of the one intact (wild-type) MMR allele permits normal MMR activity in the cell [20,21]. Loss of the remaining wild-type allele from a colonic epithelial cell in Lynch syndrome causes loss of DNA MMR activity and permits accelerated accumulation of point mutations and insertion/deletion mutations in simple repetitive sequences such as A_n or $(CA)_n$, which are present $> 10^5$ times throughout the genome [1]. Therefore, Lynch syndrome is mechanistically different from FAP, since FAP involves germline activation of a structural gene that restrains cell proliferation, whereas Lynch syndrome is caused by mutational activation of a gene required to maintain genomic integrity, which then permits mutations at “target genes” that actually regulate cell growth [22,23]. The genetic lesions that cause familial colorectal cancer are of clinical importance: loss of the *APC* gatekeeper in the colon gives rise to a very large number of adenomas in FAP; inactivation of the DNA MMR caretaker in Lynch syndrome permits accelerated progression of the adenoma-to-carcinoma sequence, and provides an explanation of the necessity for shorter colonoscopic screening intervals in this situation [24].

Hamartomatous polyposis

Germline mutations in the *PTEN* gene can lead to the development of hamartomatous polyps (typically juvenile polyps). The histologic features of these polyps suggest that an alteration in the lamina propria or other supportive tissues is the underlying lesion that leads to polyp growth. Thus, one can think of the development of these lesions as a result of a defect in the environment in which the epithelial cells grow, and these genes have been tentatively termed “landscape genes.”

Multistep carcinogenesis and sporadic polyps

Sporadic adenomatous polyps

Sporadic adenomatous polyps are not homogeneous lesions. Some are initiated by loss of the *APC* gene [25], followed by the sequential mutation of oncogenes and inactivating mutations at TSGs. In a classic series of papers, Vogelstein and colleagues [26,27] outlined the

sequence of events by which this takes place. They found that allelic losses in the vicinity of the *APC* gene (on chromosome 5q) in a proportion of adenomatous polyps were present in a similar ratio regardless of whether polyps were small, large, or malignant. Thus it was concluded that inactivation of the *APC* gene was sufficient to permit formation of the adenoma but *APC* loss did not directly participate in progression to a more advanced lesion. Mutations in the *K-ras* oncogene were almost never found in tiny adenomas, were present in half of larger adenomas, and in about 90% of very large villous adenomas [6,7,26]. In this instance, it was concluded that *ras* mutations mediated accelerated growth of the adenomas but were not sufficient to initiate the adenoma. Thus, *K-ras* mutations were assigned as a “second” step in the multistep process. It was subsequently found that biallelic inactivation of the *p53* gene mediated the adenoma-to-carcinoma transition [28]. Thus, two genes were given specific temporal locations in the tumor development scheme, in which *APC* inactivation marked the initiation of the adenoma and *p53* inactivation marked the conversion to carcinoma [29].

Alternative pathways for neoplastic evolution (Fig. 31.3)

Once the *APC* gene was identified as the gatekeeper for the initiation of the adenoma, detailed studies revealed additional key concepts. First, not all polyps have the same mutations. Alternate mutational mechanisms that inactivate *APC* were found in different adenomas. For example, some polyps have point mutations that create premature stop codons in *APC*; about half of tumors have LOH events that delete *APC*; other adenomas have the *APC* gene silenced by promoter methylation [30]. Varying combinations of these alterations can be found in any polyp, as both *APC* alleles must be inactivated in the adenoma. It is my opinion that all colorectal neo-

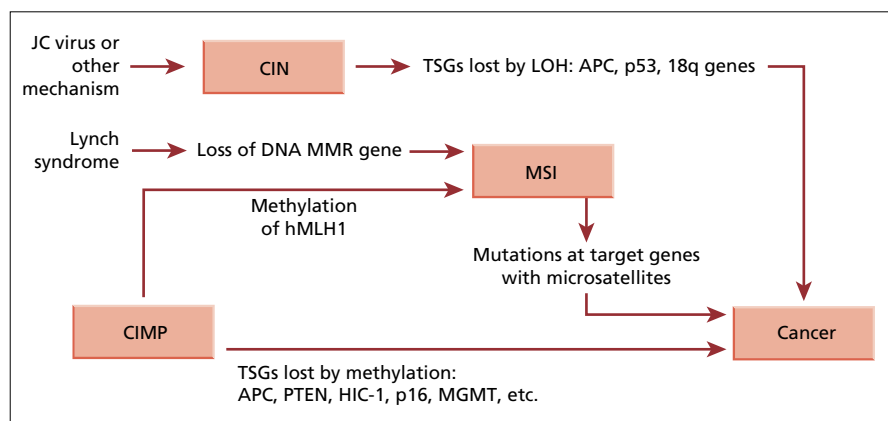
plasms begin as benign lesions, incapable of invasion or metastasis, and that progressive malignant behavior “evolves” from this by the chance occurrence of additional mutations (abetted by genomic instability). This is followed by “natural selection” of those new clones that have gained additional advantages in growth (e.g. an activating *K-ras* mutation) or survival (e.g. inactivating mutations in *p53* or *BAX*).

APC

Some adenomatous polyps have one or two wild-type copies of the *APC* gene. This conundrum was resolved when the function of *APC* was more fully understood. The *APC* gene regulates a signal transduction pathway in which the WNT ligand stimulates cell proliferation. WNT signaling leads to the expression of the β -catenin gene, which then activates a cascade of genes involved in cell proliferation; β -catenin also participates in the intercellular adhesion complex. Together, these functions lead to an increased rate of proliferation and an enhanced ability of adenoma cells to adhere to one another, as opposed to being sloughed into the lumen. When signaled to do so, the *APC* protein is produced in the developing colonic cell, which leads to degradation of β -catenin, which inhibits cell proliferation and allows the cell to die and detach from the crypt [31].

As mentioned, some colorectal adenomas have wild-type copies of *APC*. These polyps often have mutations in the β -catenin gene that prevent this protein from being degraded on interaction with the *APC* protein. Additionally, inactivating mutations have been found (albeit less commonly) in other genes that are downstream in the WNT signaling cascade, such as *WISP-3* [32]. Thus, although inactivation of *APC* is the most common way to initiate the adenoma, it is not the only way this happens. It has also been proposed that other mechanisms not requiring the WNT signaling pathway may lead to tumors [33].

Fig. 31.3 Integrating all the concepts proposed, tumors can develop via chromosomal instability, microsatellite instability (MSI), or CpG island methylator phenotype (CIMP) pathways. MSI may develop either from Lynch syndrome (the hereditary form) or via the CIMP pathway (a presumably acquired form). Ultimately, all pathways converge pathologically as cancer. (Adapted from Boland [11].)



K-ras

Similarly, not every adenomatous polyp or colorectal cancer has a mutated copy of the *K-ras* gene. Some tumors progress through the adenoma stage, develop *p53* mutations, and convert to cancers without incurring *K-ras* mutations. Colorectal neoplasms with *K-ras* mutations tend to be exophytic, while those without this mutation tend to be the flat adenomas and cancers [34,35].

p53

In this context, it is not surprising that the *p53* gene can be inactivated by multiple different pathways. The most common form of genetic inactivation of *p53* is a point mutation of one allele followed by an LOH (deletion) event in the other. Interestingly, the point mutations most commonly found in *p53* simultaneously inactivate the functional characteristics of the p53 protein and stabilize it. Therefore, immunostaining of the adenoma reveals excessive expression of p53, although the protein itself is inactive. In certain other experimental systems, *p53* can be inactivated by the overexpression of a normal cellular protein that binds and inactivates it (MDM-2), or by the presence of a viral oncoprotein such as T antigen or other transforming gene.

MSI and CIMP

As discussed earlier, some proportion of colorectal neoplasia develops via the MSI (about 12–15%) or the CIMP (uncertain proportion) pathways, and these may overlap. In many of these tumors, one may not find alterations in the *APC*, *K-ras*, or *p53* genes. It is not entirely certain how these tumors develop; however, in the presence of MSI, one frequently finds stabilizing mutations in the β -catenin gene that render it resistant to phosphorylation and inactivation in the presence of wild-type *APC* [31]. Neoplasms in the MSI pathway typically have mutations in microsatellite sequences that occur in a coding region of a critical gene required for cell growth. An example is the transforming growth factor- β receptor II (*TGF- β RII*) gene, which has an A₁₀ sequence in an expressed exon [36]. The majority of colorectal neoplasms with MSI have a single base-pair deletion mutation in the A₁₀ sequence that inactivates this gene. Tumors with this lesion fail to respond to the growth-suppressing effects of TGF- β . Likewise, the TSG *BAX* has a G₈ sequence that is mutated in a proportion of colorectal neoplasms with MSI [37]. Other genes that participate in regulating cell behavior that have a microsatellite in a coding region include the insulin-like growth factor 2 receptor (*IGF2R*) gene [38] and, curiously, the minor DNA MMR genes *MSH6* and *MSH3*

[39,40]. The exact sequence of events by which these sequences are mutated and their impact on cell growth is not understood as well as those neoplasms with CIN; however, experimental evidence indicates that the accumulation of mutations in microsatellite sequences may occur very rapidly.

Summary

Adenomatous polyps are not homogeneous lesions and are caused by mutations in genes that regulate cell growth and other behaviors. Colorectal neoplasia begins with the adenoma, which is usually caused by a lesion that abrogates the growth-restraining function of the WNT signaling pathway. This usually, but not always, is caused by inactivation of both alleles of the *APC* gene. Most colorectal neoplasms are characterized by a form of genomic instability, which permits accelerated accumulation of mutations. As the adenoma grows in the context of hypermutability, more mutations may occur, permitting successive waves of clonal evolution with progressively more aggressive growth characteristics. Our current knowledge of the genes involved in this process is expanding, and we will soon begin to tailor preventive and therapeutic strategies based upon the mutational signatures of the neoplasm.

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Chapter 32

Colon Polyps: Prevalence Rates, Incidence Rates, and Growth Rates

Bjørn Hofstad

Introduction

The malignant potential of adenomas has been recognized for more than a century [1] but most knowledge has been collected in the last 30 years. The earliest information emerged from autopsy studies, while clinical material only appeared after the advent of fiberoptic endoscopy where the whole colon may be inspected without surgical intervention. Both symptomatic and asymptomatic individuals can be investigated by flexible sigmoidoscopy or colonoscopy. Other methods may include surgical material, which is highly selective and includes mostly large polyps, and radiologic studies, in which no information on histologic type is available.

A polyp may be defined as any protuberant lesion in the mucosa. Most of the polyps in unselected material consist of hyperplastic polyps, although about 15% of smaller polyps [2] are not histologically different from the normal mucosa and have often been termed "mucosal tags." Nonneoplastic polyps, which may comprise 70–80% of unselected endoscopy material, have no malignant potential, except possibly as markers for synchronous or metachronous adenomas [3,4]. Therefore most attention has been drawn to adenomas.

The evidence that adenomas are indeed precursors of most colorectal cancers (adenoma–carcinoma hypothesis) is circumstantial and based on several observations.

- 1 High- and low-risk areas for colorectal cancer and polyps are correlated [5–7].
- 2 Both polyps and cancers are located more often in the proximal and distal part of the colon than in the middle. They are both more frequent in the left side in younger persons, with a shift toward the right side of the colon at older ages [8].
- 3 Malignancy increases with the size of the polyp, and with increasing dysplasia and villous structure of the adenoma [9–11].
- 4 Remnants of adenomatous tissue are found in a high proportion of colorectal cancers limited to the submucosa (60–85%), whereas this is found in only 7% of cases with extension beyond the serosa [9,11,12]. This has been interpreted to indicate that cancers arise in adenomas, which are destroyed as the cancer grows.
- 5 Nearly 100% of patients with familial adenomatous

polyposis (FAP) develop cancer if not treated surgically [9].

Prevalence

The results from autopsy and endoscopy studies differ in their reported prevalence rates for various reasons. More small and proximal adenomas will be detected if a pathologist can scrutinize a dissected colon in an unstressed situation, opening up folds and crevices, straightening bends for concealed lesions, or applying a magnifying lens [13–16].

The factors that lead to a postmortem examination for a deceased person vary for the different populations within a country and change over time. Prior to 1970, autopsy rates for most academic centers in the USA ranged around 40% [17]. Since then, autopsy rates have declined in many countries and is at present around 5% in the USA. This increases the selection factors so that studies from more recent times must be viewed with skepticism. Autopsies on younger individuals may overrepresent those with conditions that negatively affect the probability of having colorectal neoplasia.

The persons included in colonoscopy studies are usually symptomatic patients and will also present a selection bias. Moreover, persons who voluntarily submit to colonoscopy are likely to be more health conscious.

Autopsy studies

The first autopsy study in the USA was published in 1947 but first appeared in Europe in the late 1920s. Table 32.1 presents the prevalence of colorectal adenomas in several autopsy studies in relation to the cancer risk of the area. These studies are old and for many of these countries the cancer risk has increased considerably over the last decades. The yield of adenomas is very low in low-risk areas of the developing world, evident in large series from Colombia and Costa Rica; in the largest reported series, no polyps were found among 14 000 autopsies of South African Bantus. Even if the prevalence may be underreported, the differences in high-risk areas are considerable, reaching more than 50% prevalence of adenomas in older males. One factor that might

Table 32.1 Age- and sex-related prevalence of adenomas (%) in autopsy studies in relation to risk of cancer.

Reference	Location	Risk of cancer	Males < 60 years (* < 65 years)	Males > 60 years (* > 65 years)	Females < 60 years (* < 65 years)	Females > 60 years (* > 65 years)
Stemmerman & Yatani [18]	Hawaii, USA	High	50–67	66–70	0–70	59–63
Rickert <i>et al.</i> [19]	New Jersey, USA	High	22–33	48–70	12–42	50–63
Williams <i>et al.</i> [20]	Liverpool, UK	High	20–34*	44–52*	15–20*	35–33*
Vatn & Stalsberg [8]	Oslo, Norway	High	6–21	36–53	7–28	19–43
Clark <i>et al.</i> [7]	Aberdeen, UK	High	16–32*	44–64*	4–18*	40–48*
Helwig [21]	St Louis, USA, whites	Intermediate	4–16	23–26	9–21	17–20
	St Louis, USA, blacks	Intermediate	1	9–13	2	14
Sato <i>et al.</i> [22]	Akita, Japan	Intermediate	23	46	6	37
Correa <i>et al.</i> [23]	São Paulo, Brazil	Intermediate	5–14	30	8–14	23
Clark <i>et al.</i> [7]	Tromsø, Norway	Intermediate	15–17*	40–45*	21–15*	14–41*
Coode <i>et al.</i> [24]	Hong Kong	Intermediate	18–21	36–49	10	14–25
Clark <i>et al.</i> [7]	Kupio, Finland	Low	4–17*	4–16*	8–0*	22–11*
Sato [25]	Miyagi, Japan	Low	4	23	5	17
Correa <i>et al.</i> [6]	Cali, Colombia	Low	2–7	18	2–10	15
Correa <i>et al.</i> [23]	Costa Rica	Low	0–6	13	2–4	9
Bremner & Ackerman [5]	Bantu, South Africa	Low	0	0	0	0

affect the reported prevalence figures is that not all studies used a magnifying lens, which may increase the yield by up to 100% [22]. Conversely, applying interobserver testing of the histologic evaluation may reduce the prevalence by as much as one-third [7]. Apparently there are no ethnic differences, although a lower prevalence of adenomas was found in blacks compared with whites in the study from St Louis in 1947.

Endoscopy studies

Most of the initial colonoscopy studies were retrospective evaluations from hospital endoscopic units [26–29] and the patients included were referred for abdominal symptoms. The majority are referred for gastrointestinal bleeding, although other symptoms such as persistent abdominal pain or change in bowel habit are frequent. The symptoms might select persons with a higher prevalence of adenomas and hence not be representative of the population in general. Several sigmoidoscopic and colonoscopic screening studies of average-risk asymptomatic persons have been published, but most of them are also subject to selection bias. All but one are non-randomized; in the case of randomized invitations to participate, compliance is vital and response rate at invitation can be as low as 6% [30]. In general, participation in screening studies will be influenced by such factors as health consciousness, friends or close family with colorectal cancer, socioeconomic status, and health insurance.

Table 32.2 shows the results of sigmoidoscopy and colonoscopy screening studies of asymptomatic persons, primarily from the USA and western world. With the flexible sigmoidoscope, an insertion depth of close to

60 cm is expected, including the whole of the rectosigmoid colon, although very often the full depth of insertion is not obtained due to bowel cleansing, technical difficulty, patient discomfort, and the skill and determination of the examiner. Conversely, in 15–20% of the investigations, extension beyond the rectosigmoid junction is achieved. For the age group most often selected (55–65 years) most polyps will be distal, within reach of the sigmoidoscope, but around 40% will be proximal to this (Tables 32.2 & 32.3). However, if all persons with detectable distal adenomas are then referred for colonoscopy, a considerable portion of the proximally located lesions will also be revealed. Even then, 13–70% of patients with proximal adenoma have no distal “index” adenoma [30,32–36].

In the screening sigmoidoscopy studies presented in Table 32.2 generally low prevalence figures are quoted (1–16%), which include only the polyps found at sigmoidoscopy and not the additional ones found by follow-up colonoscopy. The exception is the study by Brady and colleagues [37], who reported a 48% yield that is largely unexplained. In this study, 45% of screenees were examined during a total colonoscopy where the authors only included the polyps of the distal 60 cm. This estimation of sigmoidoscopy yield may include too many polyps compared with an actual sigmoidoscopy.

While sigmoidoscopy is a rapid examination with little discomfort in general [38], total colonoscopy is more time-consuming, resource-demanding, and causes more discomfort to the patient as a result of both bowel cleansing and the endoscopic procedure. Therefore colonoscopy is generally considered unsuitable as a screening method. Despite these limitations, some screening colonoscopy studies have been published (Table 32.2). The

Table 32.2 Studies of neoplasia prevalence in asymptomatic screenees.* (Adapted from Neugut *et al.* [31] with permission.)

Reference	Country	Number of patients	Adenomas (%)	Group/age	Mean age (years)	Males (%)
<i>Flexible sigmoidoscopy studies</i>						
Ujaszasy <i>et al.</i> (1985)	Hungary	3863	8	County hospital, > 40 years		
Riff <i>et al.</i> (1990)	USA	329	8	Primary care practice, > 50 years	63	
Cauffman <i>et al.</i> (1992)	USA	1000	4	FOBT negative, > 45 years	61	47
Krevsky <i>et al.</i> (1992)	USA	202	12	Chemical plant employees	53	99
Matter & Campbell (1992)	USA	101	12	> 50 years	68	96
Brady <i>et al.</i> (1993)	USA	162	48	Asymptomatic, FOBT/FH negative, > 50 years	62	80
Brint <i>et al.</i> (1993)	USA	116	9	FOBT negative, > 45 years	57	76
Maule (1994)	USA	2611	11	> 45 years	60	45
Sakamoto <i>et al.</i> (1994)	USA	866	1	FOBT negative and NF > 50 years	62	44
Cannon-Albright <i>et al.</i> (1994)	USA	206	14	FH negative, > 25 years, males	52	100
Cannon-Albright <i>et al.</i> (1994)	USA	200	6	FH negative, > 25 years, females	52	0
(2002)	UK	20 519	16	Males, recruited from GP practice, 55–64 years		100
(2002)	UK	20 155	8	Females, recruited from GP practice, 55–64 years		0
<i>Colonoscopy studies</i>						
Johnson <i>et al.</i> (1990)	USA	90	21	Armed forces and dependants, > 50 years	65	68
Rex <i>et al.</i> (1991)	USA	210	25	Asymptomatic, average risk, 50–75 years		71
DiSario <i>et al.</i> (1991)	USA	119	41	FOBT and FH negative, 50–79 years	64	100
Lieberman & Smith (1991)	USA	105	41	FOBT negative, > 50 years	64	100
Guillem <i>et al.</i> (1992)	USA	83	8	Asymptomatic, average risk, 31–78 years	55	55
Rex <i>et al.</i> (1993)	USA	621	25	Healthcare professionals/spouses, 50–75 years	60	62
Brady <i>et al.</i> (1993)	USA	162	55	FOBT and FH negative, > 50 years	62	80
Thiis-Evensen <i>et al.</i> (1999)	Norway	109	47	Population randomized, males, 63–72 years	67	100
Thiis-Evensen <i>et al.</i> (1999)	Norway	84	38	Population randomized, females, 63–72 years	67	0
Lieberman <i>et al.</i> 2000	US	3121	38	Recruited from medical centers, > 50 years	63	96

* For details of individual studies, readers should consult reference 31.

Table 32.3 Anatomic distribution of colorectal adenomas in autopsy studies.* (Adapted from Neugut *et al.* [31] with permission.)

Reference	Country	Sex/race	Number	Cecum (%)	Ascending colon (%)	Transverse colon (%)	Descending colon (%)	Sigmoid colon (%)	Rectosigmoid colon (%)	Rectum (%)
Helwig (1947)	USA	Male	139	10	14	18	8	31	19	19
Helwig (1947)	USA	Female	—	16	24	10	6	27	16	16
Correa <i>et al.</i> (1972)	Colombia		35	46	—	—	—	10	—	—
Stemmerman & Yatani (1973)	USA		125	10	34	22	11	15	1	1
Sato (1974)	Japan		89	2	41	23	15	13	2	2
Sato <i>et al.</i> (1976)	Japan		90	4	42	20	18	8	3	3
Correa <i>et al.</i> (1977)	USA	Black	146	10	44	22	6	12	3	3
Correa <i>et al.</i> (1977)	USA	White	57	7	40	21	6	9	5	5
Marigo <i>et al.</i> (1978)	Brazil	Male	52	67	—	—	28	—	—	—
Marigo <i>et al.</i> (1978)	Brazil	Female	52	51	—	—	39	—	—	—
Vatn & Stalsberg (1982)	Norway		148	19	12	25	14	9	12	12
Clark <i>et al.</i> (1985)	UK/Norway/ Finland		174	28	—	28	15	21	—	—
Coode <i>et al.</i> (1985)	Hong Kong		60	17	21	17	11	13	12	12
Bombi (1988)	Spain		46	8	21	27	7	29	8	8

* For details of individual studies, readers should consult reference 31.

number of persons with adenomas in these studies is strikingly higher than the 20% increase expected from the figures found in the sigmoidoscopy studies. The prevalence ratio ranges from 21 to 55%, with the excep-

tion of one study [39] that included a smaller number of participants, a lower male ratio, and mean age lower than the rest of the studies. The colonoscopy studies are generally male dominated and there might be a

Table 32.4 Anatomic distribution of colorectal adenomas in endoscopy studies.* (Adapted from Neugut et al. [31] with permission.)

Reference	Study period	Country	Number	Cecum (%)	Ascending colon (%)	Transverse colon (%)	Descending colon (%)	Sigmoid colon (%)	Rectosigmoid colon (%)	Rectum (%)
Shinya & Wolff (1979)	1969–79	USA	6942	13	—	12	23	46	—	6
Gillespie et al. (1979)	1972–79	UK	275	8	—	14	19	47	—	13
Granqvist (1981)	1969–76	Sweden	264	20	—	36	—	44	—	—
Fruhmorgen & Matek (1983)	Before 1983	Germany	1280	2	8	4	15	48	—	25
Webb et al. (1985)	1975–82	USA	274	13	—	12	21	—	53	—
Bat et al. (1986)	1980–84	Israel, Ashkenazi	279	9	—	21	52	—	—	19
Wegener et al. (1986)	1982–85	Germany	282	4	13	18	17	24	—	21
O'Brien et al. (1990)	1986–88	USA	2362	8	14	10	18	43	—	8
Thiis-Evensen et al. (1999)	1996	Norway	203	6	13	19	16	18	—	28

* For details of individual studies, readers should consult reference 31.

considerable selection bias, as the method of recruitment and the number that declined to participate is often not stated. In a study from Norway [40] the subjects invited were randomized from the population registry and 60% attended, which is considered a high rate.

Age and sex

In autopsy studies [7,8,19], there is an increase in adenoma prevalence with age for both men and women, with very low figures for persons under 50 years of age (although high prevalence was reported from Hawaii). The prevalence steadily increased for each 10-year age group to more than 50% in high-risk areas and 15–20% in low-risk areas, for males. An exception was found in the Oslo study, where the middle age group of women had a reduced prevalence. An age increase is also confirmed in the colonoscopy studies [33,34,41], with increasing prevalence from 21–28% in the age group 50–59 years to 53–58% in the age group > 70 years. As people live longer, the age-related prevalence will have some implications for the total prevalence in a community. In some studies an increased size of the adenomas with increasing age has been demonstrated [8,20], although this was not confirmed in others [19,22].

Contrary to a 1 : 1 sex ratio for the incidence of colorectal cancer, the prevalence of adenomas is higher among men in all age groups, approaching a 1 : 2 ratio in some studies [24,42], both in high-risk [20] and low-risk [23,25] areas. The sex difference is most consistent in the middle age group (60–69 years). The shift from male-dominated prevalence of colorectal adenomas to an equal ratio for cancer is puzzling. One might speculate as to whether women harbor more malignant polyps. A higher proportion of large and dysplastic adenomas was seen in women in an autopsy study [8]. Contrary to this, in clinical studies a lower proportion of large or dysplastic or multiple adenomas has been observed

in women compared with men [40,42]. A higher rate of malignant transformation of adenomas in women can only be explained by sex-related factors.

Subsite distribution

Tables 32.3 and 32.4 present autopsy and endoscopy studies showing the anatomic distribution of adenomas in the colon. The autopsy studies generally predate the endoscopy reports and the age groups are not properly defined in many. Autopsies are more precise in defining the correct segment localization, which is often incorrectly judged during endoscopy. The existing endoscopic studies are all from symptomatic patients in hospital endoscopic units, except one [40] that is population based and randomized, although the distribution is not essentially different from the others. Autopsy studies [8] have clearly demonstrated a marked preponderance of adenomas on the left side in the age group < 60 years, with a shift to the right side in the age group > 70 years and a more even distribution in the middle age group. This holds true for both men and women but is less evident in the latter. The middle part of the colon, represented by the transverse colon, is the area harboring the least adenomas. The distribution of large and villous adenomas is similar. Hyperplastic polyps show the same age shift as adenomas for men but are more evenly distributed in women in all age groups. Age differences in the material from the different studies may account for some of the variations, although a high proportion of right-sided polyps was found in the material from Colombia and Brazil [6,43], where the data are expected to include younger persons. Subjects belonging to families with high risk of colorectal cancer (hereditary non-polyposis colorectal cancer, HNPCC) have an increased tendency to right-sided polyps (and cancer).

In endoscopic studies, which usually have a higher proportion of smaller polyps, the smaller adenomas

Characteristic	UK*	USA†	Germany‡	USA†	Norway‡
< 5 mm	} 60		45	38	69
5–9 mm		40	22	36	24
10–20 mm	23	46	17	} 26	} 7
> 20 mm	17	14	16		
Severe dysplasia	8	12	4	6	2
Villous components	25	35	27	13	8
More than one adenoma	8	17	—	45	27

* Surgery/rigid endoscopy material [9].

† Hospital routine endoscopy material [10,11,47].

‡ Randomized colonoscopy screening material [40].

(< 5 mm) occur more often in the rectum, whereas the sigmoid colon has more middle-sized (5–9 mm) and larger (> 9 mm) adenomas [40].

The age shift in anatomic distribution of polyps has also been observed for colorectal carcinomas [44,45], as have correlated time trends [46] between the two, and this forms some of the evidence for the adenoma–carcinoma sequence hypothesis. The highest proportion of left-sided cancers are actually located in the rectum, constituting 30–40% of all colorectal cancers; however, most studies place the bulk of the polyps in the sigmoid colon. If the rectosigmoid junction area were treated as a separate entity, some of this difference would be nullified.

Size, dysplasia, and villous structure

The first large report to show the size, dysplasia, and villous structure of adenomas and their interrelationships was published in 1975 [9], later supplemented by large endoscopic studies. The work by Muto and colleagues consists of material from surgery or rigid endoscopy, and would favor large polyps. To a lesser degree this is true for retrospective hospital studies. In a randomized study with average-risk persons [40], more than two-thirds of the adenomas were less than 5 mm in diameter (Table 32.5). High-grade dysplasia and villous components (tubulovillous and villous adenoma) were rare in the reported series. In addition, 46% of all polyps removed were hyperplastic and 23% were mucosal tags, so that nearly three-quarters of the polyps were nonneoplastic.

The studies have demonstrated a clear relationship between the size of adenomas, villous architecture, grade of dysplasia, multiplicity, and rate of malignant transformation [9–11]. While polyps < 1 cm are hardly ever malignant, up to 50% of those > 2 cm are malignant (Table 32.6). Tubular adenomas are malignant in 4–5% of cases, while the malignancy rate for villous adenomas is 40–50% [9]. This may be partly due to the observation that 86% of the villous adenomas are more than 1 cm in

Table 32.5 Prevalence (%) of polyp characteristics.

Table 32.6 Relationship between size and risk of malignancy of colorectal adenomas based on clinical and autopsy material. (Data from references 9, 10, 48, 49.)

Polyp diameter (mm)	Malignancy (%)
< 5	~ 0
5–9	0.9
10–20	5–10
> 20	10–50

diameter. The rate of malignancy increases from 6% with mild dysplasia to 35% with severe dysplasia. Moreover, malignancy appears in 8% of adenomas when these are single but in 29% of patients when they have six adenomas [10], although multiplicity is the factor least correlated with malignant transformation compared with other polyp characteristics.

The National Polyp Study clearly demonstrated the increased risk of polyps containing high-grade dysplasia in older patients, and in patients harboring medium-sized and large adenomas, while the presence of multiple adenomas was not a separate risk factor [47].

Polyps may be pedunculated or sessile in appearance. Very few small polyps are pedunculated, while 41% of large and left-sided polyps have this characteristic [50]. It is not possible to judge the histologic type from the macroscopic appearance alone, except that histology is correlated with the size of the polyp [2], since small polyps (< 0.5 mm) are likely to be nonneoplastic, while only 16% of hyperplastic polyps grow beyond this size [51]. In expert hands, however, inspection of the pit pattern using high-resolution chromoendoscopy with indigocarmine dye may reliably separate neoplastic from nonneoplastic polyps [52].

Multiplicity

Multiple adenomas appear to a varying degree (see Table 32.5). The larger recent studies report a frequency of 35–45% among adenoma-bearing patients [47,53,54].

Autopsy studies demonstrate an increased multiplicity of adenomas with increasing age of patients in different parts of the world [7,8,19,20,23]. The tendency to multiplicity may be more pronounced in high-risk than low-risk areas [18]. A higher degree of multiplicity has also been documented for males compared with females.

Multiple adenomas may be spread over the total colorectum; however, two studies have demonstrated a significant spatial clustering, increasing the chance for two polyps to be located in the same or a neighboring segment [55,56], although this was not true for rectal polyps.

Risk factors for adenoma prevalence

Age and male gender have already been discussed as risk factors. One sigmoidoscopy study [57] and one colonoscopy study [39] have found family history of colorectal cancer as a separate predictor for adenoma prevalence, although this is not substantiated by others [30,34,40]. In case-control studies kindreds of colorectal cancer patients have a relative risk of around 1.5–2 for prevalence of adenomas [39,58,59]. Smoking as a risk factor has been found in most studies [60–63], although the data on alcohol are not consistent [64–66]. Regular aspirin users may have a lower prevalence of polyps [67].

The role of dietary factors, body mass index (BMI), and physical inactivity, which have been thought to account for most of the difference in prevalence of

colorectal cancer and adenomas between the developing and the industrial countries, is not well substantiated [68,69].

High BMI and fat intake [68,70–72] has been found to be associated with increased polyp prevalence. A reduced prevalence has been found with high intake of dietary fiber [68,71,73], carbohydrates [70,71], vitamin A [74], vitamin B₆ [73,75,76], vitamin C [73], folic acid [73,76], magnesium [73,75], zinc [73], and iron [70].

Incidence

The term “prevalence” rather than “incidence” should be applied to the individual who has an adenoma detected for the first time, since the adenoma has been present for an unknown period of time because polyps (with the exception of some large polyps) do not cause symptoms. Knowledge of polyp incidence or new polyp formation must be collected from follow-up studies after a colon has been inspected and certified free from polyps.

Postpolypectomy incidence

For more than 20 years it has been common in western countries to perform regular endoscopic follow-up after polypectomy of adenomas, and therefore a large number of studies from initially symptomatic patients with index adenomas have been published (Table 32.7).

However, patients with adenomas may have a higher biologic potential for new polyp formation, giving a

Table 32.7 Adenoma incidence (recurrence) in symptomatic patients after polypectomy.

Reference	Country	Number of patients	Recurrence rate (%)	Mean follow-up (years)	Follow-up period (years)	Comments
Henry <i>et al.</i> [77]	USA	154	30	7		Sigmoidoscopy and barium enema
Waye & Braunfeld [78]	USA	133	56	1		
Morson & Bussey [79]	UK	1697	18	5		Follow-up method not stated
Neugut <i>et al.</i> [80]	USA	118	15–39	2.2	1 to > 3	
Wegener <i>et al.</i> [81]	Germany	66	32–54	2.6	1 to > 3	
Kronborg & Fenger [82]	Denmark	552	16	4	4	
Holtzman <i>et al.</i> [83]	USA	49	50		1–4	
Nava <i>et al.</i> [84]	USA	44	59	2.8		
Olsen <i>et al.</i> [85]	USA	500	26	4.4	1–10	Including nonneoplastic polyps?
Eckardt <i>et al.</i> [86]	Germany	220	32	4.3		Only polyps > 1 year included
McKeown-Eyssen <i>et al.</i> [87]	Canada	137	46	2	2	Intervention with vitamins C and E
Yashiro <i>et al.</i> [88]	Japan	58	29			Different follow-up intervals
Woolfson <i>et al.</i> [89]	Canada	109	50	1	0.9–1.5	Including nonneoplastic polyps?
Winawer <i>et al.</i> [90]	USA	973	30	3.2		
Triantafyllou <i>et al.</i> [91]	Greece	44	36	2	2	
van Stolk <i>et al.</i> [92]	USA	479	35	3	3	Intervention with antioxidants; only polyps > 1 year included
Alberts <i>et al.</i> [93]	USA	1303	49	3	3	Intervention: fiber supplement
Schatzkin <i>et al.</i> [53]	USA	1905	40	3	3	Intervention: high-fiber, low-fat diet
Bonithon-Kopp <i>et al.</i> [54]	Europe	552	16	3	3	Intervention: calcium/fiber supplement

higher rate of subsequent polyps than in persons without polyps. Moreover, the risk of overlooking polyps at index colonoscopy is far greater where one or more polyps are present. The miss rate of polyps at colonoscopy is discussed in Chapter 30. When a polyp is missed at index colonoscopy, it will appear as a recurrence at follow-up examination. This will lead to an overstatement of the true incidence rate in this subpopulation. Partly to make up for this, one study [78] included a “clean colon” at the start, which entailed a colonoscopy performed 1 year after polypectomy, where no polyps were detected. Subsequent follow-up 1 year later resulted in a lower recurrence for those with baseline single polyps (13%) but not for those with multiple polyps (80%), as compared with another group (56%) 1 year after polypectomy without an intermediate clean colon. Other studies have performed a repeat colonoscopy after 1 year, excluding those polyps as overlooked at the initial examination [86,92].

There is a wide variety of adenoma recurrence rates reported, although most surveillance studies state that the range is 30–50% after a mean or median follow-up period of 1–4 years. Four recent large intervention studies report no effect of the intervention medication, except for a nonsignificant beneficial effect of calcium and slight promoting effect of fiber in the European study [54]. This latter study reports a lower recurrence rate than most others.

In some studies the patients have undergone multiple follow-up endoscopies, and in these the first examination detects more polyps than the succeeding ones. This may imply that some polyps, detected in the first follow-up, are in fact overlooked at the index examination. In all cases the new polyps at follow-up are smaller in size and

with a more benign histology than at index colonoscopy. It has been argued that if a large polyp with advanced histology is detected after a short interval, it must certainly have been overlooked at the previous examination, judging from present knowledge of polyp growth rates. Even with repeated endoscopy, there is a possibility of missing polyps, even those of a significant size. On the other hand, even if most polyps grow very slowly or hardly at all in 3 years [16], it may be that some unusual ones can evolve with an explosive growth pattern.

In one study newly developed polyps were detected in 81% of patients in the same segment as the index polyps [84], while others report a higher frequency in the proximal part of the colon compared with the index examination [16,89], a finding more in line with the known age shift of polyp distribution.

More important than the recurrence of small tubular adenomas with low-grade dysplasia is the detection of significant lesions at follow-up. Significant or advanced lesions are often defined as adenomas either > 1 cm in diameter (with villous components) or with high-grade dysplasia, in addition to, of course, invasive carcinoma.

Significant lesions are not often found on follow-up colonoscopy. The National Polyp Study found pathologically advanced adenomas in 2.9% compared with 29.5% for any adenoma, but in this study villous elements were not included. Two other reports found advanced adenomas, including villous elements, in 6.6% [94] and 11.4% [91].

Incidence in polyp-free individuals

Information on polyp incidence in individuals who were initially polyp-free is less available. Table 32.8 shows

Table 32.8 Adenoma incidence in asymptomatic and symptomatic screenees.

Reference	Country	Number of patients	Adenomas (%)	Group/age	Follow-up interval	Mean age (years)	Males (%)
<i>Flexible sigmoidoscopy studies</i>							
Riff <i>et al.</i> [95]	USA	257	5	Asymptomatic, FOBT negative	1 year	64	
Riff <i>et al.</i> [95]	USA	140	6	Asymptomatic, FOBT negative	2 years	65	
Brint <i>et al.</i> [96]	USA	101	1	FOBT negative, > 45 years	1 year	58	45
Maule [97]	USA	894	5	Asymptomatic, FOBT negative, > 45 years	30–53 months	60	42
Krevsky & Fisher [98]	USA	64	8	Chemical plant employees, > 40 years	Mean 17 months	54	99
Rex <i>et al.</i> [99]	USA	259	6	Asymptomatic, FOBT negative, > 45 years	Mean 41 months	60	90
Platell <i>et al.</i> [100]	Australia	361	8	60–69 years	5 years		
<i>Colonoscopy studies</i>							
Hixson <i>et al.</i> [101]	USA	11	36	Symptomatic patients	2 years		98
Squillace <i>et al.</i> [102]	USA	29	41	Symptomatic patients	5.7 years	63	97
Neugut <i>et al.</i> [103]	USA	99	24	Symptomatic patients	Mean 36 months	61	47
Rex <i>et al.</i> [104]	USA	158	27	Asymptomatic, average risk, 50–75 years	Mean 66 months	66	66
Thiis-Evensen <i>et al.</i> [105]	Norway	178	33	Population randomized, 64–69 years, index examination sigmoidoscopy	13 years	67	46

FOBT, fecal occult blood test.

seven follow-up sigmoidoscopy and four colonoscopy studies of persons without a previous history of colorectal polyps who were free of polyps at index endoscopy. The recurrence figures are consistently low in the sigmoidoscopy follow-up reports, and are remarkably different from the colonoscopy studies. It is apparent from the sigmoidoscopy reports that repeated sigmoidoscopy in persons with previous negative examinations is not very cost-effective.

The incidence rate for colorectal adenomas in the four studies of subjects with a polyp-free colon at enrolment varies from 24 to 36%, which is somewhat but not considerably lower than the recurrence rate after polypectomy. In one study [101], patients were involved in a tandem colonoscopy project, in which two examinations by different endoscopists were performed in the same session to evaluate the miss rate of colorectal polyps. Eleven of these patients with "clean colons" were re-examined 2 years later, where polyps were detected in four (36%). Studies such as this are of particular value as a clean colon at baseline was certified to a higher degree than in other studies. In the study by Neugut and colleagues [103], 99 patients with a prior negative colonoscopy from different clinical practices were reexamined 3 years later, finding incident polyps in 24%. In another group of 178 patients who had undergone prior polypectomy, 46% incident polyps were detected during the same follow-up period. However, this latter group was 5 years older, with a higher male ratio. In a parallel setting to the previous study, Squillace and colleagues [102] found an adenoma incidence of 41% in 29 patients. Rex and colleagues [104] reexamined a subset of colonoscopy screenees who had participated in a previous prevalence study [30]. The participants were asymptomatic, average risk, and tested negative on occult blood, and the follow-up interval was 4–7 years (mean 5.5 years). The incidence rate in this study was 27%. Finally, sigmoidoscopy screenees, randomly selected from a population registry in a polyp growth study, were reexamined by colonoscopy 13 years later [105]. Only those with polyps went on to colonoscopy at baseline. A total of 178 persons with negative sigmoidoscopy at baseline had 33% new adenomas, comparable to 37% in a randomly selected control group not previously examined but less than those who had polyps detected and removed 13 years previously (63%).

Risk factors for polyp incidence (post polypectomy)

The risk factors for adenoma recurrence have been amply evaluated. Multiple polyps at index endoscopy is a consistent risk factor for new adenomas. It is logical to anticipate that these patients have a higher biologic potential to develop polyps than those with a single polyp. However, in the case of multiple polyps, the risk

of overlooking some at index examination is far greater, reducing the true risk of recurrence. Nevertheless, both probabilities make a case for closer surveillance intervals of those with multiple adenomas.

Other risk factors for polyp recurrence have been reported less consistently. Although the National Polyp Study found by multivariate analysis, in addition to multiplicity, that increased risk exists in the presence of a medium-sized or large adenoma and when patients are > 60 years of age, this has been supported by very few others [106]. Other studies [77,92,106] have found villous/tubulovillous adenomas to be a risk factor.

Increased recurrence of polyps after polypectomy has been found in smokers [107] and in patients with high intake of fat and total fiber [74]. In intervention studies, vitamin C supplementation produced polyp reduction [108] or reduced polyp volume [109] in patients with FAP and ileorectal anastomosis. The same has been found with sulindac, a nonsteroidal antiinflammatory drug, in open intervention studies [110–112].

Of the three intervention studies examining the effect of antioxidant vitamins on sporadic polyp recurrence [87,113,114], only one reported a significant reduction in recurrence of polyps with a combination of vitamins A, C, and E [113]. Another three adenoma recurrence intervention studies have recently been published, two of them giving supplementation with wheat bran [93] and calcium or ispaghula [54] for a period of 3 years, and the third giving intensive counseling in a diet that was low in fat and high in fiber. Only the European study found an effect of intervention, calcium being nonsignificantly protective, with a weak but significant promoting effect of fiber supplementation.

The National Polyp Study [90] found baseline multiplicity of polyps to be the only risk factor for advanced adenomas at follow-up. This was supported by Triantafyllou and colleagues [91], while van Stolk and colleagues [92] did not detect any significant risk factors.

Growth

Most colorectal cancers are believed to arise in preexisting adenomas through a multistep process of genetic events, which implies that malignant transformation may occur after an accumulation of at least five significant genetic faults [115]. A small polyp may grow for a period of perhaps 10–15 years before it is transformed into a malignant growth. Generally polyps are discovered earlier in life than cancers, by a period of at least 4 years [9,85]. The exact time from the formation of a polyp and its progression to cancer to onset of symptoms is uncertain. Polyps > 1 cm in diameter followed by X-ray show a cumulative risk of malignancy at the polyp site of 24% after 20 years [116]. Small adenomas are hardly ever malignant, whereas the malignant potential

increases with the size of the polyp [9,10,48,117] (see Table 32.6). This makes the growth rate of colorectal polyps an interesting issue. However, as studies on polyp growth are a cumbersome task, few studies exist.

An approximate evaluation of growth rate might be estimated from the time elapsed after a clean colon by colonoscopy to the discovery of new, size-estimated, polyps. This would, however, tend to overestimate growth rate. Polyps are frequently missed at colonoscopy, and many newly discovered polyps have been previously overlooked. Besides, it is not possible to know when the actual initiation of the polyp occurred. Moreover, polyps having a regression in size will not be included.

Another indirect method of investigating dietary or chemotherapeutic effects on the growth of colorectal polyps may be to evaluate the effect on the incidence of small and large polyps. One could argue that an effect on prevalence of large polyps, that was not seen on small polyps, is in fact affecting polyp growth.

The best method for evaluation of growth rate of polyps is to leave the polyp *in situ* and to measure the size of the polyp at regular intervals. This requires a reliable method for size estimation of polyps *in situ*. Moreover, the problems involved in such studies need to be discussed.

Estimation of polyp size

Precise measurement of polyps *in situ* is mainly an issue when polyps are left for studies of polyp growth. Otherwise, polyps would be best measured with a ruler or caliper after polypectomy and removal. However, smaller polyps < 5 mm in diameter are often removed with hot biopsy and would tend to disintegrate if removed by snare resection, making measurement afterwards impossible.

In clinical practice, polyp size has mostly been stated as an educated guess based on visual estimation or comparing the polyp with an open or closed forceps. The validity of these measurements has been tested in latex colon models with ball bearings of different sizes [118] or plastic molds of artificial polyps [119], where there is a consistent underestimation of 20–30% regardless of skill and training of the endoscopist. Measurements of artificial ulcer models also report an average underestimation of size of 42% [120]. The latter study used an image-processing system to correct for lens distortion and thus reduced the average underestimation to 1.8%.

Applying the open forceps method in the human colon resulted in a consistent overestimation of polyp size (average 18%) compared with postpolypectomy measurements, both for smaller (< 5 mm) and for intermediate (5–10 mm) polyps [121,122]. It appears that visual estimation of polyps without object comparison is

equally good, or may be even more accurate, than the open forceps method [123].

The reason for the consistent difference in size between artificial models and the human colon, as evaluated by the open forceps method, is speculative [121,124]. The extracted polyp, measured with a ruler or caliper, may have changed in size and shape compared with the time before polypectomy. Snare resection may shrink the tissue as a result of cauterization, especially small sessile polyps. Moreover, at the start of a snare polypectomy venous congestion is obvious, followed by vascular collapse at the final transection, a process that could lead to an unpredictable increase or decrease in polyp volume. In addition, the polyp graspers may deform the polyp and alter the largest diameter during extraction. This would be even more exaggerated if the polyp were brought out through the biopsy channel. Polyp size is not significantly altered by formalin fixation [121,122].

Endoscopic conditions are widely different in the artificial model and the live colon. Technical endoscopic difficulties are numerous in the live situation. Insufficient bowel cleansing is probably the most important cause of missed polyps. Frequently, it is difficult to view the polyp fully when hidden behind folds, inside of curvatures, or behind flexures. Contractile movements may make the situation difficult: a soft polyp changes shape during contraction. The polyp may even alter its shape somewhat if the bowel is insufflated with large amounts of air. Finally, the time spent with the polyp in full view may sometimes be too short for adequate measurement of the diameter.

The endoscopic lens is wide-angled to improve peripheral view. This introduces a distortion, so that the 1-mm units may be reduced by 10% at the periphery compared with the center of the view [125]. This can be corrected by image-processing methods, which will reduce measurement errors when applying the open forceps method [120]. In practice, the measuring device and polyp should be placed close to each other in the center of the picture (Fig. 32.1). Moreover, it is important to place the measuring device at the same distance from the endoscope as the polyp, preferably at the middle of the polyp. In large polyps great variation in diameter readings will occur, whether the measuring device is placed in front or behind the polyp.

The optimal *in situ* measurement of colorectal polyps is achieved with a linear measuring probe positioned at 90° to the direction of sight (Fig. 32.1). The scale units should be in either 1- or 2-mm divisions. One prototype (Polyprobe) [16] is 12 mm long; this is preferable to a longer one, which may be too long to rotate into proper position in the narrow sigmoid colon. Since *in situ* measurements of polyps are mainly needed for studies of polyp growth, 12 mm is sufficient, as follow-up of polyps

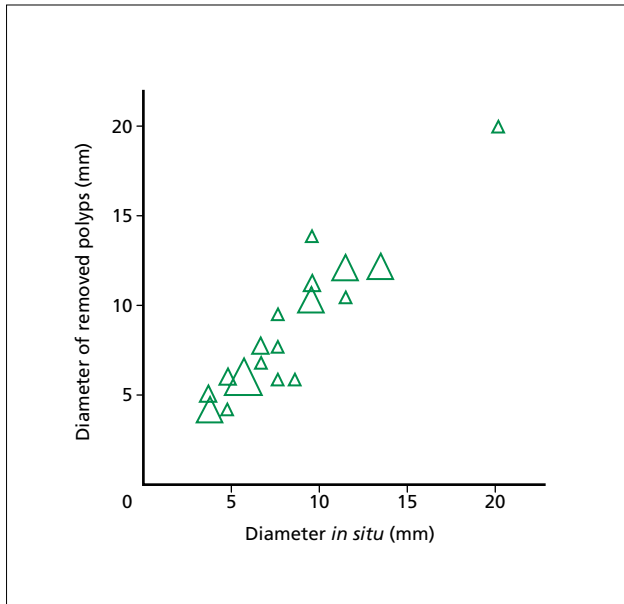


Fig. 32.1 Correlation between diameter measured *in situ* and diameter measured after removal of the polyp (larger points indicate exact overlaps); $n = 36$, $r = 0.94$. (From Hofstad *et al.* [124].)

larger than 10 mm cannot be accepted for ethical reasons. Moreover, it is technically more difficult, at times impossible, to maneuver larger polyps into full view, a necessity for a correct reading.

The reliability of *in situ* measurements with a linear measuring probe supersedes other methods [123–125] (see Fig. 32.1) and is equally good for fiberoptic and video systems [125]. The correlation coefficient for comparison of diameter measured *in situ* and after polypectomy exceeds 0.9 [124,125] (see Fig. 32.1). Moreover, the correlation coefficient between diameter to the third power measured *in situ* and weight of the polyp is more than 0.9. In another study, Gopalswamy and colleagues [126] compared the three working methods for *in situ* polyp size evaluation with ruler measurement of the resected polyp and showed a mean difference vs. the actual size of 3.4% for the linear probe, 6.4% for visual estimation, and 12.3% for the forceps.

If a picture of the polyp is taken with the measuring probe in position, an alternative size evaluation to linear measurement can be made. Using computerized image analysis, the area of the polyp on the picture can be calculated. Ideally, this would provide a more sensitive growth estimation, as polyp growth is three-dimensional and a small increase in diameter may double the volume. However, this measurement was shown to correlate less well with the weight and volume of the removed polyp than the linear measurement [124,125]. This may have been caused by problems in maneuvering the probe and polyp into the correct position.

The most sensitive estimation of polyp growth would be an *in situ* volume or weight estimation, but no prototype has been devised. An approximate value might be calculated from measurements of the area of the polyp and depth of the polyp measured with an ultrasound probe through the working channel of the endoscope.

Problems with studies of polyp growth

So far, few studies on polyp growth have been published [38,127,128]. As polyps grow slowly, they need to be observed for many years. The main technical problems are associated with *in situ* measurement, redetection, and reidentification of polyps. This kind of study is laborious, with demand for a large number of patients with few dropouts.

In situ measurement

The problems of *in situ* measurement have been discussed. A linear measuring probe has been shown to give a reliable size evaluation; with a picture of the polyp, computerized image analysis of the area of the polyp can be obtained.

Redetection

The problems of detection and redetection of polyps is well known to all colonoscopists. Polyps may be hidden by inadequate emptying, located behind folds or on the inside of curvatures, and contractile movements may occlude the view. Judged by repeat endoscopies within 3 months, the miss rate of polyps by single endoscopy was estimated to be 25% of polyps < 5 mm and 5% of polyps > 5 mm in diameter in one study [13], and 13% for all sizes in another study [129]. This is comparable with the results of tandem colonoscopies by two alternating examiners, revealing a miss rate of 16–27% for polyps < 5 mm, 12–17% for polyps 5–9 mm, and less than 5% for polyps > 1 cm [14,15].

In a study of polyp growth, the examiner will be aware of the location of previously detected polyps at follow-up (but not the size), and a redetection rate of 75–90% for polyps < 1 cm has been demonstrated [2,16,130]. There is a considerable difference in redetection rate of polyps situated proximal or distal to the splenic flexure. Of polyps < 5 mm, 76–89% were redetected when the polyp was located in the left colon compared with 54–86% in the right side of the colon [2,16]. The redetection rate of polyps 5–9 mm was 91–96% in the left side compared with 76–90% in the right. Location of the polyp at redetection (measured as distance in centimeters from the anus with a straightened endoscope) correlates well with initial endoscopy [2,16], resulting in a mean distance difference of 0.8 cm [16].

Reidentification

Between 35 and 45% of adenoma-bearing patients have multiple polyps. Multiple polyps, especially in the same segments, may cause problems in deciding which polyps are redetected and which may be new (or previously overlooked). Polyp recurrence is substantial in follow-up studies, varying from 16 to 56% after 1-year follow-up. Tattooing in the area of the follow-up polyp has been used with success [127]. The tattoo stain has been reported to last for years [131]. However, for individual polyps, it is a laborious technique, with possible hazards [132,133], and has seen limited use.

In studies of polyp growth, a strategy might be to remove all but one polyp so that reidentification will be simpler. However, this will destroy information concerning the growth of different polyps within one patient, and might lead to removal of adenomas while retaining a hyperplastic polyp. More than three-quarters of polyps < 5 mm are nonneoplastic [2,134] and cannot be separated visually from adenomas [2]. Moreover, this might lead to a tendency to keep the distal polyps, which are technically easier to follow-up, discarding information on the growth pattern of the proximal polyps.

For the identification of polyps during follow-up, the following data should be collected at each examination:

- 1 distance from anus by straightened endoscope;
- 2 segment localization;
- 3 description of body and base;
- 4 size;
- 5 distance from other intraluminal structures;
- 6 photographs [16].

By applying these data, a full agreement between two investigations was achieved in 79% [130]. As no absolute criteria can be applied to separate multiple polyps, it was of particular value to have several observations for each patient from the annual examinations [16].

Cancer risk and ethics

There might be a reluctance against not removing a potentially malignant structure or a structure that might turn into malignancy. Polyps > 1 cm are at considerable risk of malignancy (see Table 32.6). However, polyps < 1 cm are very rarely malignant. The reported incidence of invasive cancer in polyps 5–9 mm in diameter is 0.5–0.9% [10,11], while in several large studies no polyps < 5 mm were found to be malignant [11,49,85]. In a study where 196 polyps < 5 mm in 106 patients were followed up for 2 years, with a redetection rate of 74%, none of the polyps finally removed were found to be malignant or showed signs of high-grade dysplasia [2]. In another study where 259 polyps < 1 cm in 116 patients were left *in situ* for a period of 3 years, 89% were redetected in 104 of the patients [16]. During annual colonoscopy, nine

polyps had to be removed before the end of the study. None of the polyps followed up showed signs of invasive carcinoma. Two polyps contained areas of intramucosal carcinoma, and there was high-grade dysplasia in four polyps. One patient developed an invasive carcinoma at the second year of follow-up, probably due to incomplete removal of a large polyp at enrollment without obtaining histologic examination. In a poorly characterized study of 257 patients with rectosigmoid polyps 2–15 mm in diameter left unresected for a period of 3–5 years, with follow-up examinations every 6–12 months, polyps were removed if they attained a size of 15 mm [127]. In two patients, invasive carcinoma developed from polyps of 7 and 10 mm respectively. The smaller polyp was removed by snare resection, with no signs of malignant tissue at the excision base.

Despite limited experience, we feel that growth studies of colorectal polyps should be considered safe, provided that polyps are < 10 mm in diameter and that frequent follow-up examinations are carried out. Cytologic smears of polyps can be performed at enrollment, but as part of scientific studies we cannot recommend biopsies, as this may shrink small polyps considerably and we do not know whether this may change the growth pattern. Such follow-up of polyps left *in situ* must be part of a predetermined study protocol. Until better markers of malignancy are found, all polyps must be removed during routine clinical practice in order to achieve a complete histologic examination.

Observational polyp growth studies

In a retrospective study before the advent of colonoscopy, polyps > 1 cm in diameter on X-ray were followed up for a mean period of 7 years (range 1–19) [116]. The cumulative risk of cancer at the polyp site at 5, 10, and 20 years was 2.5, 8, and 24%, indicating that the interval before malignant transformation may be long and that many polyps will never turn malignant. During the period of surveillance, 37% of the polyps enlarged and 4% could not be demonstrated at later radiography. Histology was unknown, although judging from the size we can assume that with few exceptions they must have been neoplastic. Ultimately, 47% of the polyps were removed and all were neoplastic.

Knoernschild [127] followed 213 patients with an unspecified number of polyps 2–15 mm in diameter for 3–5 years before removal. A small tattoo mark was placed in the mucosa near the base of the polyp. He reported that only 4% of the polyps increased significantly in size, 70% were unchanged, while 8% decreased in size and 18% disappeared entirely, with the tattoo stain giving mute evidence of previous location and existence.

Hoff and colleagues [38] discovered polyps in 35% (201 polyps in 112 persons) of 400 invited men and

women aged 50–60 years, randomized from the local population registry. Polyps < 5 mm were not removed. At the 2-year follow-up examination, 74% of the polyps were redetected, in addition to 44 new polyps in 30 persons. All polyps were measured with a 2-mm linear measuring probe. No polyp increased in size beyond 5 mm. Only 35 of the redetected polyps were adenomas (25%); 17 of the adenomas showed growth from a mean of 2.8 mm to 4.1 mm, 13 remained unchanged, and five showed a mean regression of 1.2 mm. There was an overall mean increase of 0.5 mm for all the adenomas. Moreover, the hyperplastic polyps also significantly increased in size by a mean of 0.5 mm in diameter, while the mucosal tags remained unchanged. This compares well with another study [16], where 58% of the adenomas < 5 mm increased in size ($n = 31$), with a mean of 0.5 mm in 3 years. Hoff and colleagues also calculated the increase in polyp mass, with a 16% mean increase in diameter of the adenomas, resulting in a 136% increase in calculated polyp mass.

In an intervention study [128], 116 polyp-bearing patients were followed for 3 years with annual colonoscopic examinations, leaving all polyps < 10 mm *in situ*. The patients received a placebo-controlled daily mixture of β -carotene 15 mg, vitamin C 150 mg, vitamin E 75 mg, selenium 101 μ g, and calcium carbonate 1.6 g, with the intention of reducing polyp growth or polyp recurrence. The surprising finding was that while adenomas or hyperplastic polyps < 5 mm showed significant growth, those 5–9 mm showed a slight net regression in size, although not significantly [16] (Figs 32.2–32.4). This was true for both the patients receiving placebo and those receiving active medication, and was also demonstrated using computerized picture analysis to estimate polyp area. This is contrary to the expected growth of adenomas 5–9 mm in diameter. It may be speculated that most polyps grow to a certain size between 5 and

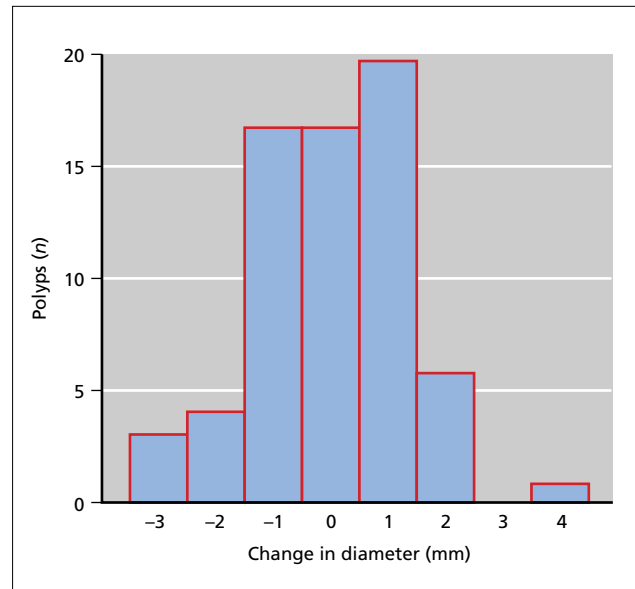
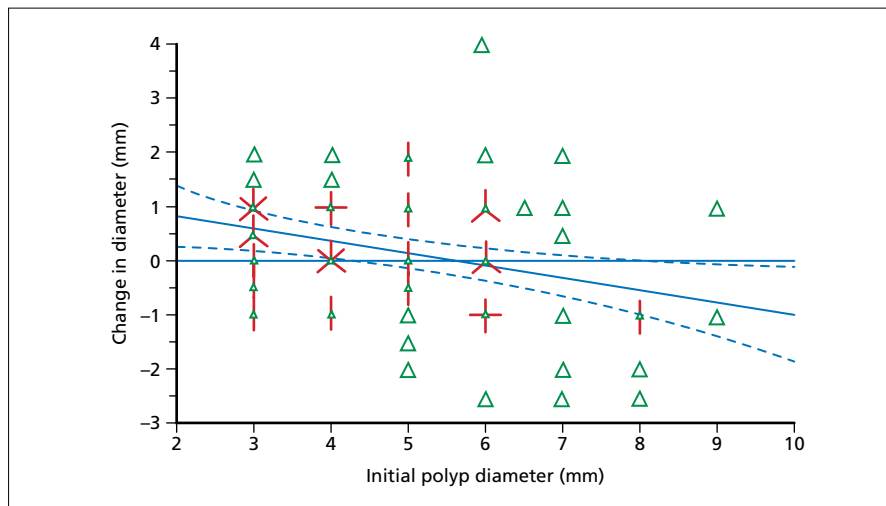


Fig. 32.2 Change in diameter of 68 adenomas in 40 patients taking placebo for a period of 3 years. (From Hofstad *et al.* [16].)

10 mm, and thereafter turn into spontaneous regression. However, this “rise and fall” of the polyps is not readily explained by any biologic model. However, it may partially explain the discrepancy between the prevalence of colorectal polyps and the incidence of cancer. Only few adenomas would be expected to grow to a size that increases the malignant potential. In order to test this hypothesis further, a much longer period of observation is required, and for ethical reasons polyps > 10 mm will have to be removed.

In the same study, Hofstad and colleagues [16] observed polyps regressing (Fig. 32.5), remaining unchanged, and growing (Fig. 32.6) in the same patient in 22% of cases. No specific tendency to growth or

Fig. 32.3 Change in diameter of 68 adenomas in 40 patients taking placebo after an observation period of 3 years, in relation to initial size of the polyps. The scatterplot is presented as a flower diagram, in which each line emanating from a point represents an exact overlap. Nonoverlapping registrations are presented as triangles. Regression line with confidence limits are drawn. (From Hofstad *et al.* [16].)



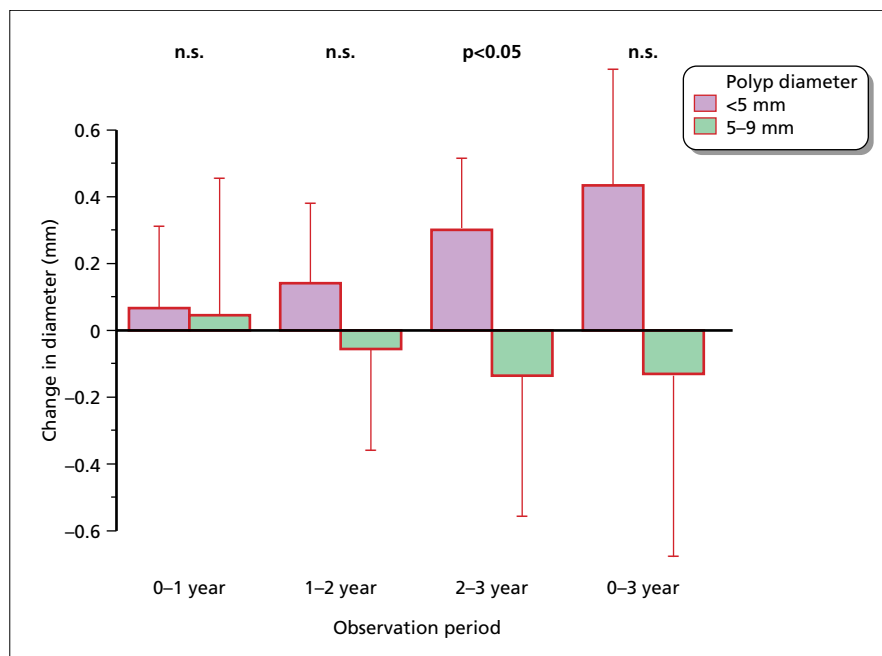


Fig. 32.4 Mean change in diameter of the adenomas (95% confidence interval) in patients taking placebo at each annual endoscopic follow-up and from inclusion to the third-year control (0–3 years) for polyps < 5 mm ($n = 27$ –43) and polyps 5–9 mm in diameter ($n = 32$ –43). P -values for the differences between growth of the smaller and larger polyps are indicated on top. (From Hofstad *et al.* [16].)

regression has been seen in different colonic segments. Significant growth in adenomas in younger patients (50–59 years) has been observed, but this comprised only 10 patients. Moreover, the patients with multiple adenomas (> 2) had a significantly larger growth than those with only one polyp. There was no difference in polyp growth between the genders. Two polyps showed an intramucosal carcinoma on removal, one had regressed from 9 to 7 mm in diameter over 3 years, and another had increased from 8 to 11 mm in 1 year. Another four tubular adenomas with high-grade dysplasia changed minimally over 3 years, except one that grew from 8 to 12 mm in 2 years. The rest of the polyps showed only low-grade dysplasia.

Risk factors for polyp growth

Colon carcinogenesis is a multistep process involving initiation, growth, and finally malignant transformation of the polyp. The factors influencing the different steps may not be identical.

In order to identify risk and protective factors for polyp growth, some studies have regarded small and large polyps separately, with the presumption that factors influencing the prevalence of large polyps, but not small polyps, affect polyp growth. Hoff and colleagues [70] found that dietary fat intake was higher while fiber and iron was lower in patients with polyps > 5 mm, but not in patients with only smaller polyps. The same was found in another study for patients with small (< 5 mm), medium (5–9 mm), and large (≥ 10 mm) polyps [69]. It was reported that patients also consumed less car-

bohydrates, and the women had lower intake of calcium and vitamin C than the controls. Moreover, BMI [72] and alcohol [66] were found to be promoters of adenoma growth, with no effect of tobacco [63]. In another study, adjusting for smoking, alcohol use, and BMI, a low rice consumption and high meat intake was associated with increased risk of polyps > 5 mm, while this was not found when all the polyps were smaller [135]. Finally, alcohol intake was higher in patients with polyps > 1 cm compared with those with smaller adenomas [76].

Only one study analyzing the effect of nutrients on growth of polyps has been published [136]. Over a period of 2 years, the relative risk of increased mass of the polyps (5 mm or smaller), both including and excluding new polyp formation, showed a trend toward an inverse relationship for intake of dietary fiber, non-fiber carbohydrate, and cruciferous vegetables, reaching significance only for fiber in men. The relative risk of increased adenoma mass for men increased with higher fat intake.

A small intervention study on the effect of sulindac and piroxicam on growth of colorectal polyps showed no change in size of the polyps after 6 months [137]. In another negative study [138] in patients with polyps < 10 mm followed for 3 years, a placebo-controlled mixture of calcium, vitamins A, C, and E, and selenium had no effect on polyp growth (adenomas or hyperplastic polyps), on polyps in the different segments of the colon, for the patients with family history of cancer, nor was a gender difference found. A significant protective effect of the trial mixture was found in a small group of patients 50–60 years of age.

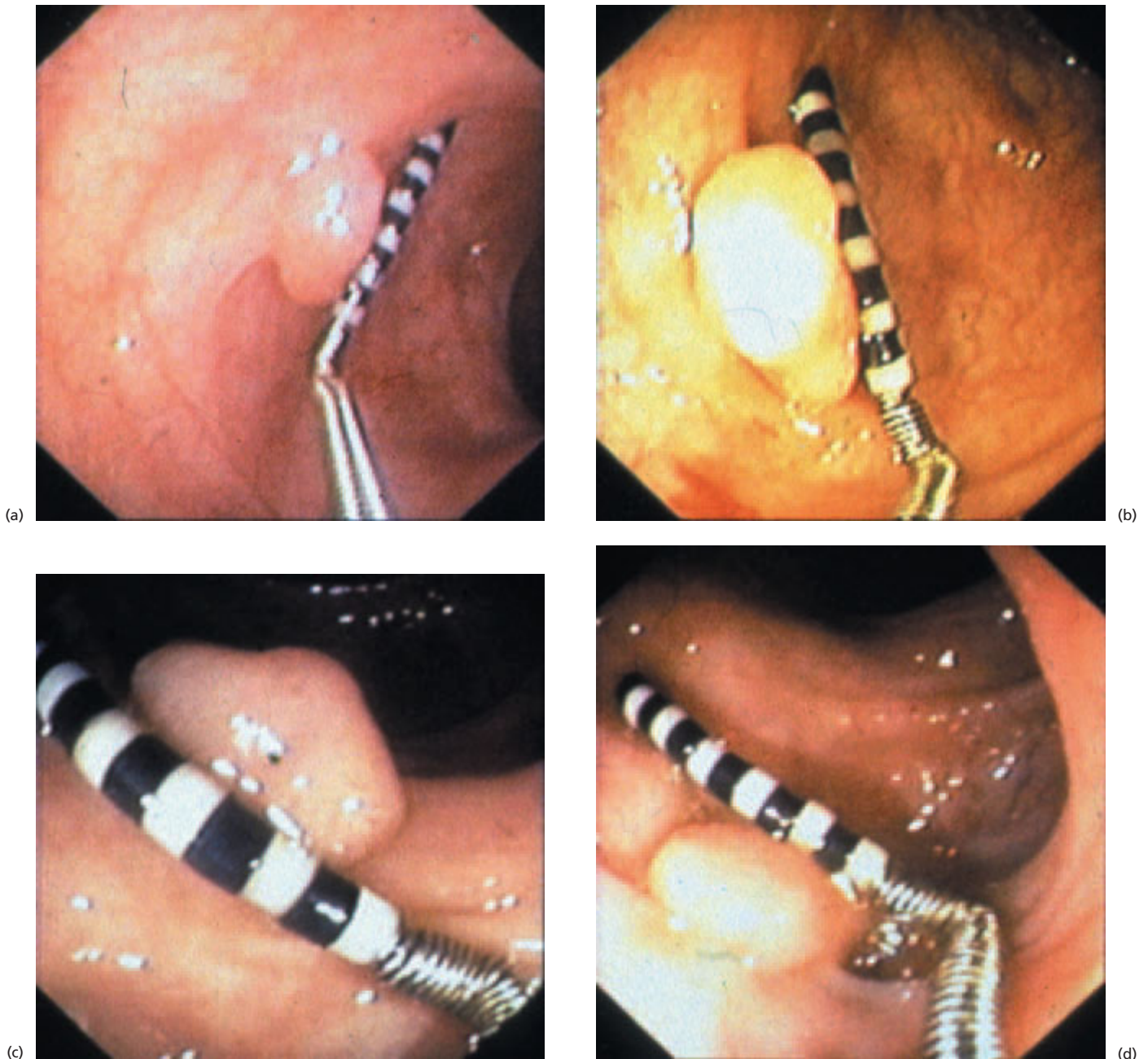


Fig. 32.5 Images of a regressing tubular adenoma, from 8 to 6 mm in 3 years: (a) polyp at enrollment; (b) first-year follow-up; (c) second-year follow-up; (d) third-year completion.

Summary

At present we have considerable knowledge about the prevalence of polyps and the incidence after polypectomy, while few studies on polyp incidence in polyp-free individuals and on polyp growth have been conducted. In future studies on polyp growth, inter-

est should be concentrated on the search for specific markers in intermediate-sized adenomas (5–9 mm) that show further growth potential.

Recent years have seen the publication of large intervention studies using dietary factors, micronutrients and antioxidants, and chemotherapeutics, with polyp recurrence as primary endpoint. These give insight into the possibility of primary prevention of colorectal cancer. Research in the future should be in combination with the advancing information from molecular biology.

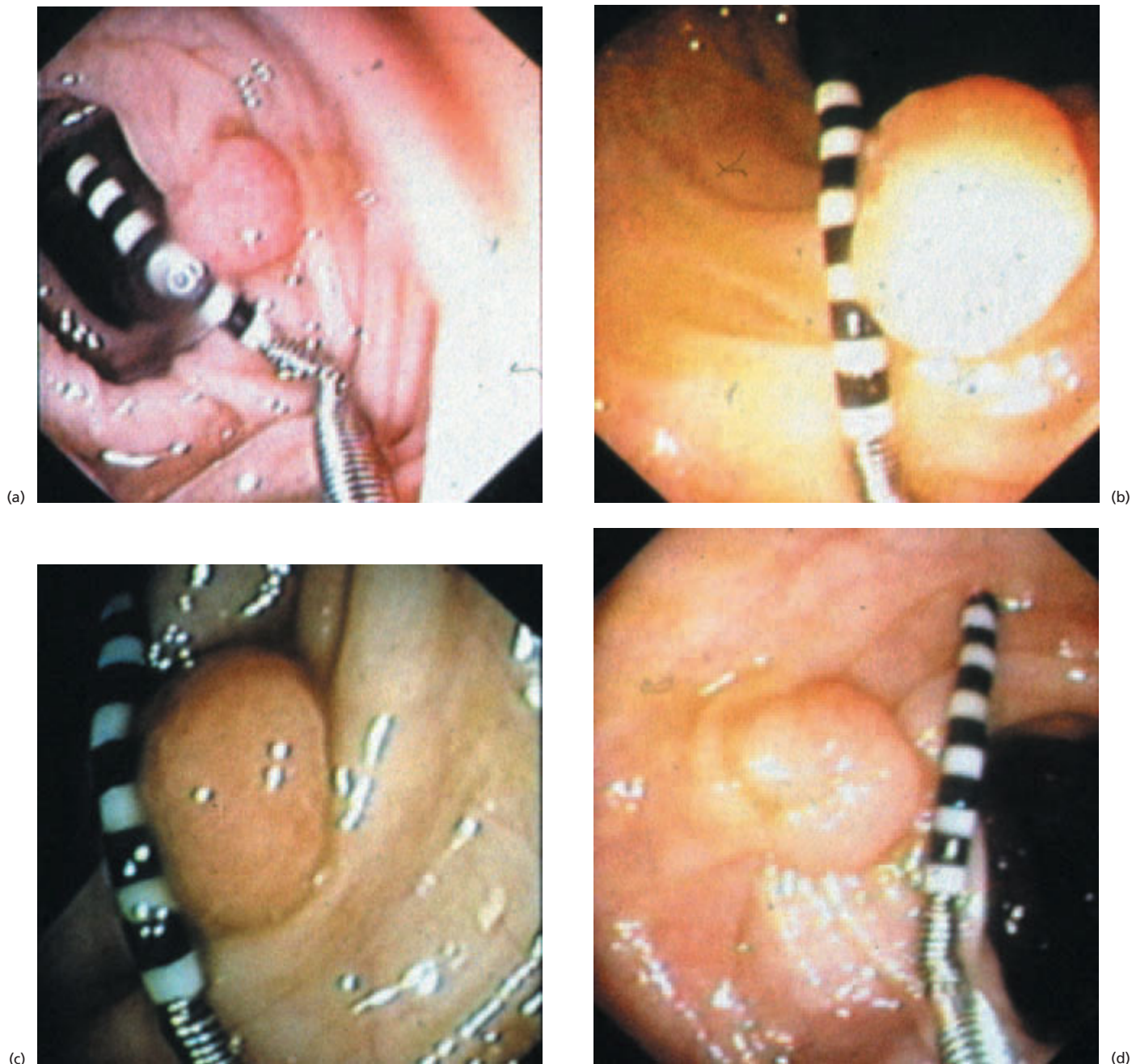


Fig. 32.6 Images of an adenoma increasing in diameter from 5 to 7 mm in 3 years, presented in the same sequence as in Fig. 32.5.

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Chapter 33

Pathology of Colorectal Polyps

Noam Harpaz

Introduction

The term “colorectal polyp,” though often used synonymously with “adenoma” by gastroenterologists, refers more accurately to any excrescence or well-circumscribed protrusion into the bowel lumen. Undoubtedly, adenomas account for the majority of polyps in western societies, most other polyps falling into a limited number of categories such as hyperplastic, inflammatory, and juvenile polyps. Collectively, however, colorectal polyps encompass a diverse assortment of benign and malignant neoplasms of epithelial, mesenchymal, neural, and mixed compositions, as well as inflammatory, mechanically induced, and other nonneoplastic lesions (Table 33.1) [1].

In addition to reviewing the essential pathologic features of some of the more common types of colorectal polyps, this chapter highlights key technical and diagnostic issues that can impact on the pathologic evaluation of polypectomy specimens, discusses their corresponding clinical implications for the postpolypectomy patient, and points out certain technical and procedural precautions that endoscopists and pathologists should observe to assure quality of care. Although the emphasis is on sporadic polyps, much of the morphologic detail applies equally to their counterparts in corresponding polyposis syndromes.

The pathologic evaluation of endoscopically resected colorectal polyps assumes a decisive role in the management of patients who have undergone polypectomy, providing the principal basis for sound decision-making regarding such issues as surgery, surveillance, and family screening. The quality of the pathologist’s evaluation depends on four main components: (i) *technical factors* related to specimen preservation and processing, (ii) *clinical and endoscopic data* provided by the clinician, (iii) *accurate interpretation* of the histologic findings and appreciation of their clinical significance, and (iv) *communication* of the findings to the clinician in a complete and meaningful form.

Diagnostic accuracy

There have been few systematic efforts to verify the

accuracy of surgical pathologists in classifying polyps and to evaluate their specific strengths and weaknesses [2,3]. In a recent study of general community pathologists challenged with a small assortment of colorectal polyps, correct classification was achieved for 94% of adenomas and 75–80% of hyperplastic, inflammatory, and juvenile polyps, but only 20% of hamartomatous and prolapsing mucosal polyps, which are less common in routine practice. Significantly, 9% of malignant polyps were misdiagnosed as benign, half were reported without indication as to tumor grade or status of the transection margins, and 22% of benign polyps with high-grade dysplasia were incorrectly interpreted as malignant [3]. Several other studies dealing with finer histologic distinctions related to growth patterns and the grading of dysplasia have reported only fair to moderate levels of intraobserver and interobserver agreement [4–7].

Histologic artifacts

Good tissue morphology, a prerequisite for accurate diagnosis, is sensitive to various technical factors that affect the preservation, sampling, and orientation of the polypectomy specimen. Substantial artifacts may be introduced during the polypectomy procedure itself, most commonly those caused by thermal electrocoagulation and crushing. The combined effects depend on the severity of the insults relative to the size and geometry of the polyp, and range anywhere from mild nuclear distortion to complete effacement of morphologic detail. Diminutive polyps are especially vulnerable to distortion artifact. A recent series of 119 diminutive polypectomy specimens reviewed independently by three pathologists reported an average of 16.5% nondiagnostic specimens resulting from thermal electrocoagulation artifact. The rates of pathologist agreement decreased with diminishing polyp size, discrepancies being most apparent below 2 mm [8].

Large polyps subjected to prolonged or multiple exposure to snare electrocoagulation, such as those with thick pedicles or requiring piecemeal resection, incur tissue artifacts along the transection lines. These rarely preclude classification of the polyp, but in the case of

Table 33.1 Colorectal polyps.

<i>Neoplastic polyps: benign</i>
Adenoma
Serrated adenoma
Composite adenoma–hyperplastic polyp
Composite adenoma–carcinoid
Polypoid dysplasia in inflammatory bowel diseases
Leiomyoma
Benign gastrointestinal stromal tumor
Lipoma*
Hemangioma*
Lymphangioma*
Granular cell tumor*
Neuroma*
Schwannoma*
Ganglioneuroma*
Mast cell tumor*
<i>Neoplastic polyps: malignant</i>
Adenoma containing invasive adenocarcinoma (“malignant polyp”)
Polypoid adenocarcinoma
Carcinoid tumor
Malignant gastrointestinal stromal tumor
Metastatic tumors (carcinoma, melanoma, etc.)
Leiomyosarcoma
Extranodal malignant lymphoma
Granulocytic sarcoma
Kaposi sarcoma
<i>Nonneoplastic polyps</i>
Hyperplastic polyp
Inflammatory polyp
Juvenile polyp
Polyp of Cronkhite–Canada syndrome
Inverted diverticulum
Mucosal prolapse-associated polyp
Inflammatory fibroid polyp
Hamartomatous polyp
Myoglandular polyp
Lymphoid polyp
Pneumatosis coli
Fibroepithelial polyp
Amyloidoma
Malakoplakia
Endometriosis
Gastric heterotopia
Elastofibroma

* Indicates no future risk of malignancy.

malignant polyps can interfere with the evaluation of cancer near the transection margins, as discussed below.

Adequate fixation of polyps requires immersion in a 10–20-fold volume of fixative for at least several hours, larger specimens requiring longer fixation. Submission of a specimen by the endoscopist in inadequate volumes of fixative not only incurs needless processing delays but, worse, can lead to inadvertent processing of the partially fixed specimen and unacceptable loss of morphologic detail.

Polyp orientation and sampling

The transection margin is an important landmark that guides the proper orientation of polyps during gross sectioning and paraffin embedding and is especially critical to the evaluation of malignant polyps (Fig. 33.1). It typically presents as a white patch on the surface of the polyp but may retract spontaneously into the polyp’s core. To assure its identification, the endoscopist should

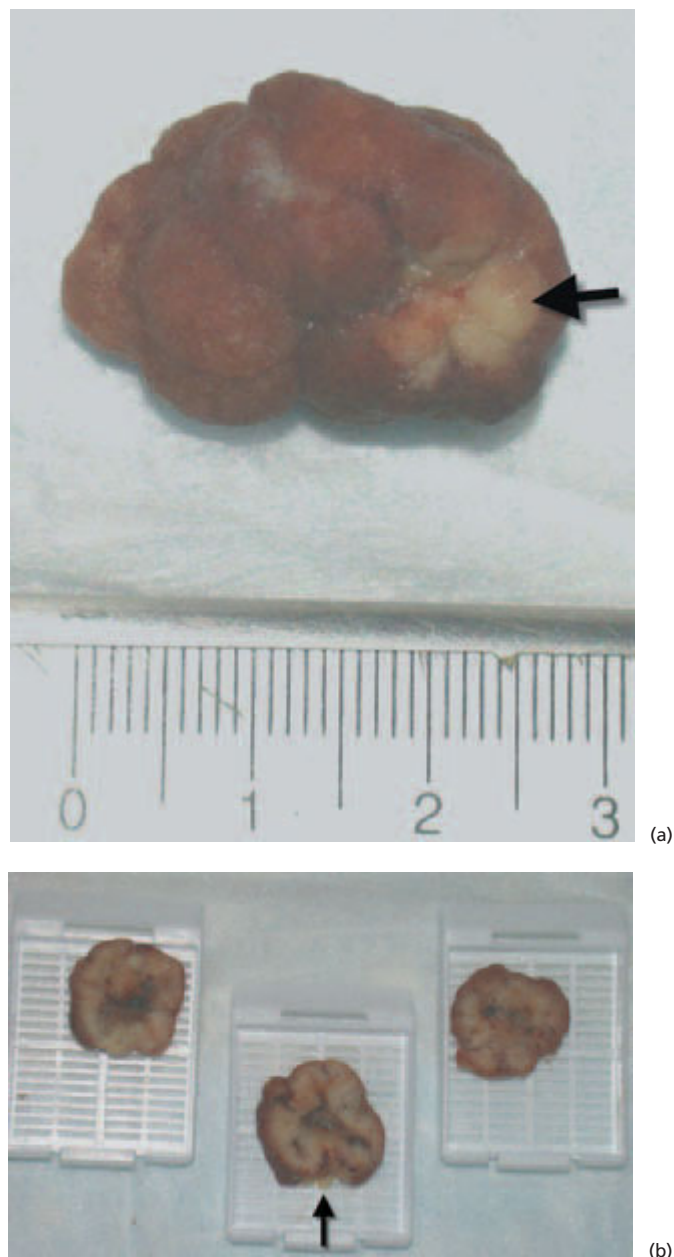


Fig. 33.1 (a) Before a polyp is sectioned, the transection line is identified, usually presenting as a pale patch (arrow). (b) The polyp is sectioned sagittally on either side of the midline and each section placed in a cassette for processing. Arrow denotes the transection margin.

routinely mark the base of polypectomy specimens with India ink or impale specimens on a pin.

Inherent in the processing of three-dimensional polyps into two-dimensional slides are variations among different planes of section. Theoretically, sampling error could be eliminated if each tissue block were sectioned exhaustively into slides; however, the costs in terms of laboratory and pathologist resources would be unrealistic. In practice, the thoroughness with which polyps are sectioned is determined individually and empirically by each individual pathologist or laboratory.

Polypectomy specimens small enough to be embedded intact as a single tissue block are reportedly subject to false-negative rates (i.e. no histologic evidence of a polyp) of 10–32% [9–11]. Given that diminutive polyps identified at endoscopy frequently correspond to insignificant mucosal irregularities or lymphoid follicles, most laboratories understandably report their initial negative findings without requesting deeper sections of the tissue block. However, a study of polyps whose initial slides were negative reported a 23% yield of new microscopic findings in additional slides, including a 10% incidence of neoplastic polyps such as adenomas, the corresponding incremental costs being approximately \$10 per case and \$95 per adenoma [9]. Nonetheless, costs notwithstanding, any clinical or endoscopic input from the endoscopist suggesting that a significant finding has been overlooked should automatically elicit a more aggressive search by the pathologist.

The potential for clinically important sampling error is greater for large adenomas, especially those that might be harboring cancer. Such polyps are initially sectioned sagittally, two to three sections per centimeter diameter on either side of the midline, and each section then embedded in paraffin as a separate tissue block for processing into slides (see Fig. 33.1). Mere sampling of large polyps in lieu of total embedding is strongly discouraged, as it incurs a substantial risk of missing important pathology. A recent study based on a series of large but grossly benign-appearing polyps calculated that a typical “1 slide per cm” sampling protocol would have reduced the likelihood of detecting carcinoma to unacceptably low levels in four of five malignant polyps and would have missed high-grade dysplasia in 7 of 12 benign polyps [12]. The optimal number of slides or step sections for each block of the polyp has not been studied systematically; however, a minimum of three slides has been recommended on empirical grounds [13].

In conclusion, it is the responsibility of the pathologist who oversees the laboratory to assure that protocols for the processing of polypectomy specimens into slides are established, that they are adhered to by laboratory personnel, and that all technical aspects of slide preparation are subject to a rigorous quality assurance program.

Clinical–pathologic correlation

(see Chapter 27)

As in any other consultative arrangement, pathologist access to the patient’s clinical history, endoscopic findings, and the particulars of the procedure itself can have a critical bearing on the accuracy of the interpretation. For example, the distinction between “look-alike” polyps such as adenomas and dysplastic polyps in inflammatory bowel disease, or between certain juvenile and inflammatory polyps, may depend entirely on clinical and endoscopic context provided by the gastroenterologist. Similarly, the wording and therapeutic implications of a cancer diagnosis may be quite different if rendered on a complete polypectomy specimen or an incomplete biopsy, yet slides of the two may be indistinguishable. Accordingly, a conscientious effort by the endoscopist to provide adequate clinical and endoscopic data should be regarded as a sound investment in quality care.

Adenomatous polyps

Adenomatous polyps, defined as circumscribed benign neoplasms of the large intestinal epithelium, account for approximately two-thirds of endoscopically resected intestinal polyps in the USA. They are the direct precursors of most, if not all, colorectal cancers in the general population, each carrying a roughly 5% lifetime probability of progressing to malignancy. This concept, the adenoma–cancer sequence, has been validated clinically, epidemiologically, morphologically, and by genetic analysis, and provides the principal rationale for the management of patients with adenomatous polyps.

The pathologic classification of adenomas is based on four features:

- size;
- gross configuration (sessile, semisessile, pedunculated, or flat);
- growth pattern (tubular, tubulovillous, or villous);
- grade of dysplasia.

Adenomas vary dramatically in size, from microscopic unicryptal neoplasms at one extreme to carpet-like growths involving entire colonic segments at the other. According to data from the US National Polyp Study (which pertain only to endoscopically resectable polyps), 38% of adenomas are < 5 mm, 36% are 6–10 mm, and 26% are > 10 mm [14]. Size correlates in turn with other important pathologic and clinical parameters, such as gross configuration, growth pattern, grade of dysplasia, prevalence of invasive cancer, incidence of local recurrence, and incidence of synchronous and metachronous adenomas. Parenthetically, measurements of polyp size after resection are not affected by formalin fixation; however, polypectomy itself results in shrinkage of 18%

on average compared with measurements made *in vivo* [15].

Once resected, pedunculated and sessile adenomatous polyps are not easily distinguished, since pedunculated polyps may be resected with little or none of the stalk and, conversely, sessile polyps may include a pseudopedicle formed from adjacent mucosa. Microscopically, a clue to resection from a well-formed stalk is the presence of thick-walled blood vessels in the submucosa. Nonetheless, the final word on this point rests with the endoscopist.

Tubular adenomas account for approximately 99% of diminutive adenomas and 87% of all resectable adenomas [14]. Microscopically, they consist of parallel, crowded, neoplastic crypts that retain the basic architecture of normal colorectal mucosa, occupying either the full height of the mucosa or its superficial portion (Fig. 33.2). With increasing polyp size, crypts grow

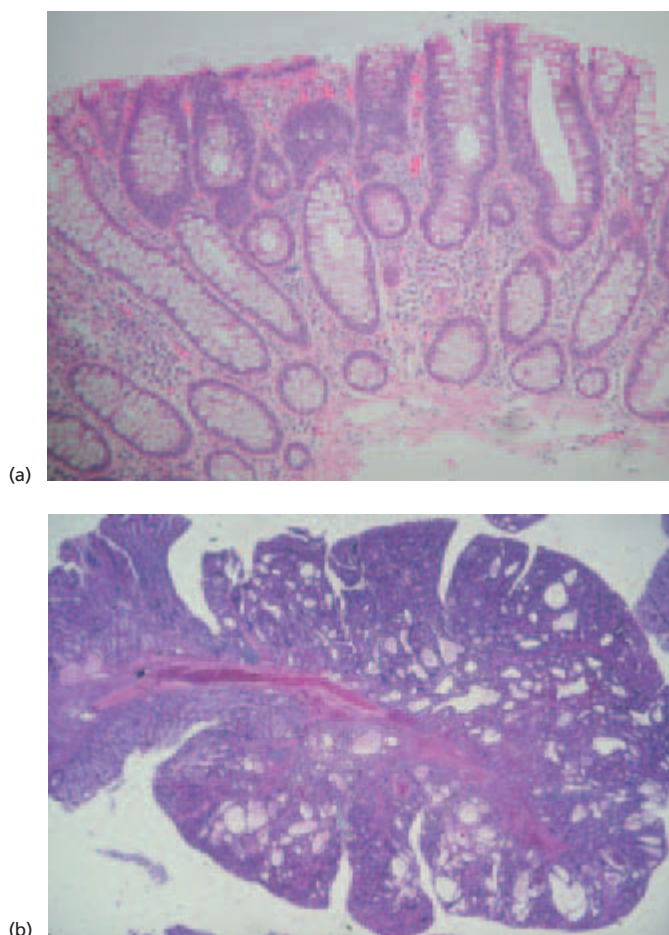


Fig. 33.2 Tubular adenomas. (a) Diminutive tubular adenoma corresponding to a collection of slightly crowded crypts occupying the upper half of the lamina propria. The dysplastic epithelium, with its crowded elongated nuclei and reduced mucin content, stands out from the background of normal crypts. (b) Pedunculated tubular adenoma.

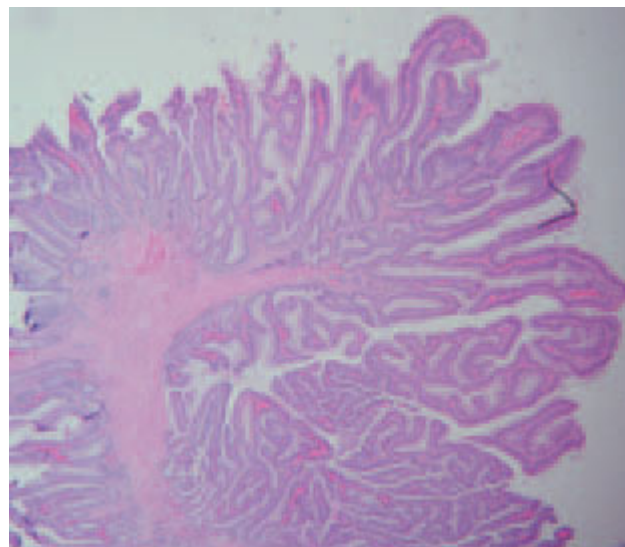


Fig. 33.3 Tubulovillous adenoma.

progressively elongated and coiled and may develop villous characteristics. Tubulovillous adenomas maintain admixed tubular and villous growth patterns, each occupying 20–80% of the polyp (Fig. 33.3). Although accounting for 8% of adenomas overall, tubulovillous adenomas account for approximately half of adenomas in the 1–2 cm range and one-third of adenomas exceeding 2 cm [14,16]. Villous adenomas consist of parallel villiform processes comprising at least 80% of the polyp. They account for approximately 5% of adenomas overall, 60% of adenomas exceeding 2 cm [16], and virtually all large carpet-like adenomas (Fig. 33.4). The villous growth pattern correlates with the presence of high-grade dysplasia and invasive carcinoma independently of other pathologic characteristics [14,16].

Dysplasia: definition, grading and terminology

The defining histologic feature of all adenomas is dysplastic epithelium. Dysplasia, synonymous with intraepithelial neoplasia, refers to a constellation of histologic abnormalities suggesting that the epithelium has undergone clonal genetic alterations causing inappropriate proliferation, abnormal differentiation, and a predisposition to malignancy [17] (Figs 33.5 & 33.6). By definition, it excludes epithelial abnormalities judged to be regenerative or reactive, epithelia whose neoplastic nature is equivocal, and neoplasia that is no longer intraepithelial, i.e. that has invaded beyond the crypt base-membrane into the surrounding lamina propria.

In keeping with this definition, the abnormalities in dysplasia are both nuclear, corresponding to inappropriate proliferation, and cytoplasmic, corresponding

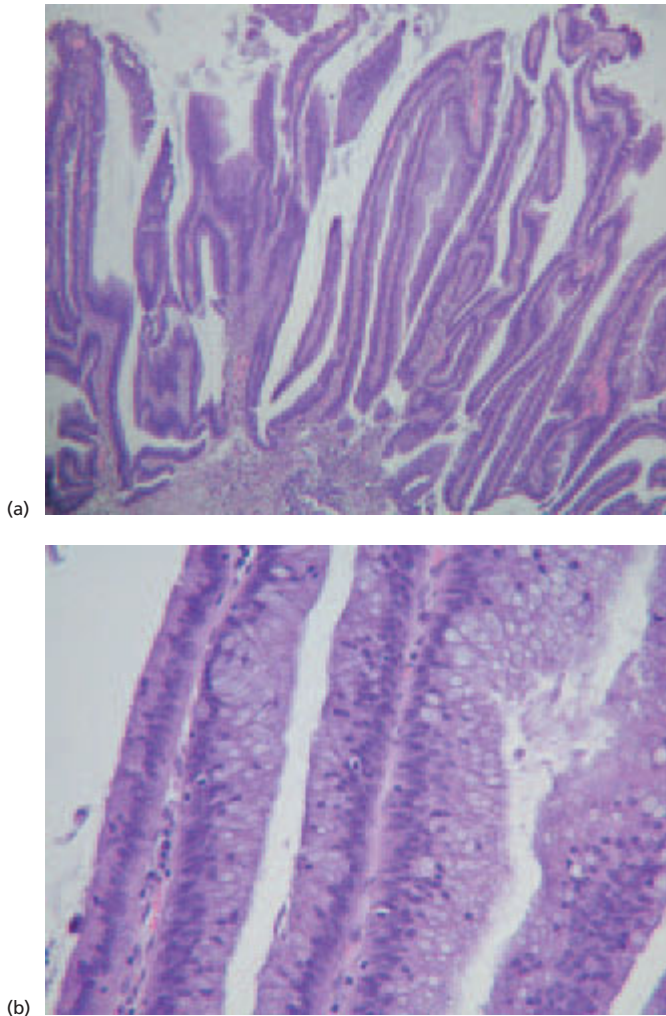


Fig. 33.4 Villous adenoma. (a) The polyp is broad-based and composed of long slender villi with tapered tips. (b) At high magnification, the dysplastic lining contains crowded dark-staining nuclei. Most of the cells contain mucin vacuoles, which could result in mucoid secretions.

to abnormal differentiation. The nuclei are typically enlarged relative to total cell volume and exhibit varying combinations of crowding, stratification, hyperchromatic staining, irregular contours, or prominent nucleoli. Mitotic activity, normally confined to the basal zone of normal crypts, occurs instead throughout the dysplastic crypt axis. The cytoplasmic abnormalities can be characterized as blurring or loss of the distinctive cell phenotypes that characterize normal colorectal epithelium.

Dysplasia in adenomas is graded on a two-tier scale of low and high grade adapted from the nomenclature of dysplasia in inflammatory bowel disease [18]. The distinction between grades is based principally on retention or loss of cellular polarity as reflected by the degree of nuclear stratification. In low-grade dysplasia, the nuclei, albeit enlarged, elongated, and crowded, are

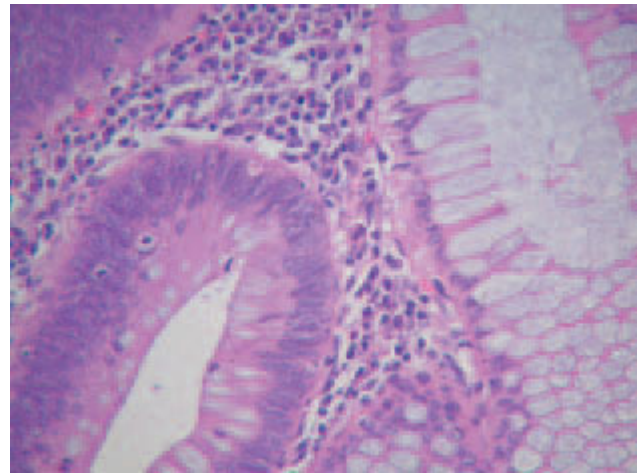
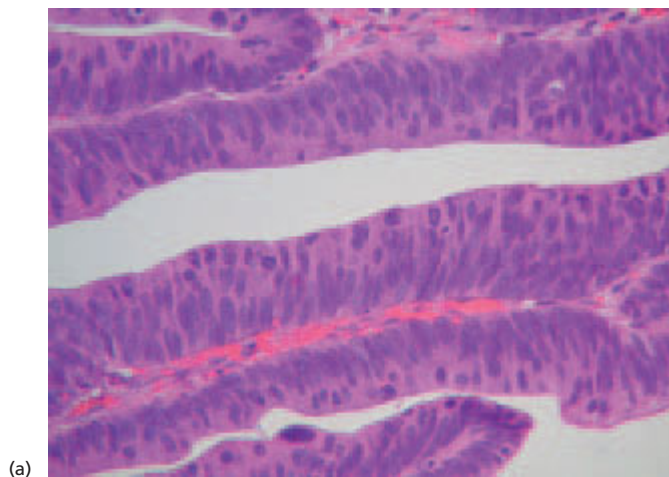


Fig. 33.5 Low-grade dysplasia. Contrast the dysplastic epithelium on the left with normal epithelium on the right. Normal epithelium contains small, round, pale nuclei and two distinct cell phenotypes, goblet and absorptive cells. The dysplastic epithelium contains elongated, crowded, dark-staining nuclei in a so-called “picket fence” pattern. The identities of the cells are blurred and goblet-cell mucin is reduced. Location of the dysplastic nuclei in the basal half of each cell, reflecting retention of polarity, qualifies this as low grade.

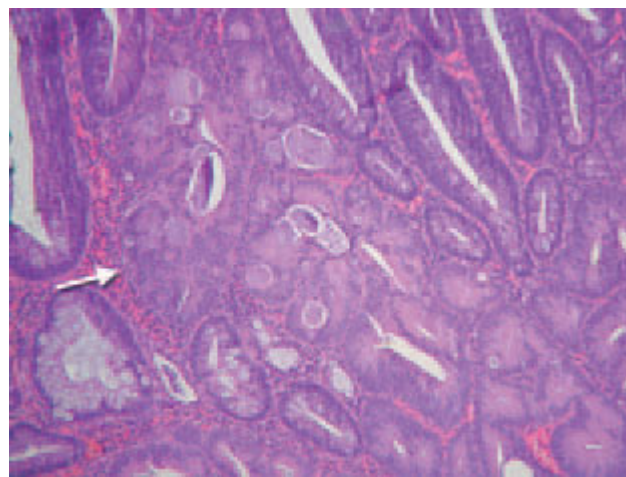
arranged uniformly along the bases of the epithelial cells (Fig. 33.5). In high-grade dysplasia, by contrast, the nuclei are stratified haphazardly with many located in the apical portions of the cells (Fig. 33.6). They also tend to be larger, more heterogeneous in size, and more cytologically atypical, exhibiting such abnormalities as irregular nuclear membranes, macronucleoli, or abnormal mitotic figures. As a rule, the cytoplasm in high-grade dysplasia retains less differentiation, e.g. goblet cells or Paneth cells, than in low-grade dysplasia. Of course, all these changes lie on a continuum. As a result, the grading of dysplasia in adenomas, like in inflammatory bowel disease, is subjective and prone to high levels of interobserver variation [7].

Although still used by some pathologists, the term “adenoma with dysplasia” as a synonym for adenomas with high-grade dysplasia is inappropriate since it implies incorrectly that there exist adenomas without dysplasia. Another misused term, “carcinoma *in situ*,” refers to extreme high-grade dysplasia, in which cell polarity is lost and cytologic aberrations verge on those in invasive cancers (see Fig. 33.6b). Given that metastatic spread does not occur, and the potential for causing unwarranted patient anxiety or even inappropriate surgery, the term “high-grade dysplasia” is preferred to “carcinoma *in situ*.” Indeed, the term “high-grade dysplasia” is extended, at least for clinical purposes, even to polyps containing intramucosal carcinoma, i.e. neoplastic epithelium that has breached the basement



(a)

Fig. 33.6 (a) High-grade dysplasia: the epithelium consists of undifferentiated colonocytes with stratified nuclei, many occupying the apical portion of the epithelial cells, corresponding to loss of cell polarity. (b) High-grade dysplasia incorporates “*in situ carcinoma*” (arrow), corresponding to



(b)

crypts in which the epithelium is arranged in a cribriform, or sieve-like, pattern, manifesting extreme loss of cell polarity. Nonetheless, the smooth rounded outline indicates that there is no penetration beyond the basement membrane.

membrane and invaded the lamina propria (Fig. 33.7). Albeit a more advanced stage of neoplastic progression from the biologic standpoint, this lesion likewise lacks metastatic potential, probably because near-absence of lymphatic channels in the large intestinal mucosa limits tumor access to this route of spread.

Whether the grade of dysplasia in totally resected adenomas ought to be specified at all outside the investigational setting is a matter of individual preference [19]. Most pathologists report high-grade dysplasia when present, one rationale being that it may, in combination

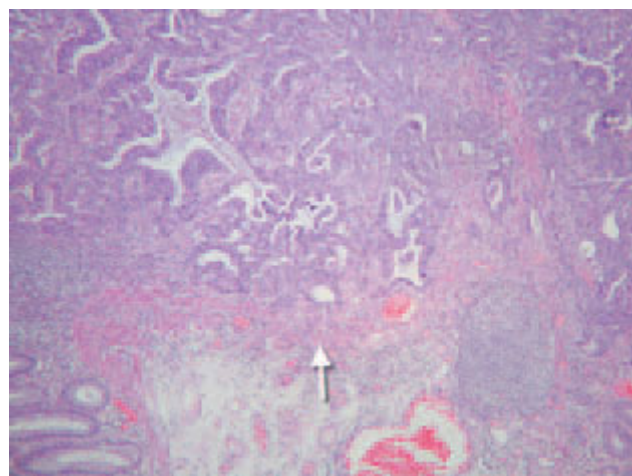


Fig. 33.7 Intramucosal carcinoma corresponds to neoplastic glands that have penetrated beyond the basement into the lamina propria but have not invaded the submucosa. Note the intact muscularis mucosae (arrow). If removed completely, the risk of metastasis is nil, and the term “high-grade dysplasia” is therefore considered appropriate.

with other variables such as polyp multiplicity and size, signify an increased risk of synchronous or metachronous neoplasia and therefore warrant closer follow-up.

Misplaced mucosa: a diagnostic pitfall

Traumatic herniation of adenomatous mucosa into the submucosa, referred to as “misplaced mucosa,” occurs mainly in large pedunculated adenomas located in the rectosigmoid, where they are subject to maximal mechanical stress. Misplaced mucosa also occurs in large hyperplastic polyps, hamartomatous polyps, and mucosal polyps associated with the solitary rectal ulcer syndrome. Its main significance in all cases is the potential for confusion with invasive adenocarcinoma, discussed further below. Microscopically, the most characteristic feature is the presence of circumscribed lobules of mucosal tissue within the head and stalk of the polyp, best appreciated at low magnification. Typically, each lobule has a smooth rounded profile and consists of crypts invested by loose inflammatory tissue identical to that of the overlying lamina propria (Fig. 33.8). The stroma surrounding the lobules is usually more sclerotic and contains hemosiderin deposits. As a rule, the grade of dysplasia within the misplaced mucosa matches that of the overlying mucosa.

Adenoma variants: flat, depressed, and serrated

Flat and depressed adenomas are nonexophytic adenomas that are slightly elevated, may contain a central depression, and are usually less than 10 mm in diameter

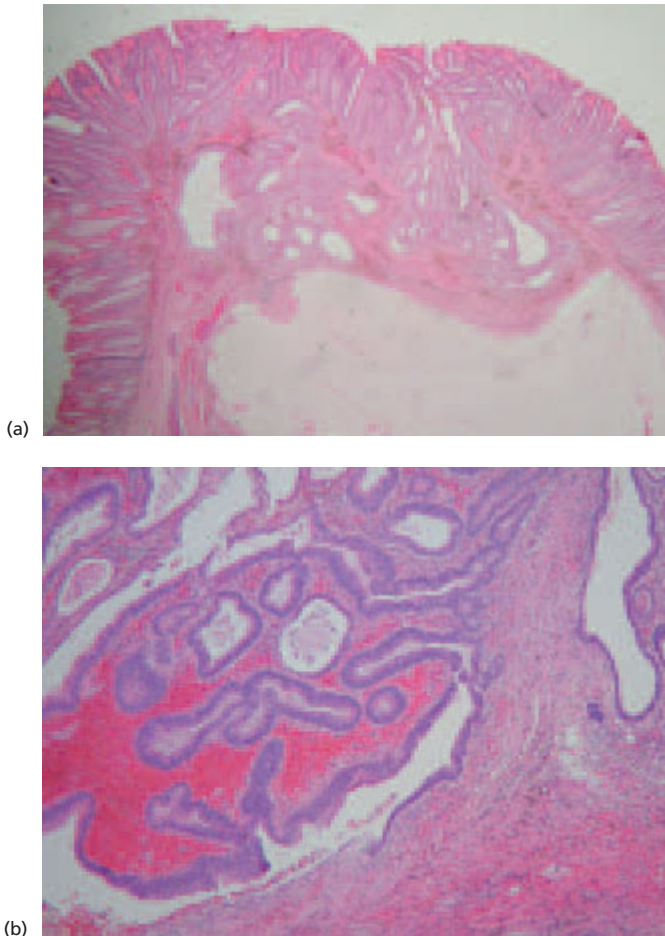


Fig. 33.8 Adenoma with misplaced mucosa in the stalk.

(a) The upper region of the submucosa contains two rounded lobules of misplaced mucosa surrounded by fibrous tissue with brown pigmentation corresponding to hemosiderin deposits. The lower region is occupied by a massively dilated misplaced crypt forming a mucocele. (b) Misplaced mucosa at higher magnification characterized by low-grade dysplastic epithelium and loose stroma.

[20]. Although difficult to detect by routine endoscopy, they are purported to harbor the potential for aggressive growth and progression to cancer without assuming a polypoid configuration.

Microscopically, they are characterized by dysplastic mucosa that is up to twice the thickness of the adjoining mucosa. The dysplastic crypts occupy the superficial mucosa overlying normal crypts, at least at the periphery, those of flat adenomas maintaining uniform height throughout and those of depressed adenomas being shorter in the center than in the periphery. However, the histologic features *per se* are not unique, occurring frequently in conventional polypoid adenomas as well [21]. Despite reports of disproportionately high rates of high-grade dysplasia and early carcinoma [20,22], particularly in the depressed subtype [23], as well as

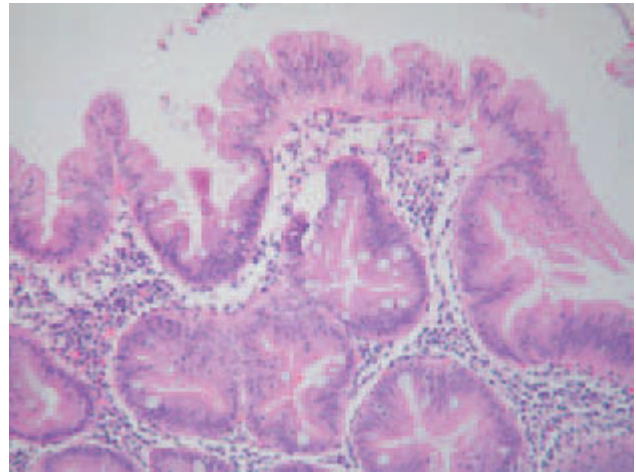


Fig. 33.9 Serrated adenoma. The serrated crypt architecture is typical of conventional hyperplastic polyps, but the nuclei are relatively enlarged, crowded, and dark-staining.

differences in the expression of certain genetic markers [24], the clinical significance of this entity remains unsettled [25].

Serrated adenomas are a distinctive histologic variant accounting for approximately 0.1% of adenomas [26]. They are distributed singly or multiply throughout the large intestine and are comparable to conventional adenomas in configuration and size, although those in the right colon tend to be flatter than those in the left. The distinction between diminutive serrated adenomas and hyperplastic polyps is difficult by conventional endoscopy [27] but seems to be feasible with use of magnification [28]. Histologically, serrated adenomas combine the architecture of hyperplastic polyps with the dysplastic cytology of conventional adenomas (Fig. 33.9). Although frequently less pronounced than in conventional adenomas [26], dysplasia in serrated adenomas is capable of spanning the full gamut including progression to carcinoma [26,29].

Molecular studies of serrated adenomas have revealed varied patterns of genetic mutations not unlike those found in conventional adenomas, suggesting similar heterogeneity in their molecular pathogenesis [30,31]. However, there is growing evidence that the histogenesis of serrated adenomas represents one of several divergent pathways of “serrated” polyp development sharing a common origin from incipient serrated polyps with specific patterns of mutations [32,33].

Malignant polyps

This term refers by convention to adenomas that are determined histologically to harbor invasive adenocarcinoma, i.e. carcinoma that has invaded at least into the submucosa [13], namely into the stalk of pedunculated

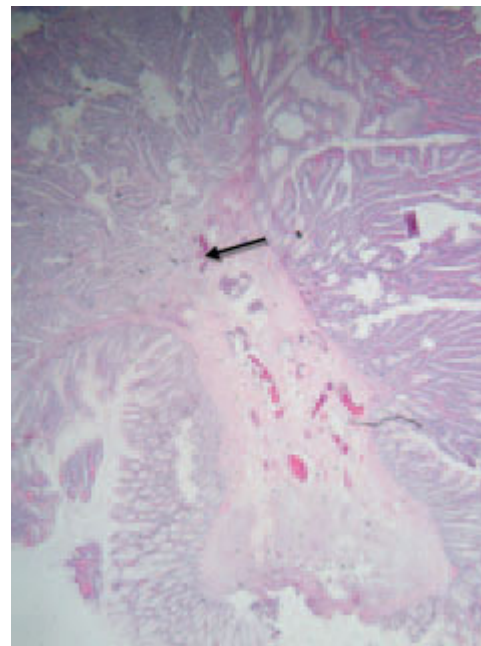
adenomas or into the intestinal submucosa beneath sessile adenomas. Histologically, invasion is usually accompanied by a desmoplastic reaction in which the nests of cancer cells are invested by reactive fibroblasts laying down collagen and mucopolysaccharide stroma (Fig. 33.10b).

Decision-making regarding management of the patient with a resected malignant colonic polyp depends on the relative statistical outcomes of colectomy compared with polypectomy and observation. Studies have concluded that these outcomes are comparable if the polyp fulfills certain favorable endoscopic and histologic criteria. Endoscopically, it should be excised completely. Histologically, the invasive cancer should be grade 1 or 2 (well or moderately differentiated) throughout, there should be a clear transection margin of at least 1 mm, and there should be no cancer invasion into lymphatic or vascular channels (Fig. 33.10). If any one of the pathologic conditions is violated, conservative therapy carries a 20–25% risk of adverse outcome, tilting the balance in favor of surgery [13,34–37].

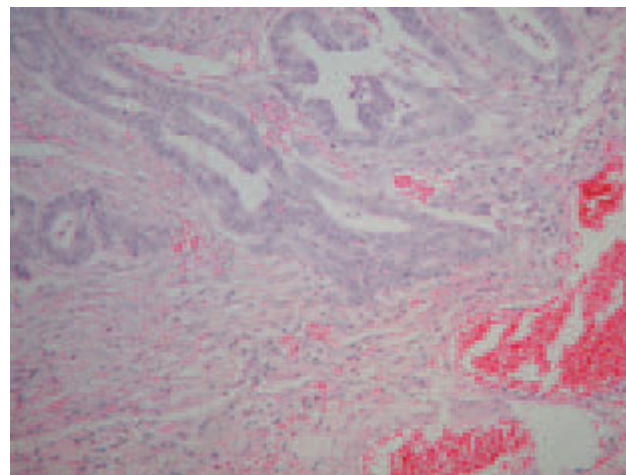
Histopathologic evaluation of the transection margin is facilitated by identifying the zone of thermal electrocoagulation artifact, corresponding to a band of magenta or blue discoloration traversing the base of the polyp. Identifying cancer cells within the coagulated zone may be difficult, but rarely to the degree of compromising the final diagnosis. Piecemeal resections, which yield multiple polypoid fragments with separate electrocoagulation zones, frequently result in indeterminate margins unless the endoscopist has taken the precaution of submitting the actual margin of the polyp as a separate specimen or unless it is identifiable histologically from its content of submucosa.

The pathology report should explicitly grade the least differentiated tumor components, since the presence of grade 3 (poorly differentiated) carcinoma is an adverse histologic feature even if the majority of the cancer is of lower grade [37]. The report should also address the presence or absence of cancer cells within endothelial-lined channels. Although lymphatic invasion is common among polyps containing grade 3 cancer, it occurs infrequently in cancers of lower grades as well. This

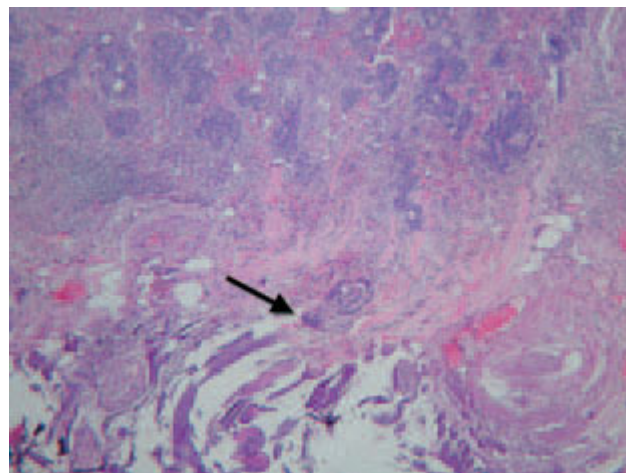
Fig. 33.10 (right) (a) Malignant polyp with invasive grade 2 adenocarcinoma invading the upper stalk. The invasive front (arrow) is located 5 mm from the cauterized margin, well above the 1-mm margin recommended for considering conservative management. (b) Higher magnification showing the point of deepest cancer invasion. The malignant glands are angulated and surrounded by cellular fibrous stroma (desmoplastic reaction). (c) Malignant polyp containing extensive invasive grade 3 adenocarcinoma with a margin of less than 1 mm from the transection line (arrow). The high grade of the cancer and the inadequate margin would each weigh independently against conservative management.



(a)



(b)



(c)

parameter may be the most difficult one to evaluate histologically, since tumor nests surrounded by stromal retraction artifact can closely resemble tumor emboli within lymphatic spaces. The use of immunohistochemical stains to make this distinction has not proven especially useful. In practice, problem cases are best resolved by examining serial histologic sections and by consensus among experienced pathologists [13,36].

In the absence of lymphatic invasion, the metastatic potential of colorectal cancer begins when it invades into the bowel submucosa proper. As a result, patients with malignant sessile adenomas are generally referred for colectomy despite fulfillment of other favorable pathologic criteria, since any cancer invasion necessarily involves the bowel submucosa [34]. For reasons stated previously, the determination whether a particular polyp is sessile or pedunculated should be made by the endoscopist rather than the pathologist. The management of malignant polyps in the mid and lower rectum involves additional considerations, including higher rates of morbidity and mortality associated with definitive surgery and the availability of alternative treatment options such as limited surgical approaches and radiotherapy.

As alluded to earlier, misplaced adenomatous mucosa may simulate well-differentiated invasive carcinoma. Microscopic features that favor malignancy include (i) a haphazard growth pattern, (ii) acute angulation of invasive tumor glands, (iii) higher grade of dysplasia than that of the overlying adenomatous mucosa, (iv) investment of glands by loose fibroblastic stroma (desmoplasia), and (v) absence of hemosiderin deposits. The distinction between well-differentiated mucinous adenocarcinoma and misplaced mucin-filled glands can be especially difficult. Malignancy is favored by the presence of free-floating complex epithelial clusters within the mucous spaces, especially if they are more dysplastic than the overlying mucosa. Nonetheless, polypectomy alone is curative in either case unless the glands extend to the transection margin.

Dysplastic polyps in inflammatory bowel disease

Dysplasia in inflammatory bowel disease is classified endoscopically as either flat, i.e. grossly indistinguishable from the surrounding mucosa, or grossly visible, corresponding to a polyp, plaque, or other mass lesion. The latter, referred to as a dysplasia-associated lesion or mass (DALM), has traditionally been regarded as an indication for colectomy even if biopsies demonstrate only low-grade dysplasia, since over 40% of patients with a DALM are diagnosed with invasive carcinoma at immediate colectomy [38].

Nevertheless, recognition that endoscopically visible dysplastic lesions are a heterogeneous group that also

includes benign endoscopically resectable dysplastic polyps, some closely resembling conventional adenomas both endoscopically and histologically, has resulted in growing acceptance of more conservative management options, particularly since fortuitous sporadic adenomas would not be unexpected in patients with inflammatory bowel disease. Whereas endoscopic removal is considered appropriate treatment of all pedunculated polyps and of polyps arising outside diseased areas of the colon, the sporadic nature of which is taken for granted, the indications for conservative management of patients with sessile dysplastic polyps within diseased colon are still evolving. Two recent studies following a total of 72 patients with ulcerative colitis who underwent colonoscopic resection of small adenoma-like polyps without long-term adverse consequences concluded that conservative management is a reasonable option in patients who have no evidence of flat dysplasia either adjacent to the polyp or elsewhere in the bowel [39,40]. Alternative molecular-based approaches to this problem are currently being pursued [41].

Hyperplastic polyps

Hyperplastic polyps (synonymous with metaplastic polyps in the British literature) are second in prevalence only to adenomas in populations where colon cancer is prevalent, occurring in 20–40% of adults in the USA and western Europe. Approximately 80% are less than 5 mm in size, accounting for approximately 40% of diminutive polyps [42], and only 1–3% exceed 1 cm [43,44]. Although the endoscopic appearances are frequently distinctive, corresponding to a hemispherical, smooth, or mucus-capped protrusion, conventional endoscopic inspection alone does not permit sufficiently clear-cut distinction between hyperplastic and adenomatous polyps to serve as a basis for decision-making [45]. In addition, endoscopically typical hyperplastic polyps may harbor microscopic adenomatous components, both conventional [46] and serrated [27]. Accordingly, there is sound justification for the practice of routinely removing putative hyperplastic polyps for pathologic examination.

Microscopically, hyperplastic polyps consist of elongated parallel crypts whose upper zone is dilated and lined by columnar epithelium with a distinctive serrated profile (Fig. 33.11). The epithelium consists of goblet cells intermingled with finely vacuolated mucin-laden columnar cells containing small, round, uncrowded nuclei and no mitoses. Approximately half of hyperplastic polyps contain a distinctive band of glassy eosinophilic collagen running along the surface basement membrane.

Although traditionally classified as nonneoplastic, hyperplastic polyps remain enigmatic entities from a histogenetic standpoint. Their serrated architecture is

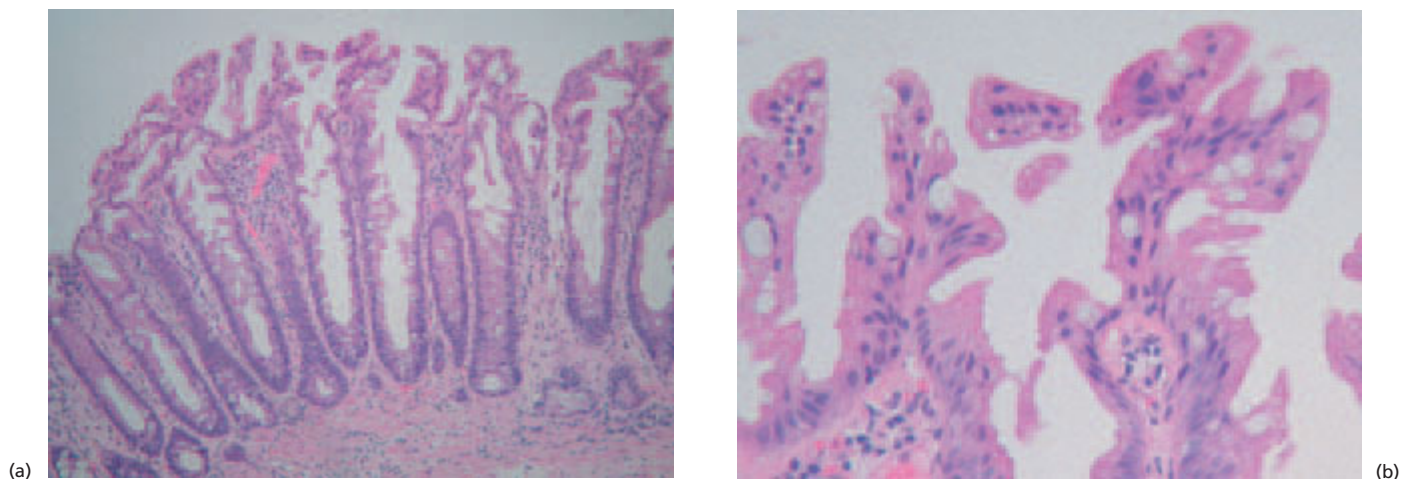


Fig. 33.11 (a) Hyperplastic polyp: the crypts are characteristically elongated and dilated, mainly in the upper zone, where the lining epithelium is prominently serrated. (b) Higher magnification reveals scattered goblet cells and intervening columnar cells with tiny mucin vacuoles. The nuclei at the surface are small, round, and widely spaced.

hypothesized to reflect a molecular defect impeding normal apoptotic shedding of senescent epithelial cells near the luminal surface, and there is accumulating evidence of specific mutations and of histogenetic similarities to serrated adenomas [32].

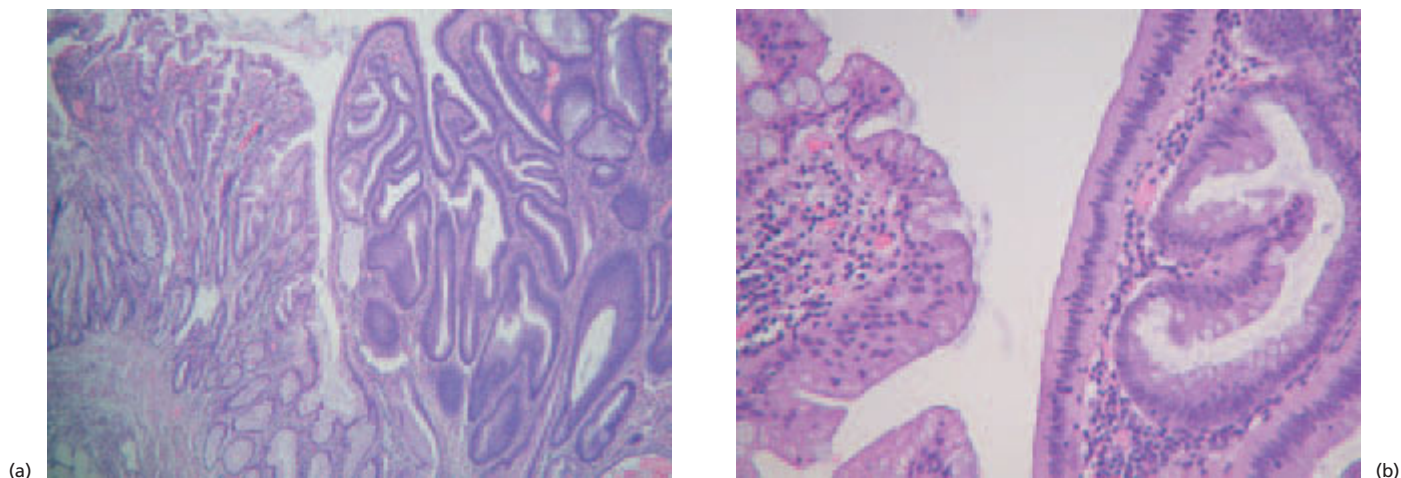
Composite or admixed hyperplastic–adenomatous polyps contain discrete hyperplastic and adenomatous

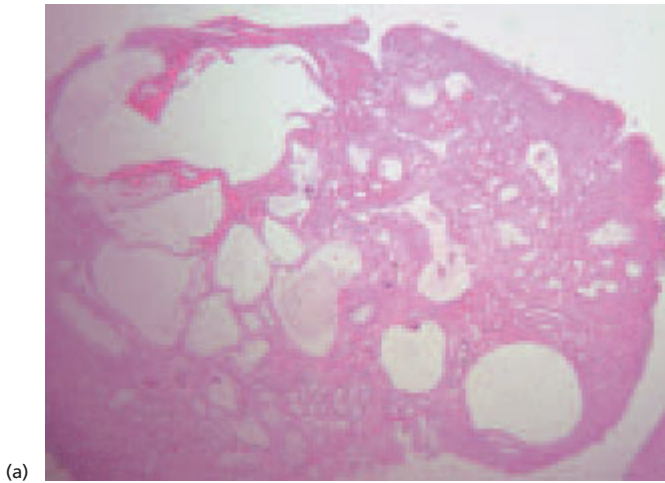
elements (Fig. 33.12). Molecular evidence suggests that some if not all reflect a direct transformation from hyperplastic to dysplastic epithelium. The practical significance of this entity is that a diagnosis of hyperplastic polyp rendered on a biopsy sampled from an incompletely excised polyp does not exclude the possibility of adenomatous tissue, a potential source of carcinoma, retained within the residual polyp.

Microscopically, large hyperplastic polyps resemble other polyps with serrated luminal profiles, especially serrated adenomas, inflammatory polyps, and hamartomatous polyps. A subepithelial collagen band, if present, is diagnostic. Serrated adenomas by definition exhibit dysplastic nuclear features and upper-zone mitoses; however, their distinction from the bland nuclei of hyperplastic polyps may be subtle at best, especially when there is superimposed mechanical stress or inflammation. The distinction from inflammatory and hamartomatous polyps is discussed later.

Inverted hyperplastic polyps are characterized by traumatic misplacement of crypts in the submucosa, analogously to adenomas with misplaced mucosa [47,48].

Fig. 33.12 (a) Composite adenoma–hyperplastic polyp consists of hyperplastic polyp with typical serrated crypt architecture on the left and tubular adenoma on the right. (b) Higher magnification shows sharp transition between hyperplastic epithelium with small, round, well-separated nuclei and dysplastic epithelium with elongated, crowded, and darkly stained nuclei.





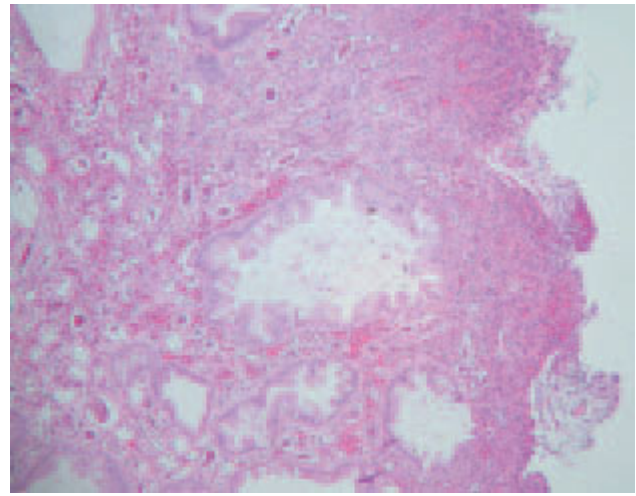
(a)

Fig. 33.13 Juvenile polyp. (a) Chronically inflamed, edematous stroma containing crypts of varying sizes and shapes, many markedly distended and containing mucin secretions. (b) Note the serrated architecture of some of the glands, especially those near the eroded surface, reflecting regenerative epithelium.

Juvenile polyps

Although juvenile polyps (synonymous with retention polyps) account for approximately 90% of intestinal polyps in the pediatric age group, approximately 40% are encountered in adults, the vast majority presenting as one or two lesions, several millimeters to 2 cm in size, located in the sigmoid colon or rectum. Patients with a solitary juvenile polyp face no excess short- or long-term risk of colorectal or other cancers, in contrast with patients with juvenile polyposis syndrome who face a substantial risk of colorectal neoplasia [49]. Barring an established family history of juvenile polyposis, where the occurrence of even one juvenile polyp should prompt a work-up, clinical investigation to exclude juvenile polyposis syndrome is recommended only when three or more synchronous juvenile polyps are encountered, whether in a child or adult [50].

On section, fully developed juvenile polyps contain distended mucus-filled cysts of varying sizes embedded in an edematous stroma. Microscopically, the cysts are lined by cytologically bland cuboidal or columnar mucinous cells and, in addition to mucus, may contain acute inflammatory cells or necrotic debris. The intervening stroma may contain scattered chronic inflammatory cells and lymphoid follicles, but smooth muscle bundles are rare, in contrast with hamartomatous polyps of Peutz–Jeghers type (Fig. 33.13). The surface is frequently eroded, eliciting reactive changes in the subsurface glands that should not be confused with dysplasia. True dysplasia rarely occurs in a juvenile



(b)

polyp outside the setting of juvenile polyposis syndrome. During their development, juvenile polyps may consist mostly of inflammatory and granulation tissue, creating the potential for confusion with inflammatory polyps [51].

Hamartomatous polyps

Hamartomatous polyps, classically associated with Peutz–Jeghers syndrome, may also occur sporadically as isolated lesions. They range in size from 5 mm to 3 cm, exhibit a coarsely lobulated surface, and are attached to the surface by a short stalk or broad base. Microscopically, they consist of lobules of mature, tubular, or serrated epithelium separated by coarse bands of smooth muscle that radiate outward from the muscularis mucosae (Fig. 33.14).

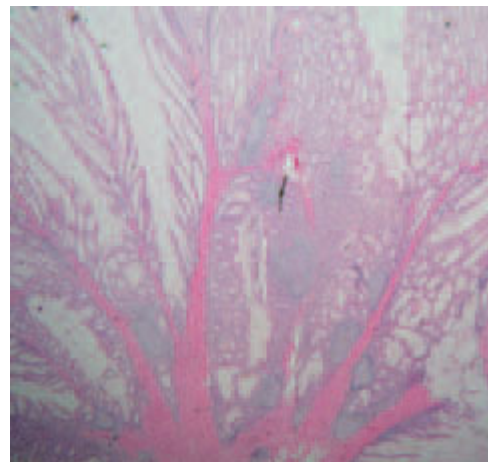


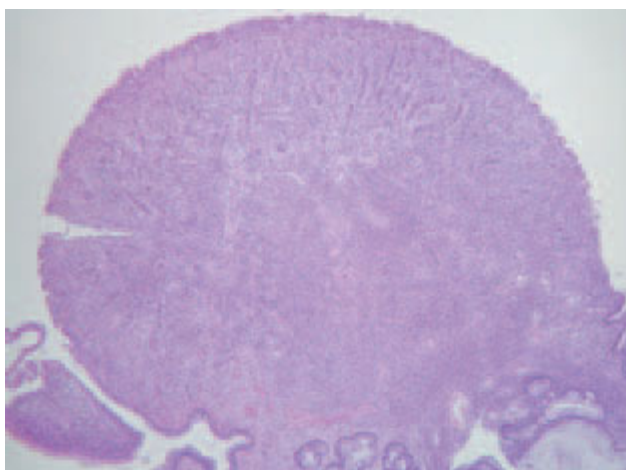
Fig. 33.14 Hamartomatous polyp. The core consists of smooth muscle bundles in an arborizing pattern. Usually, the muscle component of colorectal hamartomas is less prominent than in this example.

Whether sporadic or multiple, hamartomatous polyps of the large intestine tend to have a less prominent smooth muscle component than their small intestinal counterparts. As a result, they may be very difficult to distinguish from other serrated polyps, such as hyperplastic polyps and serrated adenomas. Misplaced elements in the underlying intestinal wall may mimic mucinous carcinoma, but are uncommon compared with hamartomatous polyps of the small intestine. Dysplasia occasionally occurs, but rarely in polyps of the sporadic type.

Inflammatory polyps

These are produced by inflammatory processes that cause undermining ulceration of mucosa, an exuberant granulation tissue reaction, or both. They occur either singly as a sequel of localized mucosal injury or more diffusely, most often as a manifestation of chronic inflammatory bowel disease, and assume diverse macroscopic appearances, including nodules, filiform excrescences, mucosal bridges, and leafy fronds. The microscopic appearances vary with the phase of inflammation (Fig. 33.15). When actively inflamed, inflammatory polyps comprise admixtures of inflamed and regenerative epithelium, edematous chronically inflamed stroma, and granulation tissue; however, once the inflammation has subsided they may revert to normal histology. The regenerative epithelium frequently assumes a serrated appearance similar to that of hyperplastic or hamartomatous polyps. The diagnosis can generally be made at low magnification based on the disorganized arrangement and marked variations in crypt sizes and shapes, which contrasts with the relative uniformity of hyper-

Fig. 33.15 Inflammatory polyps consist of granulation tissue, colorectal mucosa, or both. (a) Polypoid mass of granulation tissue. (b) Polyp consisting of relatively uninflamed mucosa. The extreme variations in the sizes and shapes of the crypts are sequelae of previous inflammation.



(a)

plastic polyps and the distinctive lobulated architecture of hamartomatous polyps.

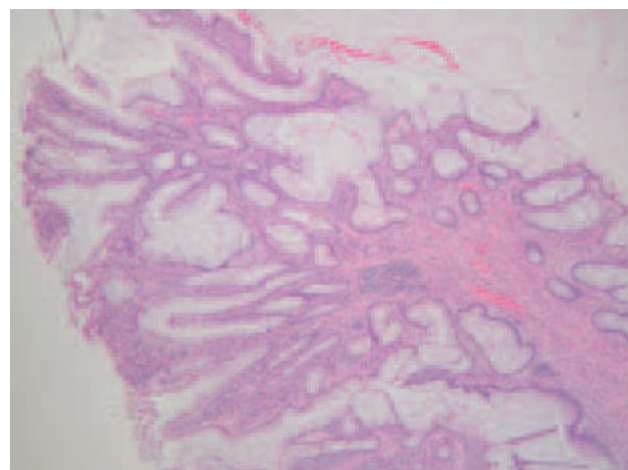
Polyps associated with mucosal prolapse

Polyps caused by mechanical stresses associated with mucosal prolapse arise in diverse settings, including diverticula, solitary rectal ulcer syndrome, rectal prolapse, hemorrhoids, and colostomy sites. Nonetheless, they share certain histologic similarities, particularly diversion of muscle fibers from the muscularis mucosae into the lamina propria and between the crypts.

Prolapsing polyps often present as reddish-brown protrusions of redundant mucosa around the mouths of colonic diverticula, where they prolapse into diverticular cavities. In addition to smooth muscle bundles, the mucosa contains elongated crypts, congested blood vessels, fresh hemorrhage, and hemosiderin deposits [52–54] (Fig. 33.16).

Solitary rectal ulcer syndrome, despite its name, may not demonstrate an ulcer, but may be associated with one or multiple polypoid lesions in approximately 40% of cases. The site of involvement is usually the anterior or anterolateral rectal wall, which may be locally indurated and mimic a neoplasm. Microscopically, the polypoid configuration results from elongation of the crypts, which often assume a villiform configuration toward the surface. The surrounding lamina propria consists of varying proportions of collagen and smooth muscle, the latter causing tapering or distortion of the lower portions of crypts (Fig. 33.17). Erosion of the surface, heralded by a band-like proliferation of granulation tissue, is accompanied by a pseudomembranous cap of mucosuppurative exudate. Analogous polypoid lesions of the anorectal transition zone are referred to as inflammatory cloacogenic polyps.

Reactive epithelium in solitary rectal ulcer may be misinterpreted as dysplastic [55], an error potentially reinforced by the clinical impression of an indurated mass,



(b)

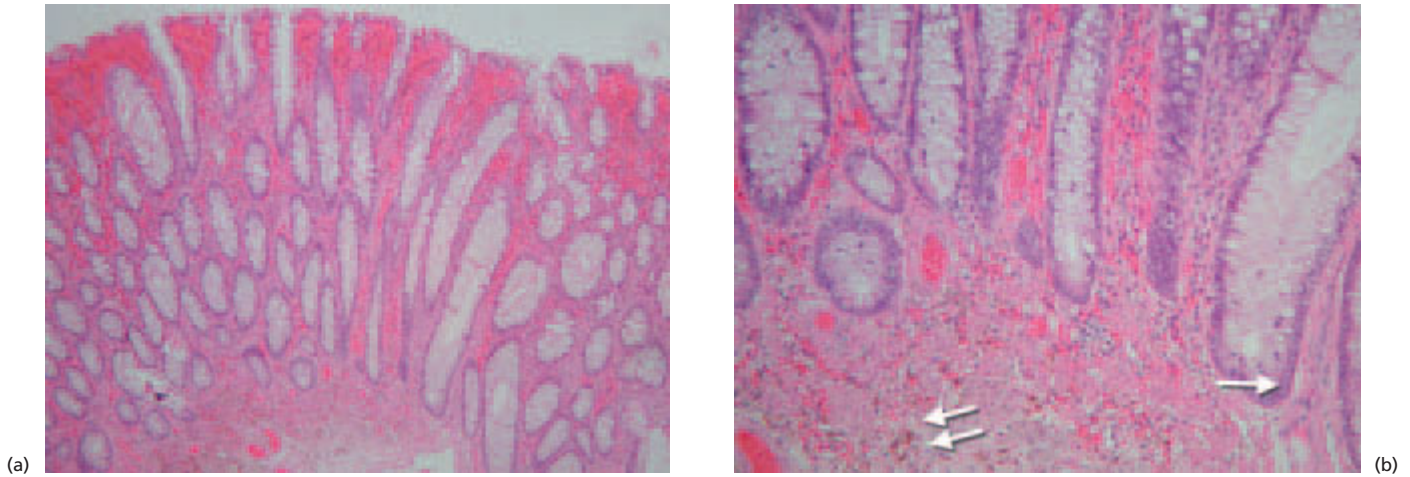


Fig. 33.16 (a) Peridiverticular prolapsing mucosal polyp characterized by elongated crypts and hemorrhagic lamina propria. (b) The base of the polyp contains occasional smooth muscle bundles extending upward between the crypts (single arrow) and prominent hemosiderin deposits (double arrows).



Fig. 33.17 Polyp associated with solitary rectal ulcer syndrome. The crypts are enveloped by smooth muscle, a manifestation of chronic mucosal prolapse.

and compounded if mucosal tissue becomes traumatically misplaced within the bowel wall, a phenomenon referred to as proctitis cystica profunda. Ultimately, the correct diagnosis depends both on awareness of the syndrome and its pathologic manifestations and on recognition of the cytologic distinctions between reactive and dysplastic epithelium.

Lymphoid polyps and polypoid lymphomas

Benign lymphoid polyps occur singly or multiply, usually in the lower rectum, and range from tiny papules

to pedunculated polyps up to several centimeters in diameter [56,57]. Their incidence is unknown since they are clinically innocuous and rarely reported. On section, they are tan and fleshy. Histologically, they consist of a circumscribed collection of well-formed, clearly separate lymphoid follicles with prominent germinal centers. The depth of infiltration of the rectal wall is usually limited to the submucosa; however, penetration into the muscularis propria is not a criterion of malignancy [58]. Local excision is curative.

Primary lymphomas present infrequently as one or multiple colorectal polyps. Most correspond to B-cell lymphomas, specifically marginal zone lymphoma of mucosa-associated lymphoid tissue (MALT) type or mantle cell lymphoma; however, rare cases of polypoid follicular lymphoma, adult T-cell lymphoma, Burkitt lymphoma, and other types have been reported. Mantle cell lymphoma, a relatively aggressive entity, typically presents diffusely as multiple lymphomatous polyposis, although similar appearances have been ascribed to other entities [59,60].

Histologically, marginal zone B-cell lymphoma of MALT type is characterized by a heterogeneous population of predominantly small to medium-size lymphocytes, including follicular center-like cells with irregular nuclear contours and abundant cytoplasm, similar cells with monocytoid features, small round lymphoid cells, interspersed blast cells with vesicular nuclei and prominent nucleoli, and sometimes plasmacytoid cells. The infiltrate often surrounds germinal centers and invades the crypt epithelium, forming lymphoepithelial lesions (Fig. 33.18).

Mantle cell lymphoma, by contrast, is characterized by a monomorphous infiltrate of small to medium-size B cells with irregular nuclear contours, frequently interspersed with macrophages to produce a “starry sky” pattern. There is no association with germinal centers or formation of lymphoepithelial lesions [61].

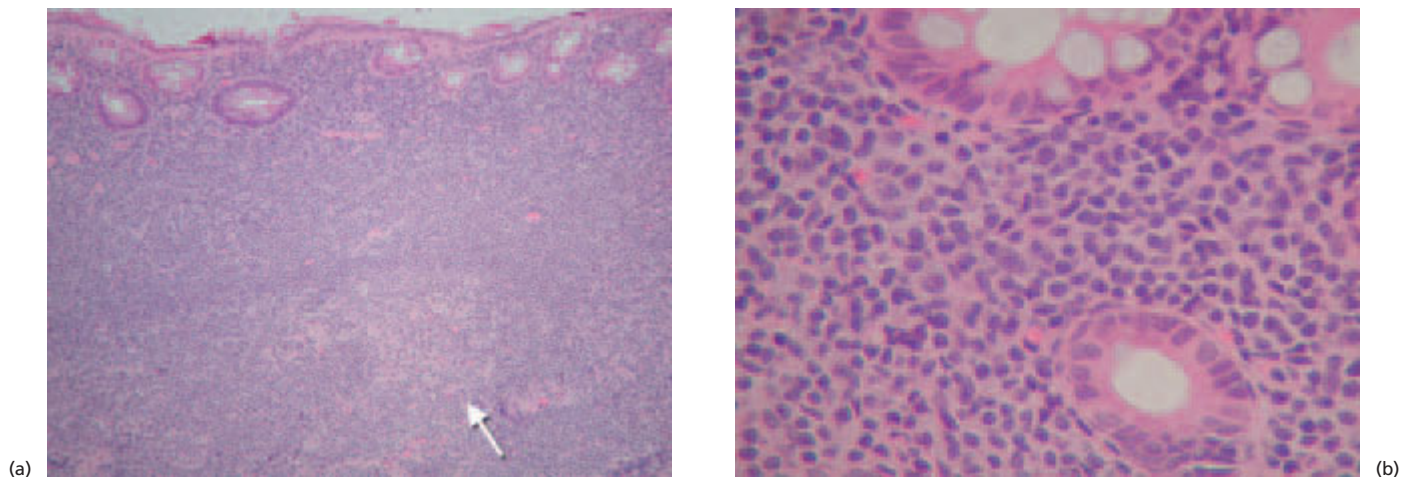
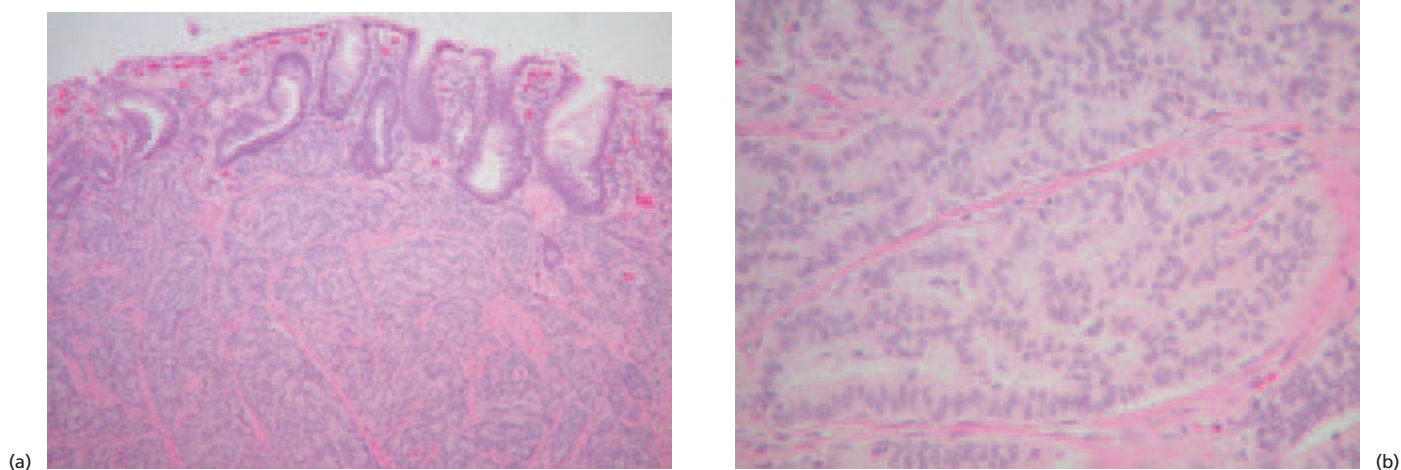


Fig. 33.18 Marginal zone lymphoma of MALT type. (a) Dense lymphocytic involving the lamina propria and submucosa. Note the residual germinal center (arrow). (b) The lamina propria is packed with mostly small lymphoid cells with slightly irregular nuclear contours. An immunohistochemical profile of CD20⁺, CD79a⁺, CD43⁺, CD3⁻, and CD5⁻ helped confirm the diagnosis.

Both MALT and mantle cell lymphomas express surface IgM and are positive for the pan-B-cell markers CD20 and CD79a and negative for the pan-T-cell marker CD3. MALT lymphomas are negative for CD5, variably positive for CD43, and do not overexpress cyclin D1, whereas mantle cell lymphomas are positive for CD5 and CD43 and overexpress cyclin D1. Negative staining

Fig. 33.19 (a) Rectal carcinoid at low magnification comprising rounded lobules of crowded glandular epithelium separated by fibrovascular septa. (b) Higher magnification showing cribriform architecture and evenly spaced, round-to-ovoid nuclei with clumped chromatin.



for CD10 is useful in distinguishing both from follicular lymphoma.

In addition to benign lymphoid polyps, malignant lymphoma must be distinguished from reactive lymphoid hyperplasia, small-cell carcinoma, granulocytic sarcoma, and other leukemic infiltrates.

Carcinoid tumors

Approximately 90% of large intestinal carcinoid tumors occur in the rectum, most presenting as solitary sessile polyps less than 1 cm in size and running a benign course [62–64]. Microscopically, the tumor cells are arranged as ribbons, solid nests, tubules, or mixed patterns, and contain round uniformly spaced nuclei with speckled or clumped chromatin (Fig. 33.19). Mitotic figures generally number less than one per 10 high-power fields. A background of hyalinized stroma accounts for the firm consistency. A substantial minority of cases do not react with stains used to diagnose carcinoids elsewhere, such as silver-based stains and immunohistochemical stains for neuroendocrine markers.

The main criteria of malignancy in a carcinoid tumor are muscularis propria invasion, size, and lymphatic invasion [63,65–67]. Tumors that invade the muscularis propria are regarded as potentially malignant regardless of size [68]. Metastasis occurs in 2–3% of tumors less than 1 cm, 5–15% of those 1–2 cm, and 60% of larger tumors [63,64,69]. Carcinoids less than 1 cm that spare the muscularis propria are generally considered adequately treated by polypectomy or local excision; however, there is a low rate of unpredictable adverse outcomes [70]. Low mitotic rates, DNA diploidy, and low cell proliferation indices do not assure benign behavior in the presence of other adverse features [62,63,68]. Colonic carcinoids are histologically similar to rectal carcinoids but as a group are larger and more aggressive, averaging 5 cm in diameter and often resembling conventional adenocarcinomas.

Composite adenoma–carcinoid tumors are quite rare. Although some seem to be fortuitous “collision” tumors, there are case reports describing intimate intermingling of the adenomatous and carcinoid components, supporting origin from a common stem cell [71,72].

Summary

The clinical approach to the patient from whom polyps have been removed is based completely on the histopathologic features of the recovered tissue. There are a vast number of pathologic entities that comprise the overall category of “polyps” and some may require further evaluation or treatment, depending on their histology. Resected polyps must be adequately examined microscopically following prescribed quality-controlled laboratory procedures. Inappropriate phrases should no longer be used by pathologists, such as the terms “adenoma with dysplasia” (since all adenomas are by definition dysplastic) and “carcinoma *in situ*.” The dialog between the clinician and the pathologist is an important communication that will provide a more accurate report, leading to a better-informed clinical decision for the patient.

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Chapter 34

Principles of Electrosurgery, Laser, and Argon Plasma Coagulation with Particular Regard to Colonoscopy

G. Farin and K.E. Grund

Introduction

Hemostasis and the ablation of pathologic tissues are the most important indications for thermal techniques in colonoscopy. However, because the colon wall is thin, it is not the ideal organ for the application of thermal techniques. The thickness of the three layers of the colon wall, comprising the mucosa, submucosa, and muscularis propria, varies from 1.5 to 3 mm (Fig. 34.1) throughout the length of the large intestine. Following insufflation, the wall can be even thinner. Since damage to the muscularis propria of the colon should be avoided during endoscopic interventions, thermal injury must not extend beyond the submucosa in order to avoid complications. As a consequence, only about half of the 1.5–3.0 mm constituting the thin wall of the colon is accessible to the endoscopist for thermal interventions. The necessity that endoscopically applied thermal techniques do not damage the muscularis propria of the colon makes their application within the colon difficult, especially when the lesion to be treated is large.

The application of thermal techniques in the colon requires knowledge of thermal effects in biologic tissues. In addition, the endoscopist must have sufficient training and master the available endoscopes, instruments, and peripheral equipment. This article deals with the theoretical principles concerning the application of thermal techniques, especially in the colon.

Relevant thermal effects in biological tissues

All thermal effects in and on biological tissues—whether intentional or unintentional—depend on the intensity and duration of temperature in the tissue (Fig. 34.2) almost regardless of the way in which this temperature is reached.

Thermal treatment is among the oldest of therapeutic techniques. Although high-frequency (HF) surgery was introduced about 100 years ago and laser surgery about 30 years ago, the terminology uses words that are centuries old and described various types of cautery. As

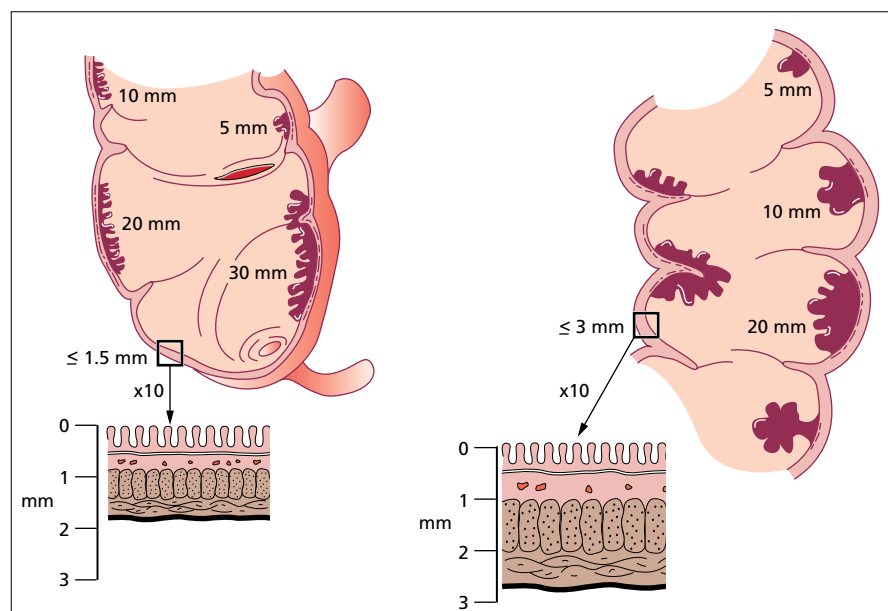


Fig. 34.1 Diagram of the wall of the right and left colon with scale representation of thickness as well as small, medium, and large adenomas.

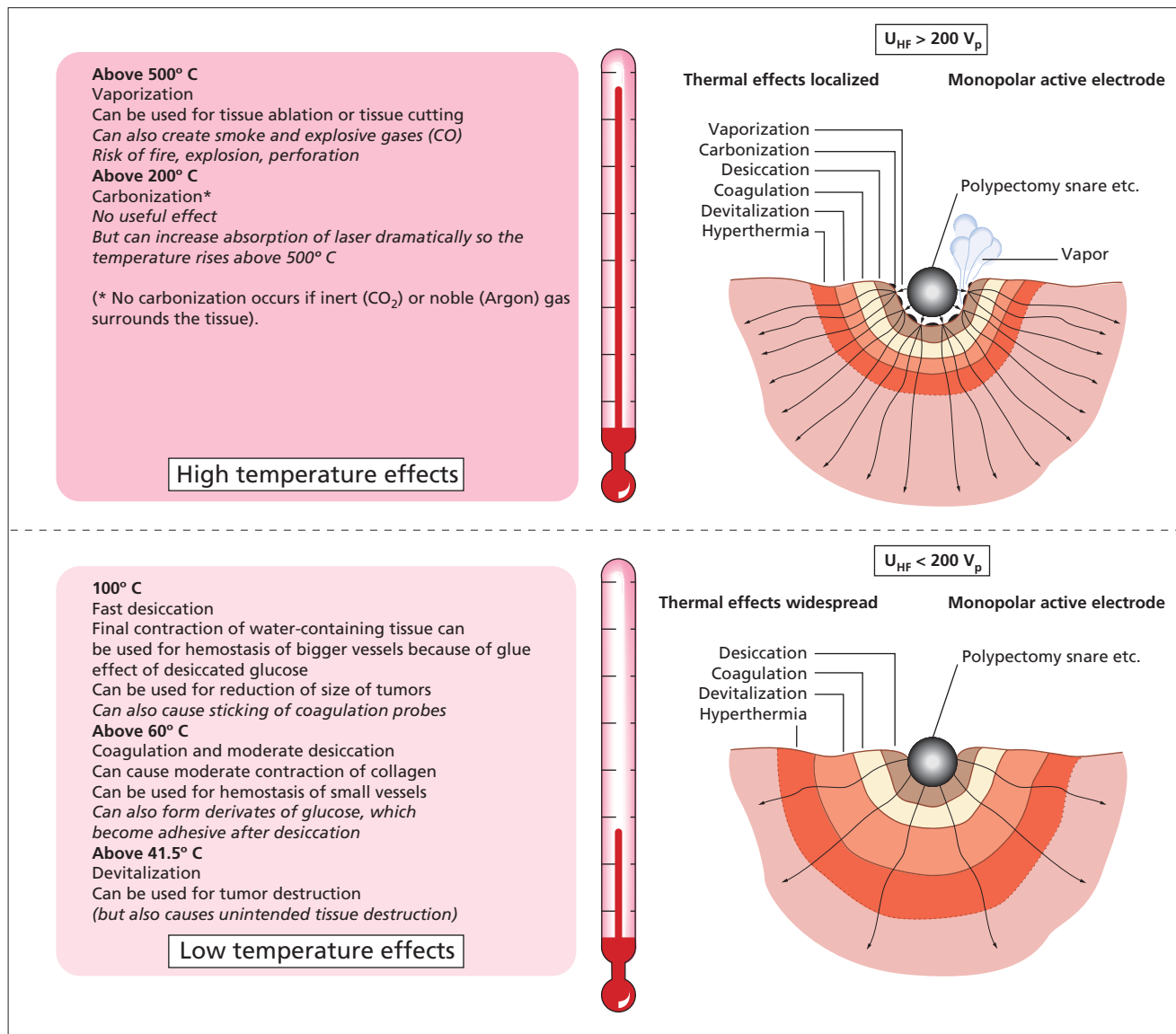


Fig. 34.2 Thermal effects in biological tissue resulting from application of high or low (peak) voltage high-frequency current.

an example, coagulation is the only term in current use to describe thermal hemostasis, even though different thermal techniques can be used for this purpose. The term “coagulation” actually encompasses many different tissue effects such as devitalization, coagulation and desiccation.

Thermal devitalization

Thermal devitalization is defined as irreversible death of tissue. More precisely, devitalization of a target tissue means irreversible as well as complete death of tissue. Biologic tissue becomes devitalized if its temperature

reaches 41.5°C. The higher the temperature, the faster the devitalization. Unfortunately devitalization is not a visible phenomenon and hence can occur in an uncontrolled fashion, and thus it is not used for destruction of pathologic tissue. Even if thermal devitalization is not employed intentionally, some degree of tissue death occurs outside the border of the coagulation zone. The depth of the invisible thermal devitalization zone depends on many different parameters, and it should be assumed for the sake of safety that it occurs in direct proportion to the visible coagulation effect.

Thermal coagulation

Thermal coagulation is defined as conversion of colloidal systems from sol to gel state. Biologic tissue becomes coagulated thermally if its temperature increases to

approximately 60°C. When this temperature is exceeded, the structure of the cell changes causing the following effects:

- change of the color of the tissue;
- formation of derivatives of collagen, e.g. glucose;
- contraction of collagen.

The change in color of the tissue is the only way to visually control intended as well as unintended coagulation. Unfortunately, color changes can only be seen on the surface but not within the tissue.

Even if thermal devitalization could be used for destruction of pathologic tissue, it is not used for this purpose because it is not controllable. Therefore the coagulation effect is used as a means of controlled devitalization. It should be noted that an invisible thermal devitalization zone of variable depth is unavoidable outside the border of the coagulation zone.

The formation of derivatives of collagen, e.g. glucose, can become adherent after desiccation.

The contraction of collagen can result in narrowing of the lumen of blood vessels and hence cause hemostasis. Even though the term “coagulation” is used as a synonym for thermal hemostasis, thermal coagulation alone is only efficient for hemostasis of small vessels. Larger vessels (> 0.5 mm) must be compressed mechanically during thermal coagulation to achieve hemostasis.

Thermal desiccation

Thermal desiccation is defined as heat-induced dehydration of tissue. If the temperature of tissue is equal to the boiling temperature of intra- or extracellular water (c. 100°C), the desiccation effect can dehydrate the tissue quickly, depending on the density of power applied to the target tissue. Thermal desiccation can cause:

- contraction and shrinkage of tissue, by dehydration;
- an adhesive effect of glucose;
- a dry layer that acts to insulate tissue electrically.

Thermal desiccation causes significant contraction by drying and shrinkage of vessels, resulting in hemostasis of small vessels. Larger vessels (> 0.5 mm) must be mechanically compressed during thermal hemostasis.

Desiccation of glucose as a derivative of collagen results in a glue effect, which in turn causes sticking of desiccated tissue to coagulation electrodes, heater probes, the distal end of laser fibers, and also to polypectomy snares.

Desiccated tissue has a relatively high specific electric resistance. A layer of desiccated tissue functions like an electric isolating layer. This can cause a problem during polypectomy if the tissue adjacent to the snare becomes desiccated. When this occurs, there is no cutting effect and the snare can get stuck within the desiccated tissue of the polyp and cannot be moved forward or backward. During use of the argon plasma coagulator (APC) the

desiccated electrically isolating layer automatically limits the maximum penetration depth of the thermal effect, described in more detail below.

Thermal carbonization

Thermal carbonization is defined as partial oxidation of tissue hydrocarbon compounds if the temperature exceeds 200°C. Because the temperature of tissue containing water does not exceed approx. 100°C, only desiccated and relatively dry tissue can become heated above 200°C and carbonized. Dry tissue will achieve temperatures above 100°C only by an electric spark or laser.

If the temperature of desiccated tissue increases above 200°C in the presence of oxygen (room air), it becomes carbonized after desiccation. However if the target tissue is bathed by a noble gas such as argon, the tissue does not become carbonized.

Even though carbonization of tissue is not a goal in therapeutic colonoscopy, it is relevant during tissue vaporization by laser, because the absorption of light increases when the tissue becomes carbonized to a black color.

Thermal vaporization

Thermal vaporization is defined as combustion of desiccated and carbonized tissue. Tissue becomes vaporized during or after desiccation and carbonization when the temperature increases to approximately 500°C and it is bathed in oxygen-containing gas, e.g. air. If the target tissue is within inert gas (e.g. CO₂) or noble gas (e.g. argon), the tissue does not become vaporized.

Thermal vaporization can be used directly for the ablation of pathologic tissues as well as indirectly for tissue cutting. In colonoscopy only laser, especially Nd:YAG laser, is used for tissue ablation by vaporization, and only high-frequency surgery is used for thermal cutting of tissue.

Generation of temperature in thermal tissue

Various energy forms, and their respective sources, applicators and application techniques are available for thermal intervention in the colon (Fig. 34.3). A description of these properties and their relevance for endoscopic applications in the colon follow.

The temperature of tissue can be increased either exogenously, e.g. by means of a heater probe, or endogenously, e.g. by means of electric current or laser; it can also be increased by a combination of both, as in high-frequency surgical cutting, where endogenous heat is caused by electric current and exogenous heat is caused by electric arcs between the active electrode and tissue.

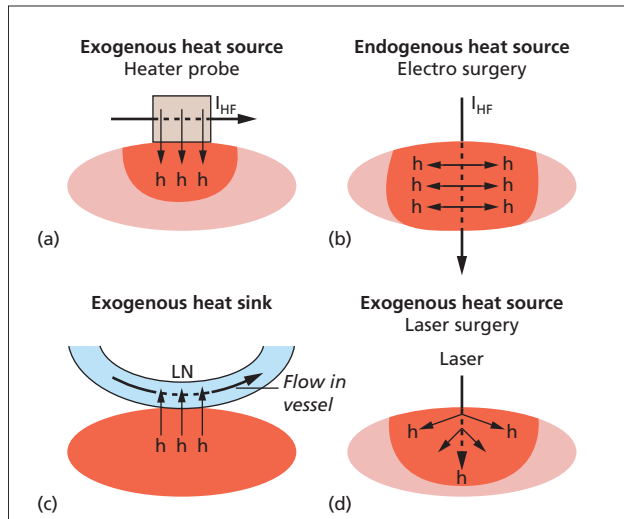


Fig. 34.3 Modalities of heat surgery. (a) Heat (h) from a heat source flows into tissue. (b) Heat (h) from the tissue flows into a heat sink such as a blood vessel. (c) Electric current I_{HF} becomes converted to heat (h) within the tissue. (d) Laser becomes converted to heat (h) within the tissue.

For thermal interventions in the colon it is important that the temperature required for an intended purpose is only delivered at the target tissue.

Unintentional thermal damage to adjacent tissues must be avoided. This stipulation is difficult to achieve since it is not possible to heat part of a tissue to a desired temperature without at the same time heating adjacent tissue. Although it is not possible to avoid heat transfer, it may be possible to keep thermal damage of adjacent tissues to a minimum. Where possible, the distance between the target tissue and deeper surrounding tissue can be increased for the purpose of limiting thermal damage by submucosal injection with physiological NaCl solution (Fig. 34.4).

Some coagulation effect to adjacent (deeper or surrounding) tissue can also be desired in some cases, especially during cutting of vascularized biologic tissue, such as during polypectomy. During polypectomy, the tissue becomes vaporized in front of a cutting electrode and heat spreads to the adjacent tissue (the cut edges) to promote hemostasis.

These aspects should be taken into account when choosing the primary energy form, its source, applicators, and application techniques.

As mentioned previously, in the colon the distances between the tissues which are the desired subject of thermal heating and those tissues which are not intended to be thermally damaged are very small; as a consequence, the diffusion of heat within the surrounding tissue also has to be taken into account. Heat flows from tissues with a higher temperature into tissues with a lower temperature (Fig. 34.5). This diffusion effect

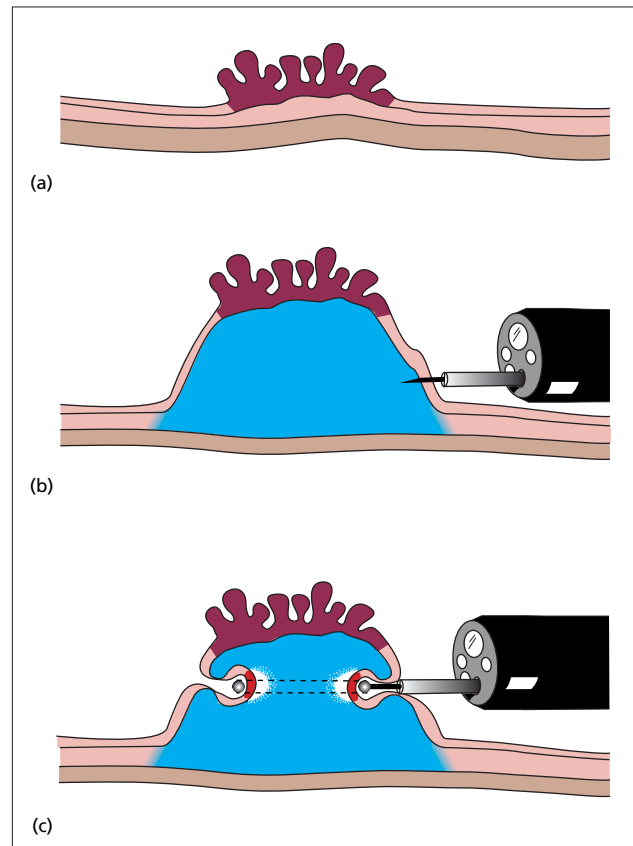


Fig. 34.4 (a,b,c) Injection of fluid into the submucosa will increase the distance between a target tissue which is to be heated and adjacent tissue which should not be heated.

is not used for therapeutic purposes in colonoscopy, and is limited by heating the target tissue to the temperature required only for the short amount of time necessary for the intended purpose.

In order to avoid unintentional damage to the tissue adjacent to the target tissue, it is necessary to know the maximum depth of the tissue injury and how to control the effect produced by the various thermal techniques.

Heater probe

Heater probes belong to the family of cautery instruments, which have a very long history. In principle, cautery instruments consist of a handle with a distal tip, which can be heated to a temperature appropriate to cause one of the specific thermal effects in biologic tissue. The heater probe consists of a catheter with a special heat-generating device built into the tip, which converts electric energy to heat energy [1,2]. The heat generated outside the tissue (exogenously) can be applied to a target tissue by touching it with the hot tip.

The temperature of modern heat probes for flexible endoscopy is adjustable and automatically controlled.

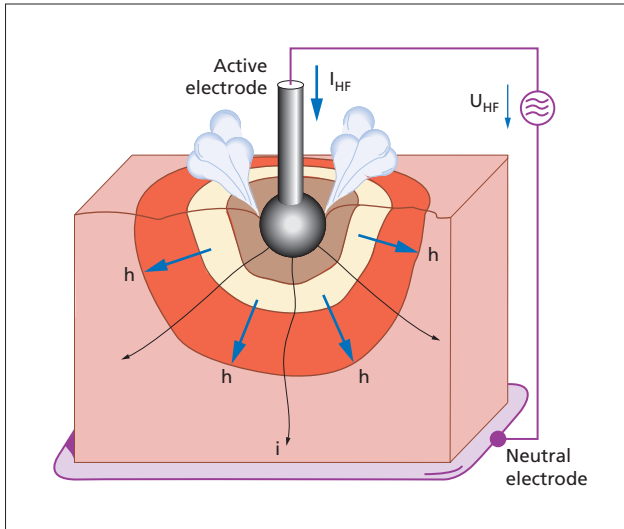


Fig. 34.5 Heat flow (h) within tissue must be taken into account during use of electrosurgery. I_{HF} , high-frequency current; U_{HF} , high-frequency voltage.

Modern heat probes are provided with irrigation from a nozzle on the tip, which can be used to clear blood from the site to facilitate a clear view and accurate positioning. A special coating on the tip prevents it from sticking to desiccated tissue.

Because heat probes can be pressed against the target tissue during heat application, even bleeding from medium size vessels can be treated by simultaneously compressing and coagulating the vessel (Fig. 34.6a). However, this should be done very carefully to avoid thermal damage to the muscularis propria (Fig. 34.6b).

High-frequency surgery

General principles of high-frequency electric devices

High-frequency surgery (HF surgery) is a thermal technique where the required temperature is reached by conversion of electric energy into heat energy within the target tissue, i.e. endogenously.

High-frequency alternating current (HF current) with frequencies greater than 300 kHz (ICE 6001-2-2) is well suited for the heating of biologic tissues because it does not stimulate either nerves or muscles. The electric energy (E) in tissue caused by the HF current becomes converted (\rightarrow) endogenously into heat energy (Q). The amount of heat energy (Q) measured in watt-seconds (Ws) which is produced in the tissue is a function (f) of the electric resistance (R) and the square of the averaged value (I^2) and the effective duration (Δt) of the HF current (Iav).

$$E \rightarrow Q = f(R, Iav^2, \Delta t) \text{ (Ws)}$$

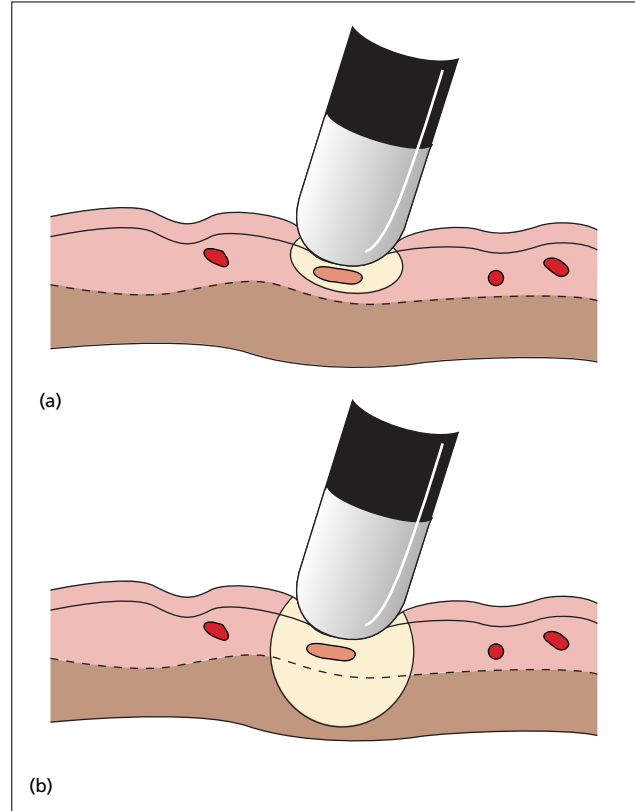


Fig. 34.6 (a) Heater probe can be used to compress and coagulate medium-sized vessels. (b) Thermal damage to the muscularis propria may result from several factors such as temperature, pressure, and duration.

The temperature of a biologic material rises proportionally to the amount of heat and inversely proportionally to the specific heat capacity of the tissue in question.

As mentioned above, a requisite for the application of thermal techniques in the colon is that the temperature required for an intended purpose is reached and becomes effective only at the target tissue, and unintentional thermal damage to adjacent or lateral tissues must be avoided. In HF surgery, this objective is achieved via the current density (j) and the current flow duration (Δt) in the target tissue. The current density (j) is a function (f) of the amount of current (i) measured in amperes (Amp) which flows through a defined area (A) measured in square centimeters (cm^2) at a certain point in time (t) or averaged over a defined time interval (Δt).

$$j = f(i/A) \text{ (A/cm}^2\text{)}$$

The partial amount of heat (q) generated endogenously through electric current either partially or at an arbitrary point within the tissue is proportional to the specific electric resistance (ρ), the square of the current density (j^2), and the effective current flow duration (Δt) at this point of the tissue.

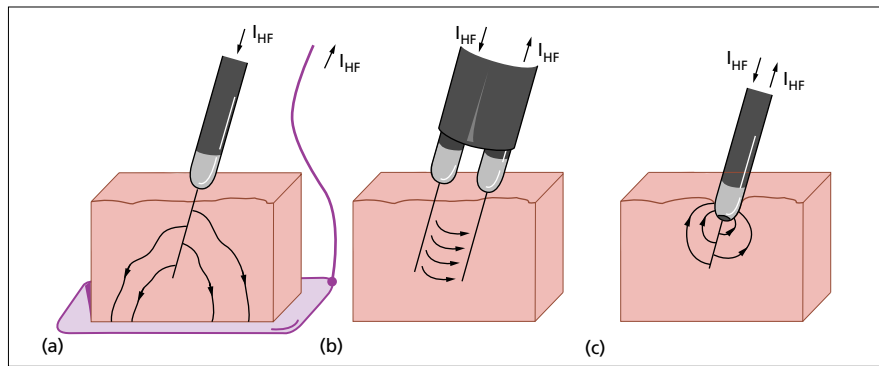


Fig. 34.7 Application techniques of electrosurgery: (a) monopolar; (b) bipolar; (c) quasi bipolar.

$$q = f(\rho, j^2, \Delta t) \text{ (Ws)}$$

Conduction of an electric current through any material requires that both poles of the electric source be connected to the tissue (through the patient) in an electrically conductive manner. Two electrodes are necessary for this purpose. The electrodes at the target tissue are called active electrodes. The electrodes through which the electric current is conducted away from the tissue (the patient), back to the energy source, without any thermal damage at this electrode, are called neutral electrodes. Applications which use an active and a neutral electrode are called monopolar applications, and the instruments used for these applications are called monopolar instruments (Fig. 34.7a). Applications which use both electrodes simultaneously as active electrodes are called bipolar applications, and the instruments used for these applications are called bipolar instruments. As a rule, both active electrodes of bipolar instruments are located close by on the same instrument (Fig. 34.7b).

The density of current within the target tissue can be varied in proportion to the size and shape of the contact surfaces of the active electrodes of HF instruments. Most active electrodes used in flexible endoscopy are in the shape of a needle, loop, or ball electrode (Fig. 34.7c).

Apart from the shape, the size of the contact surface plays an important role as regards the current density and its distribution both in the target tissue and in adjacent tissue. A smaller contact surface results in a steep reduction in the current density and in the temperature profiles in the tissue independent of the distance from the contact surface (Fig. 34.8).

HF current can flow through biological tissue only when the tissue contains water and electrolytes. As a consequence, the temperature of tissue containing water cannot rise above the boiling point of water (approx. 100°C). Tissues that contain less water and are drier, have a lower electric conductivity and less HF current can flow through this tissue. Completely dry biologic tissue is an electric insulator, hence no electric current can flow through it, and the temperature cannot rise (Fig. 34.2a). This fact is of importance during use of argon plasma coagulation.

Electric arcs

Electric arcs are ignited between an active electrode and tissues when the peak value of the HF voltage is equal to or greater than 200 V, which is typical if the active electrode consists of metal and the tissue contains water (Fig. 34.2b). Since these electric arcs reach temperatures

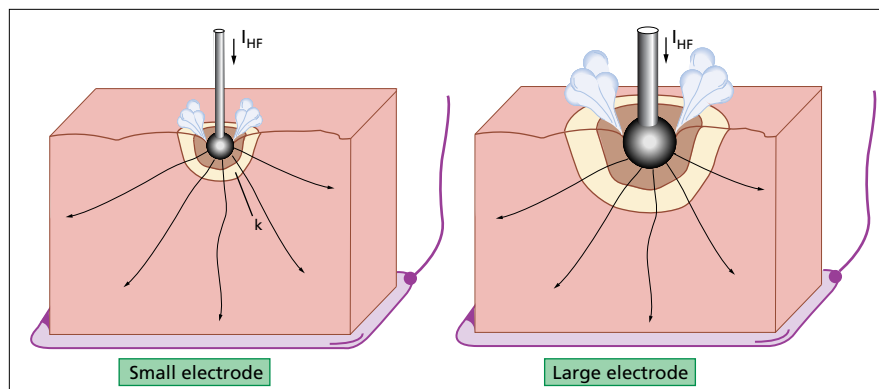


Fig. 34.8 Current density and the resulting penetration depth of thermal effect in the tissue is dependent on the size of the contact surface.

far above 300°C, they generate exogenous heat, which raises the temperature of tissue above 100°C, thus causing carbonization and vaporization of dry tissue as described above.

In colonoscopy, carbonization and vaporization of tissue caused by an electric arc is not only unnecessary, but also annoying, since it generates a certain amount of smoke which impedes visibility. Because the depth of heat penetration cannot be controlled during electric arcing, it is not used as a therapeutic tool in endoscopy.

Even if the vaporization effect caused by electric arcs is not directly used in colonoscopy, it is useful indirectly for HF surgical tissue resection.

Principles of high-frequency surgical coagulation

In general, the term “coagulation” includes the effects of devitalization, coagulation, and desiccation. In colonoscopy HF surgical coagulation can be used for thermal devitalization of pathologic tissue and for hemostasis. Thermal devitalization of pathologic tissue is performed by argon plasma coagulation (APC) or laser and is described in more detail below. Thermal hemostasis can be used to stop spontaneous bleeding as well as to prevent iatrogenic bleeding, for example during resection of polyps.

The spectrum of indications for thermal hemostasis is very wide. Equally wide is the spectrum of the techniques and instruments available for hemostasis, some of which have been developed or designed especially for application in flexible endoscopy. Because the wall of the colon is relatively thin, thermal hemostasis applied directly on the colon wall is a compromise between efficiency and thermal wall damage.

The method and instrument of thermal hemostasis is dependent on the size of the vessels causing bleeding. In small vessels, hemostasis can be achieved by thermal coagulation or desiccation alone. Control of bleeding from larger vessels requires mechanical compression during heat application. This principle is also applicable for hemostasis during polypectomy.

Monopolar coagulation instruments

In their most simple form, monopolar coagulation instruments for flexible endoscopy consist of a catheter at the distal end of which is an electrode, often ball-shaped. Because this electrode can be pushed against the target tissue, this instrument is useful for hemostasis not only of small but also of larger vessels. In the colon the risk of deep thermal wall damage has to be taken into consideration. During hemostasis, coagulated or desiccated tissue can stick to the electrode, so that the source of bleeding can be reopened when the electrode is pulled

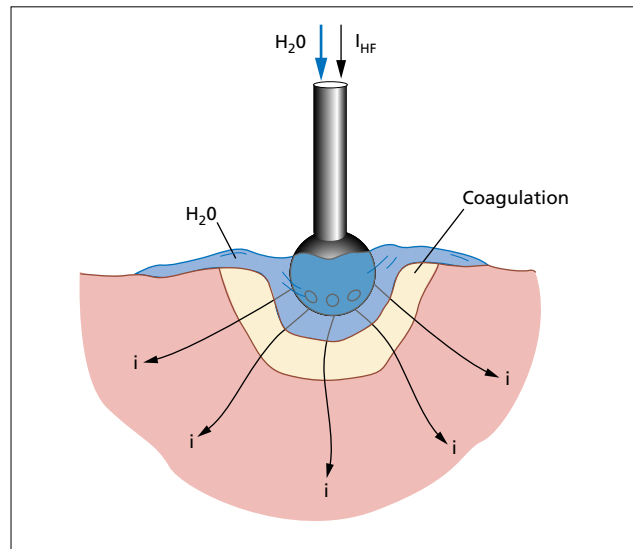


Fig. 34.9 Schematic of electro-hydro-thermo (EHT) probes.

off the site. This problem was addressed by the development of the electro-hydro-thermo probe and by addition of an antisticking coating.

Electro-hydro-thermo probes

Electro-hydro-thermo (EHT) probes for flexible endoscopy (Fig. 34.9) consist of a catheter with an electrode at the distal end (usually ball-shaped). On this electrode is a hole through which water or physiological NaCl solution can be instilled between the electrode and target tissue. When the electric current is applied the contact surface between electrode and tissue does not become dry and the electrode does not stick to the coagulated tissue [3,4]. The instillation of fluid can also be applied for the irrigation of bleeding sources. When applying EHT, the depth of the thermal effect cannot be well controlled. This problem has been addressed with the development of bipolar coagulation probes for flexible endoscopy.

Bipolar coagulation instruments

In their most simple form bipolar coagulation instruments for flexible endoscopy consist of a catheter, at the distal end of which are at least two closely placed electrodes (Fig. 34.10). The HF current flows through the tissue only between these two electrodes. They can be applied either axially or laterally. The depth of the thermal effects which can be reached is relatively small, decreasing the risk of penetration; however, the efficacy is also limited, i.e. the instruments are useful only for small lesions. Bipolar instruments often have irrigation capacity and some have integrated injection needles [5,6].

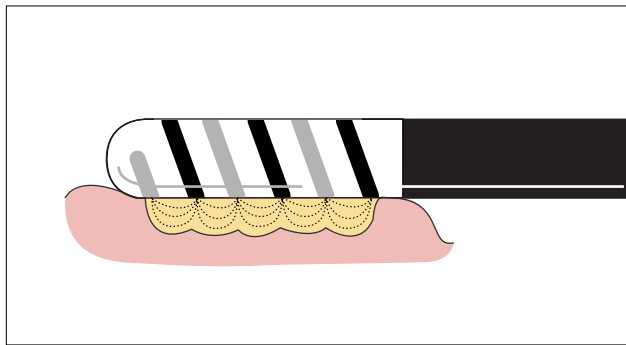


Fig. 34.10 Schematic depiction of current flow of bipolar coagulation probes.

Principles of high-frequency surgical cutting with particular regard to polypectomy

Biologic tissue can be incised electrosurgically when the HF voltage between an electrode and tissue is sufficiently high to produce electric arcs between the cutting electrode and the tissue; this concentrates the HF current at specific points of the tissue (Fig. 34.11a). The temperature produced at the interface where the electric arcs contact the tissue (like microscopic flashes of lightning) is so high that the tissue is immediately evaporated or burned away. As the active cutting electrode passes through the tissue, electric arcs are produced wherever the distance between the cutting electrode and the tissue is sufficiently small, producing an incision (Fig. 34.11b). As mentioned previously, a minimum peak voltage (U_p) of 200 Vp is required in order to produce electric arcs

between a metal electrode and biological tissue containing water. The intensity of the electric arcs increase in proportion to the peak voltage. Experience has shown that the depth of thermal coagulation along the cut edges increases with increasing peak voltage (Fig. 34.12).

In the system of HF surgical cutting, an increase of the voltage increases the electric power (P) by the square of the voltage ($P = f(U^2)$), so it is necessary to modulate the amplitude of the voltage (turn it down) to compensate for the strong influence provided by the mathematical power of the square multiplier.

The higher the peak voltage (U_p) and the degree of amplitude modulation, the deeper the thermal coagulation of the cut edges. If the voltage is not modulated and its peak value is low, the coagulation depth at the cut edges is minor or nil, it is called "cut mode," and the HF current caused by this voltage is called "cutting current." If the voltage is strongly modulated and its peak value is high resulting in deep coagulation of the cut edges, it is called "coagulation mode," and the HF current caused by this voltage is called "coagulation current." One reason for this confusing terminology is the fact that conventional HF surgical generators do not have the capacity for setting the output voltage, only the output power. Setting of the output power of HF generators is not the best option for polypectomy, but it is the standard at the present time.

In colonoscopy the depth of thermal coagulation and also the possibility of thermal devitalization outside the coagulation zone must be considered. It can be dangerous if the coagulation and/or devitalization occurs outside the desired zone of thermal devitalization. If deep thermal damage occurs, tissue histology may be

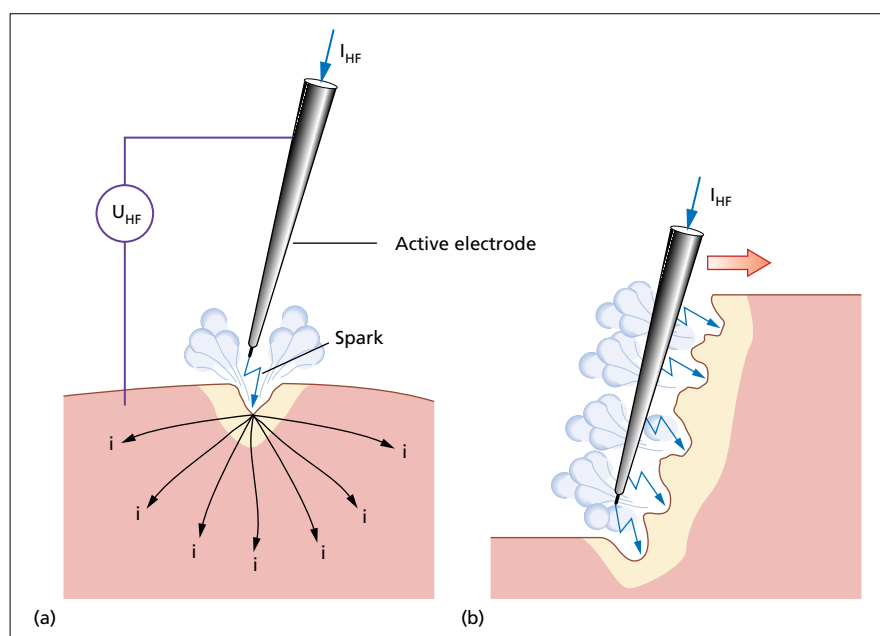


Fig. 34.11 Schematic of the electrosurgical cut effect. (a) Electric sparks ignite between an electrode and tissue if the HF voltage U_{HF} is sufficiently high. (b) The high temperature of the electric sparks evaporates the tissue adjacent to the electrode which will cause a cut if moved through tissue.

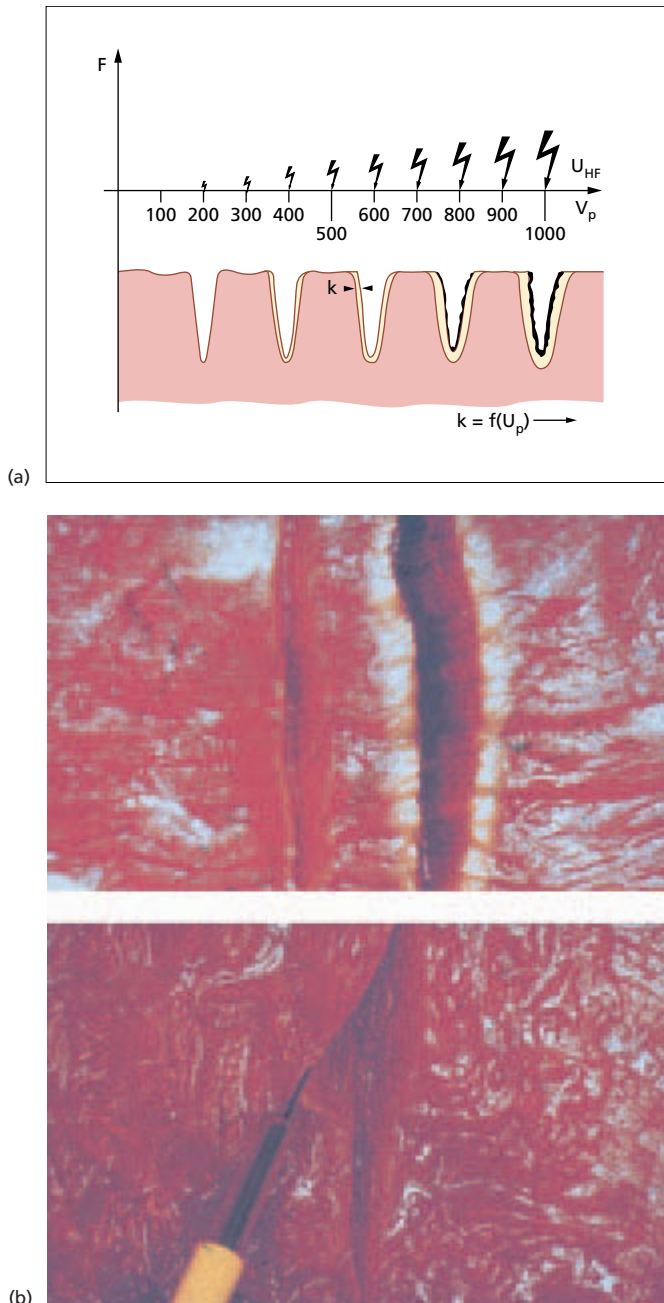


Fig. 34.12 Electrosurgical effects on tissue. The cut edges become devitalized, coagulated (k) and carbonized in proportion to the peak voltage (U_{HF}) and the intensity of the electric sparks (F). (a) Graphic depiction. (b) Photograph of effect on tissue with low and high voltage.

interfered with. A useful aspect is that coagulation of the cut edge of the colon wall can cause hemostasis, which can be used advantageously. Hence, coagulation of the cut edges always is a compromise between these three aspects in colonoscopy.

Another problem with regard to the adjustability, reproducibility and constancy of the depth of coagula-

tion common to all conventional HF surgical generators is the greater or lesser generator impedance R_i , making the HF output voltage U_a dependent on the HF output current I_a . The greater the generator impedance R_i , the more the HF output voltage U_a depends on the HF output current I_a . Conventional HF surgical generators have a generator impedance of between 200 and 1000 ohms.

$$U_a = U_0 - R_i \times I_a$$

The output voltage U_a , and hence also the intensity of the electric arcs and ultimately the depth of coagulation, vary considerably, since the load resistance R_a and current I_a vary from one cut to the next and also during each cutting process. During polypectomy for example the load resistance R_a , which is the electric resistance between a polypectomy snare and a polyp, depends among other things on the size of the polyp and increases during closing the snare because the contact between the snare and tissue becomes smaller and smaller.

Another special problem of HF surgical resection of polyps is that HF surgical cutting can be done with minor mechanical force, as long as the HF voltage between the polypectomy snare and the tissue to be cut is above 200 Vp. Because the speed of the snare while cutting through the polyp has a major influence on the degree of hemostasis of the cut edges, the speed should be appropriate to the size of the polyp's attachment as well as controlled. Control of closure speed can be very difficult or really impossible if there is mechanical friction between the polypectomy snare and catheter or between the slider and the slider bar of the handle of the instrument (Fig. 34.13).

Mechanical friction can cause uncontrolled speed of the snare and hence uncontrolled or insufficient hemostasis, especially if the snare zips through the polyp. Most of the mechanical force on the polypectomy snare is caused by closing the snare intentionally.

Technical aspects of polypectomy

(see Chapters 35 and 36)

Polypectomy is one of the most important applications of HF surgery in the colon [7–11] and hemostasis is one of the main problems with polyp resection. If the problem of bleeding caused by resection did not exist, it would be possible to resect polyps or adenoma in a purely mechanical fashion with a thin wire snare in the absence of heat. This would have the advantage that neither the resected specimen (with regard to the histology) nor the wall of the colon (with regard to the risk of perforation) would be thermally damaged. This is possible for tiny polyps, but the endoscopist must tread the path between application of sufficient heat for hemostasis and yet

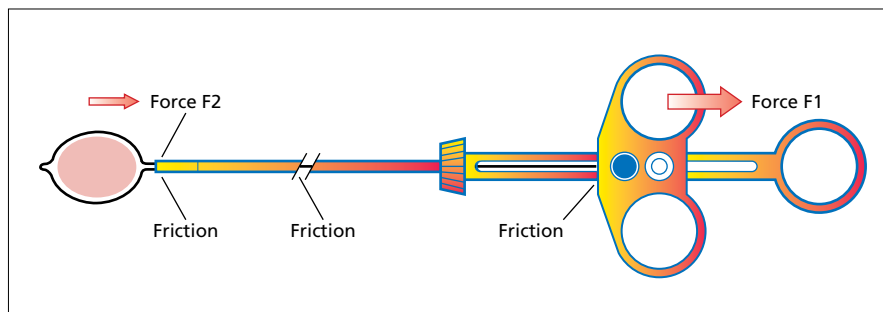


Fig. 34.13 Depiction of mechanical friction at different parts of the polypectomy snare.

avoid deep thermal damage. For safe polypectomy, the endoscopy team should be familiar with the equipment available for polypectomy [13–15].

Polypectomy snares

The ideal polypectomy snares should cut perfectly, and should not coagulate the cut edge of the polyp to permit adequate histologic examination. In addition, the ideal snare should coagulate the cut edge on the colon wall to guarantee safe hemostasis, should not coagulate through the muscularis propria, and can be applied easily and safely. Unfortunately this ideal polypectomy snare is not available, as a number of problems must be addressed. For a perfect cut and minor thermal coagulation of the cut edge on the polyp margin the snare wire should be as thin as possible. For effective coagulation of the cut edge on the wall of the colon the snare wire should be as thick as possible. For easy and safe application on all different polyps the snare should be both flexible as well as stiff and should assume the optimal size for small as well as big polyps. In reality, the available polypectomy snares offer only a compromise of all these features.

A special problem can be caused by the nose at the distal end of polypectomy snares. If this nose is too long, because it is out of endoscopic view, it can touch the mucosa behind the polyp without the operator's knowledge and cause inadvertent damage when electrically activated.

The polypectomy snare handle

Polypectomy snare handles should be designed ergonomically for both male and female hands, and should have minor friction between the slider bar and the slider. This is important to provide even loop closure allowing a consistent cut quality and even coagulation.

Polypectomy snare catheters

Polypectomy snare catheters should be flexible enough for passing through working channels of twisted and

looped endoscopes and have sufficient stiffness to prevent shortening when removing large polyps.

Safety aspects of high-frequency surgery

HF surgery can cause unintended thermal effects outside the target tissue during monopolar applications [12]. This can happen in tissue directly adjacent to the target tissue or remote from the target tissue when the HF current density is higher outside the target tissue.

To prevent thermal damage to the patient's skin, the neutral electrode must be firmly in contact with the skin as recommended in the instruction manual of the specific HF surgery generator.

HF surgery can cause interference in other electronic devices, such as a pacemaker where it can cause reversion of synchronous to asynchronous pacing or possibly pacemaker inhibition.

During polypectomy, the head of a big or stalked polyp must not touch the colon wall because HF current can flow through this contact resulting in uncontrolled thermal effects (Fig. 34.14a).

If an endoloop is used for preventing bleeding and is placed on the stalk of a polyp between the colon wall and where the polypectomy snare is placed, the HF current density in the smaller diameter compressed by the endoloop can be much higher compared with the HF current density at the polypectomy snare; this will cause the narrowest part to become heated (within the endoloop) instead of the tissue within the polypectomy snare (Fig. 34.14b,c).

If metallic hemoclips are used for hemostasis, the snare must not touch the clips as HF current will be conducted through it.

Argon plasma coagulation

The principle of argon plasma coagulation

The principle of argon plasma coagulation (APC) is relatively simple [16]. When an electrode (E) is placed at a distance (d) from the surface of a tissue (G) and a HF voltage (U_{HF}) is applied between the electrode and the

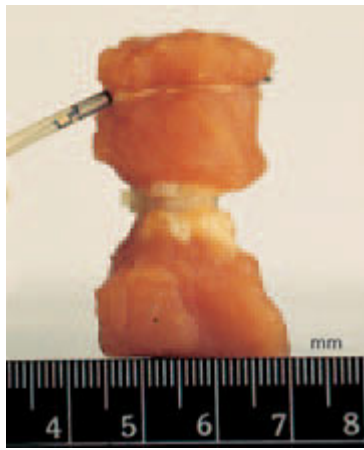
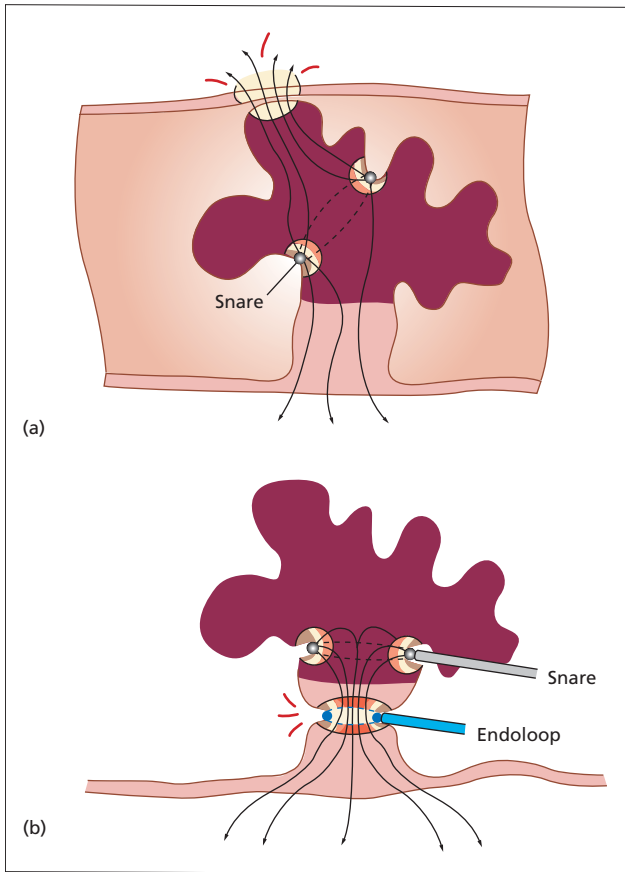


Fig. 34.14 Unintended thermal effects. (a) If part of a polyp touches the colon wall during polypectomy HF current can flow through this contact point into the colon wall. The closer the snare to this point, the higher the flow of HF current through it. (b) If an endoloop is placed around the polyp the HF current must flow through the strangulated part of the polyp and heat will increase at the point of constriction because of the higher current density. (c) Photographic demonstration of (b) with increased heat damage at point of narrowing.

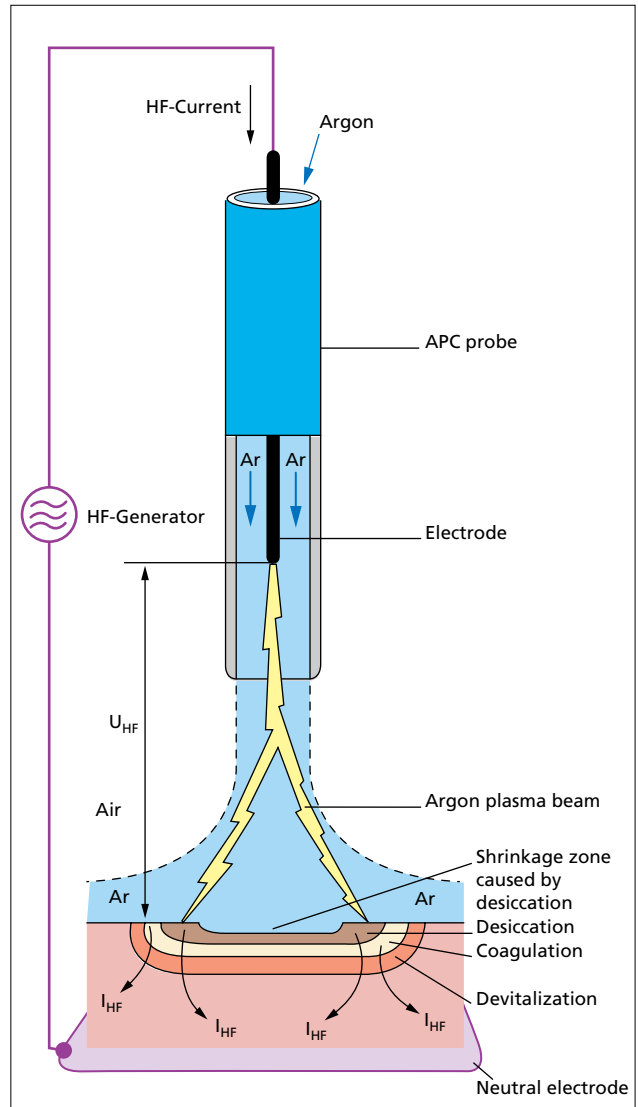


Fig. 34.15 The principle of argon plasma coagulation (APC).

tissue, the gas between the electrode and the tissue becomes ionized and hence electrically conductive when the electric field strength (U_{HF}/d) exceeds a critical level. If the gas between the electrode and the tissue is a noble gas (argon, helium, etc.), an electric field strength of about 500 V/mm is needed for ionization. Argon is preferred because of its relatively low cost. The ionized argon forms argon plasma beams between the electrode and the tissue, which can be visualized as small sparks that conduct the HF current to the tissue. An important advantage of argon in comparison to air is its inert character, which neither carbonizes nor vaporizes biologic tissue so that the thermal effects of APC are limited to the devitalization (zone 1), coagulation (zone 2), desiccation (zone 3), and shrinking of tissue (zone 4) as a result of coagulation and desiccation (Fig. 34.15).

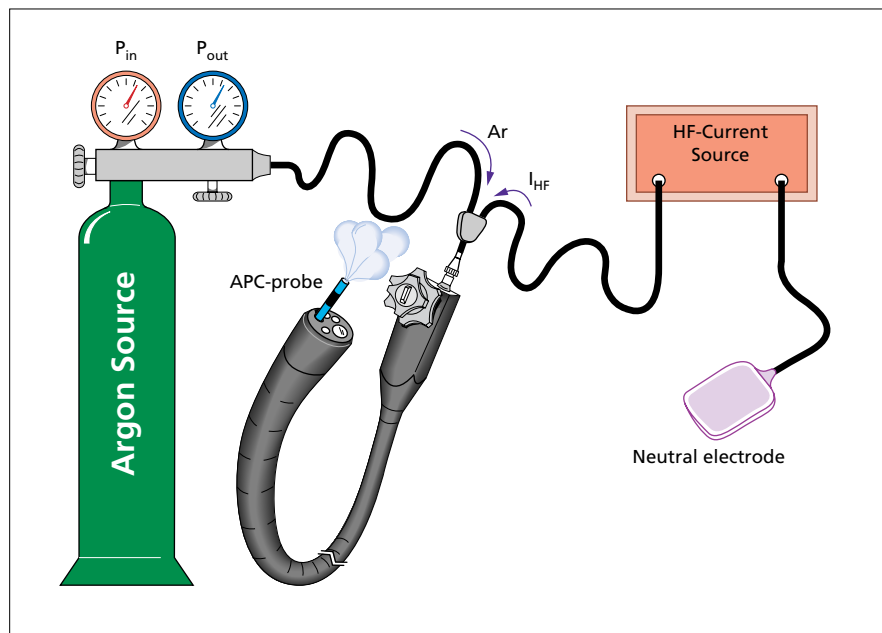


Fig. 34.16 Equipment for APC: argon tank, flow valves, probe, electro-surgical generator.

A special aspect of APC is that the direction of the argon plasma beams follows the direction of the electric field between the electrode and the tissue. The electrically active beams are directed from the electrode to electrically conductive tissue closest to the electrode, regardless of whether the tissue is in front of or lateral to the electrode. As soon as the target tissue becomes desiccated and hence loses its electric conductivity, the beams automatically move from desiccated to non-desiccated tissue until a large area of the target tissue is desiccated. As a result of the loss of electric conductivity at a treated site, the depth of desiccation, coagulation, and devitalization is limited.

Equipment for argon plasma coagulation

The argon source is an argon cylinder with a pressure-reducing valve (Fig. 34.16). For safety reasons, the argon source must have automatically controlled flow rates and limitation of the pressure. The HF current source must provide both sufficiently high HF voltage for the ionization of argon as well as sufficiently high HF current to generate adequate heat within the target tissue.

APC probes for flexible endoscopy basically consist of a nonconductive flexible tube (Fig. 34.17) through which argon flows. An electrode within the distal end is connected to the HF generator by a wire through the lumen of this tube. For safety reasons, the electrode is recessed from the distal end of the tube so that it cannot come into contact with tissue.

As shown in Fig. 34.18, the depth of coagulation depends on power setting and on application time. In addition, the application technique has a significant



Fig. 34.17 An APC probe and its distal end.

influence on the depth. Movement of the activated probe tip will result in a shallower depth of thermal effect than is produced by directing the tip at one point.

When the probe is held at one site for between about 3 and 10 s, the depth of thermal coagulation is up to about 2 mm. Above 10 s the depth increases slowly to its maximum of about 3–4 mm.

Touching the foot pedal activates the flow of argon gas and simultaneously starts the flow of electric current. The time that the foot pedal is depressed may not be the same as the activation time, which refers to the interval when the argon plasma sparks actually touch the target tissue. There may be no or intermittent sparks if the distance between the probe and the tissue is too great.

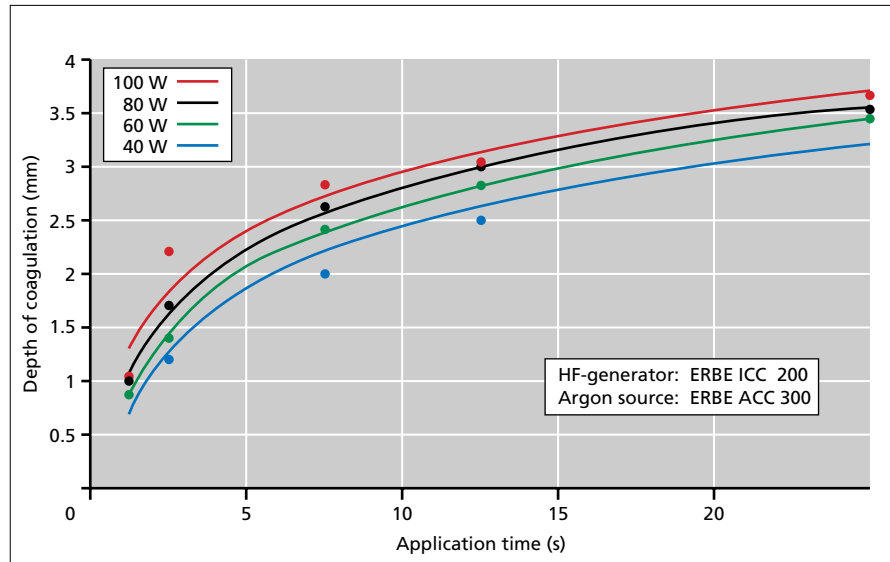


Fig. 34.18 The depth of APC coagulation depends on the application time and power setting.

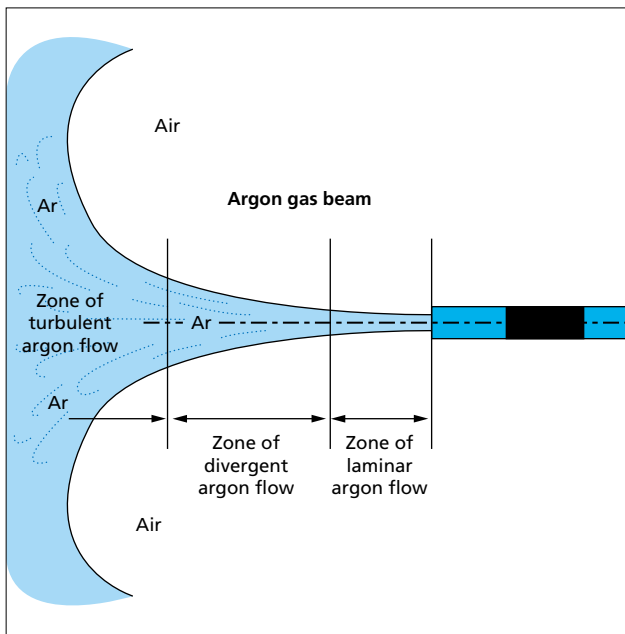


Fig. 34.19 The profile of argon gas flow from an APC probe.

Figure 34.19 shows that the shape of an argon gas beam consists of a zone of laminar argon flow, a zone of divergent argon flow and a zone where the flow becomes turbulent. Argon plasma beams can only reach the target tissue when there is argon gas between the distal end of the APC probe and the target tissue. This is the case when the argon gas beam is directed to the target tissue as shown in Fig. 34.20(a) (axial APC probe) and Fig. 34.20(b) (lateral APC probe). APC probes can be used laterally as well, but the lumen must be filled with argon. The ignited spark will direct itself to the nearest

grounded tissue (Fig. 34.20c,d). If the target tissue is not within the argon gas beam or within an argon-filled lumen the argon plasma beams will not ignite, or plasma beams of air will ignite instead. Air plasma beams do not look very different from argon plasma beams; however, air plasma beams can cause carbonization as well as vaporization of tissue and hence can cause deep damage and perforation of organs. Endoscopists typically use air plasma beams when using the tip of the snare wire to “spark” a polypectomy site to stop bleeding or destroy residual polyp fragments. Air plasma beams, consisting of ionized air, only travel over extremely short distances, and are uncontrollable.

Safety aspects of argon plasma coagulation

As in any monopolar electrosurgical procedure, the neutral electrode must be applied to the skin surface.

Because argon gas is insufflated into the colon during APC, extensive distention of the colon can occur. The distal end of the APC probe must never be pressed against the mucosa or perforation can occur. If the superficial mucosal layer is destroyed by the probe pressure against the colon wall, the flow of argon gas will create instantaneous submucosal emphysema.

Laser

Principle of Nd:YAG laser

“Light Amplification by Stimulated Emission of Radiation (LASER),” first described theoretically by Albert Einstein in 1917, and put into practice by T.H. Maiman 5 years after Einstein’s death, made possible the generation of electromagnetic radiation in the range of optical

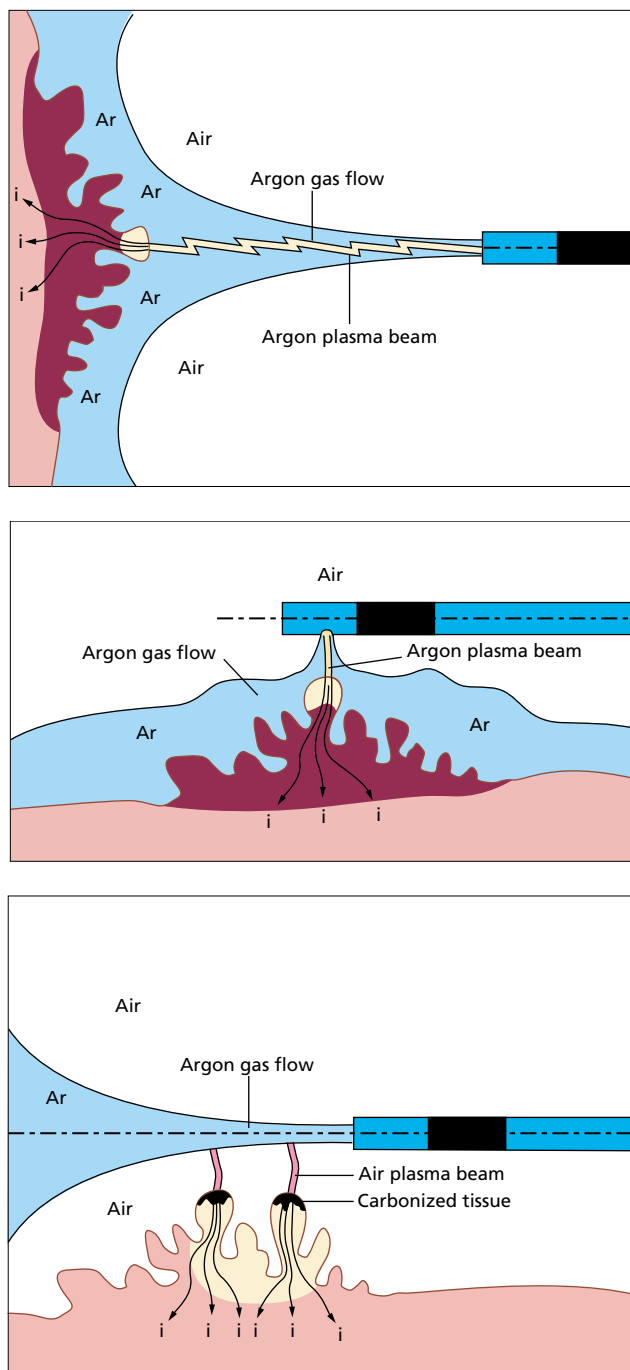


Fig. 34.20 The effects of forward- and side-firing APC probe application.

wavelengths (light) with an extremely high power density. For about 50 years, the high energy of the laser has been used in medicine. The endoscopic application of laser began in 1975 [54], and following the successful development of a flexible light conductor. Of all the different laser sources, only the argon laser ($\lambda = 488/515 \text{ nm}$, $P_{\text{max}} = 20 \text{ W}$), and the Nd:YAG laser ($\lambda = 1064 \text{ nm}$, $P_{\text{max}} = 100 \text{ W}$) can be used endoscopically because

their wavelength can be conducted through thin flexible light guides without significant loss of energy.

Specific characteristics of Nd:YAG lasers in flexible endoscopy

With an adjustable power of up to approx. 100 W, Nd:YAG laser sources are able to generate light with a wavelength of 1064 nm, which is located in the infrared range and is thus invisible to the human eye. With a light guide of 0.6 mm, this light can be guided through an instrumentation channel of a flexible endoscope. The laser light emanates from the light guide in an axial direction with a divergence of approx. 10 degrees.

The invisible Nd:YAG laser is combined with a “pilot light” in the visible range in order to see where the beam is directed.

The thermal effects within the radiated tissue are primarily dependent on the density of absorption (W/mm^2) in the tissue and the duration of effect (Δt). The density of absorption refers to the power of light (W) which is absorbed by the tissue per mm^3 . The density of absorption is dependent on several variables: the distance (x) of the distal end of the light guide from tissue (Fig. 34.21), the angle with which the light radiates onto the surface, and the absorption and reflection characteristics of the tissue. The parameters may change rapidly due to coagulation, desiccation, or even carbonization. The latter can cause a dramatic increase in absorption or a decrease in reflection, leading to intentional or unintentional vaporization of tissue or even a perforation of the colon.

For intentional vaporization of larger tumour masses, the distal end of the light guide has to be placed close to the target tissue and the power of the laser has to be set sufficiently high.

When using lasers for thermal hemostasis, the experience of the operator is most important; if the light guide is too far away the density of power could be too low for hemostasis, and if too close, the source of bleeding could be started by vaporization rather than stopped by coagulation (Fig. 34.22).

The introduction of APC into flexible endoscopy has reduced the need for lasers in endoscopy [57,60].

Safety aspects of Nd:YAG laser in flexible endoscopy

The laser can cause unintended thermal effects outside the target tissue during applications.

During Nd:YAG laser applications all persons including the patient must protect their eyes, even when the distal end of the laser fiber is within the colon, because the light guide can break outside the endoscope. Since Nd:YAG laser is invisible, a break of the laser fiber can damage the retina of unprotected eyes.

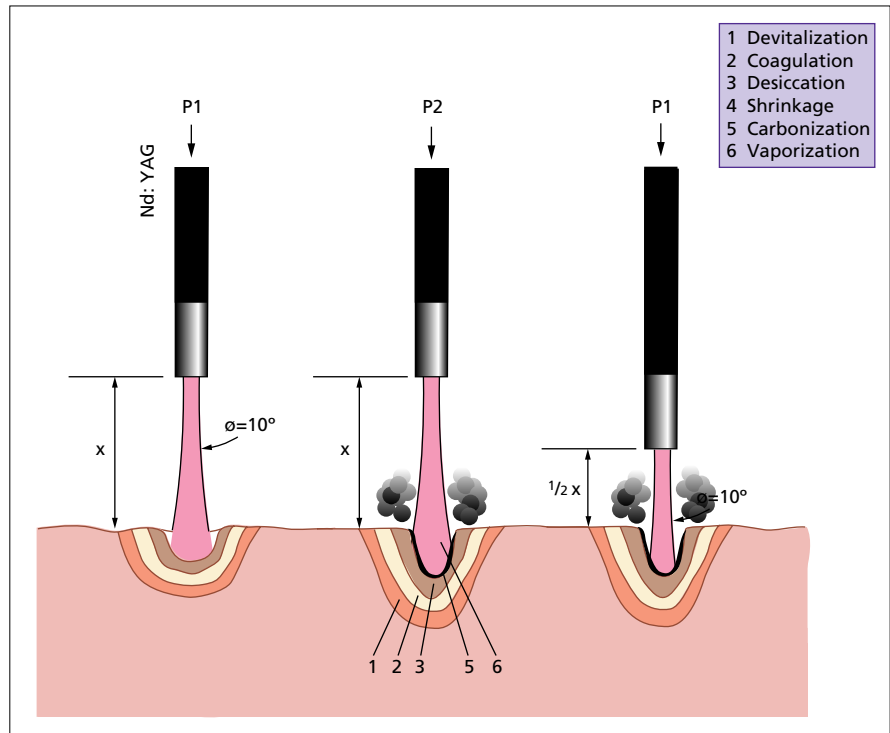


Fig. 34.21 The influence of power as well as the distance between the distal end of the laser fiber and tissue, where $P2 > P1$ and $X1 > X2$.

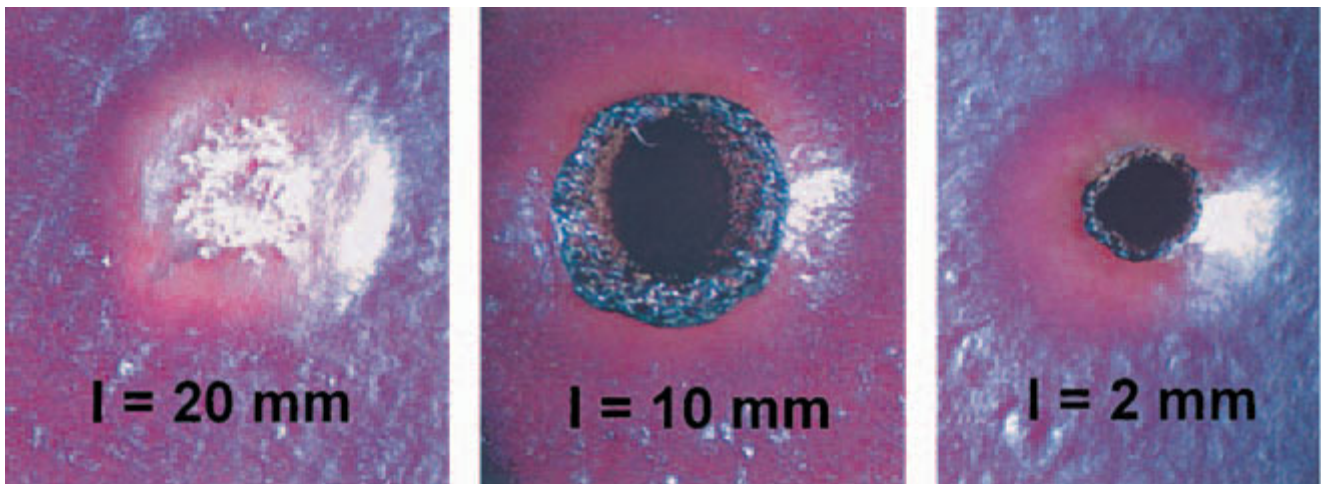


Fig. 34.22 Tissue effect is related to the distance between the distal end of the laser fiber and the tissue.

Summary

All the different thermal modalities described in this chapter have their special advantages and disadvantages. None of the methods or equipment can yet be regarded as ideal for all cases. A modern endoscopy facility should have adequate equipment to provide optimum treatment for each case as listed in Table 34.1. But endoscopists should not only have the equipment available, they should also be familiar with the physical background as well as with the advantages and dis-

Table 34.1 Optimum treatment required by case.

Treatment required	Thermal method
Thermal ablation of pathologic tissue	
By resection	HF
By devitalization	APC
By vaporization (only in the rectum, not in the colon)	Laser
Thermal hemostasis	
By coagulation (desiccation) (applicable for small vessels only)	HF, APC, HP, laser
By coagulation and mechanical compression (applicable for bleeding of larger vessels)	HF, HP, BICAP
Polypectomy	HF

advantages of all modalities, which are available in the endoscopy suite. This, combined with practical skill and experience, and last but not least competent assistance, is the prerequisite for obtaining successful results.

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Chapter 35

Polypectomy—Basic Principles

Jerome D. Waye

Introduction

The ability to find and remove colon polyps from any location in the large bowel has been the main reason for the worldwide enthusiastic embrace of colonoscopy as both a diagnostic and therapeutic tool. The removal of premalignant polyps has made an impact on the incidence, morbidity, and mortality of colorectal cancer [1,2] and is one of the major landmarks in gastroenterology during the past century. Polypectomy with flexible instruments has only been performed for the last three decades, although polyps of the rectum and distal sigmoid colon have been removed by proctologists and colorectal surgeons for many years.

Before the era of flexible endoscopy, polyps in the proximal portions of the colon could only be discovered by the barium X-ray, and if sufficiently large or irregular in contour, abdominal surgery was the only option for removal. Textbooks of radiology described various morphologic aspects of polyps, in the attempt to make the diagnosis of early malignancy or to identify those polyps which had a high probability of becoming malignant. Transanal polypectomy was limited by the fixed loops and bends of the sigmoid colon and the ability to intubate the lumen with rigid pipe-like instruments. Occasionally, polyps in the descending colon could be reached and removed by skilled operators using general anesthesia. The advent of flexible endoscopy (see Chapter 1) dramatically affected the ability to reach the proximal portions of the colon, and to see the mucosal surface in full color. The development of flexible accessories such as snare wires and forceps added the therapeutic capabilities.

Most colon polyps in the large bowel are relatively small (< 1 cm in diameter), a feature that has enabled their successful treatment and the popularity of polypectomy throughout the world. Only 20% of polyps are over 1 cm in size. All large polyps (> 35 mm) are adenomas and are usually located in the rectum or right colon. The majority of small (< 5 mm) polyps in the rectum and distal sigmoid colon are nonneoplastic, but throughout the remainder of the colon, approximately 60–70% of small polyps are adenomas [3].

Principles of colonoscopic polypectomy

Safe polypectomy requires the ability to sever a polyp while achieving hemostasis and maintaining the integrity of the colon wall. A successful polypectomy depends on achieving a balance between the forces employed whenever a polyp is transected with the electrically activated wire snare. The two complementary forces are heat, which results in cauterization (hemostasis), and the shearing force exerted by tightening the wire loop (transection). Both of the forces must be used simultaneously to result in a clean, bloodless polypectomy without an excessive amount of burn to the colon wall. Heat alone will not sever a polyp, while guillotine force alone may cut through a polyp, but can result in immediate bleeding as there is no capability for heat-sealing of blood vessels.

Coaptive coagulation

Most polypectomies are performed without any blood loss. This is because the same principles are employed as in the cessation of bleeding for the upper gastrointestinal tract. During hemostasis of bleeding ulcers, the technique is to push hard on the probe in order to tamponade the bleeding site; this coapts the walls of the bleeding vessel and stops blood flow; there is a need for only a small amount of heat to seal a coapted blood vessel in the absence of intravascular blood flow. In similar fashion, the tightened snare around the pedicle of a polyp effectively causes cessation of circulation in that polyp, enabling a relatively small amount of current to seal the arteriole and vein. Because there is no single large feeding blood vessel in a sessile polyp, it is difficult to achieve as successful hemostasis as when a stalk is present, but bunching up the polyp base in the tightly closed snare affords much the same principles, as smaller vessels are heat sealed as closure of the activated snare wire cauterizes the small vessels.

Electrosurgical unit

The power output of electrosurgical generator units is not standardized. There are no rules concerning the

number of Watt-seconds or joules used for the separation of broad or narrow attachments of polyps to the colon wall. In general, the dial settings should be medium to low and the current may be either pure coagulation or blended. Pure cutting current is never used because this type of energy output explodes cells with no hemostatic qualities. The delivery of energy should be continuous once polypectomy has commenced (there is no scientific justification for intermittent tapping of the foot switch), and the person who closes the snare should do so slowly (as opposed to a rapid closure of the slide bar) after having been requested to begin tightening following current application. Most colonoscopists do not change the power output of the electrosurgical unit. Once they are comfortable with the dial settings, the same setting is used for small or large polyps, and is not changed, even for giant polyps or those where transection is prolonged.

The type of current used for polypectomy, whether coagulation or a blend of cutting and coagulation, is a point of some controversy. Both can achieve tissue heating, but coagulation current produces a greater degree of hemostasis, while cutting current is designed to cause cell disruption. This characteristic of cutting current can result in bleeding from the polypectomy site without adequate hemostasis. A clinical trial has pointed out that use of blended current (a combination of various amounts of both types of current) had a greater incidence of immediate bleeding whereas use of pure coagulation current was associated with a higher rate of delayed postpolypectomy bleeding [4]. However, it is the preference of the author and of several colleagues who perform a large number of polypectomies to use only coagulation current when resecting colon polyps.

The colonoscope

A single-channel 168-cm-long colonoscope with a 3.8- or 4.2-mm accessory channel is the instrument most preferred for colonoscopy by all experts and most colonoscopists (see Chapter 23). The double-channel scopes are somewhat less flexible, can be difficult to pass through the entire colon, and are associated with more patient discomfort than the one-channel type. A variable-stiffness colonoscope has recently been introduced in a standard size as well as a pediatric diameter [5]. The latter has an accessory channel of 3.2 mm, which is sufficient for most polypectomies. There are only limited occasions when it is desired to pass two accessory devices simultaneously through a colonoscope, such as grasping a polyp and lifting it while placing a snare [6–8]. This maneuver would appear to be relatively easy, but in practice can be quite difficult, since the two accessories are obligated to move together (with the tip of the instrument) rather than separately; it is desirable to lift

up the portion grasped by the forceps while seating the snare downward over the polyp, but such manipulation is not possible. Attempts at use of instruments passed through both channels requires that, before grasping the polyp, the forceps must be passed through the open snare, but even when this has been accomplished, moving the scope tip to lift up the forceps to elevate the polyp also causes the snare to rise up. It is possible to use two separate endoscopes [9], one for grasping, and the other for snaring, but that is not commonly employed.

Snares

Types of snares (see Chapter 25)

Snares are available in a wide variety of shapes and sizes. The standard large snare is about 6 cm in length by 3 cm wide, and the small snare is 3 cm long by 1 cm wide. The technique is the same in all instances, whether the snare is oval, crescent-shaped, or hexagonal. The diameter of the wire is an important consideration, since thin snare wires will cut through a polyp faster than a thick wire [10]. This variable must be considered when switching from one type of snare to another.

Bipolar snares

A bipolar snare [11] is available but does not seem to have any benefit over the standard monopolar electrocautery snare.

Rotatable snares

Rotatable snares are available, but considered unnecessary by most endoscopists. With the wire loop extended, the combination of torque on the shaft and rotation of the dial controls affords much the same effect as snare wire rotation.

The handle—an information center

The snare device not only permits application of heat for hemostasis during polypectomy and the force required to transect a polyp by wire closure, but can also be used to estimate the volume of tissue enclosed within the wire loop. In addition, by making a visible mark on the handle, the assistant can close the slide bar to that mark, and prevent inadvertent guillotining of a polyp with the risk of bleeding.

The endoscopy assistant who closes the snare around a large polyp feels resistance to closure when the slide bar is retracted to the point where the wire loop is snug around the polyp. This resistance is perceived as a “spongy” resilient sensation, coupled with the inability to further close the slide bar. This “closure sensation”

means that the wire loop has encircled tissue and is tightly closed on it, and further retraction of the slide bar will result in guillotining of the polyp or the encircled tissue. If the polyp is very soft such as a villous tumour or is very small, no closure sensation will be perceived and the slide bar, in the absence of any closure sensation, may be effortlessly retracted and will inadvertently transect the encircled tissue, like a wire cutting through a soft cheese. If the assistant knows when to stop slide bar retraction, in the absence of any closure sensation, such cheese wiring of a polyp could be prevented. Knowledge of the exact point at which to stop slide bar retraction to prevent guillotining of a polyp can be readily obtained by a simple pen mark. This 1-minute preparation performed prior to snare use requires that the slide bar be retracted toward the thumb hole on the snare handle, stopping when the free tip of the wire loop (snare) is just even with the tip of the plastic sheath. Further closure of the slide bar would result in the snare tip fully entering the plastic sheath (Fig. 35.1). The assistant should make a mark on the snare handle using the slide bar as a guide [12]. The mark may be made by pencil or pen, and is a

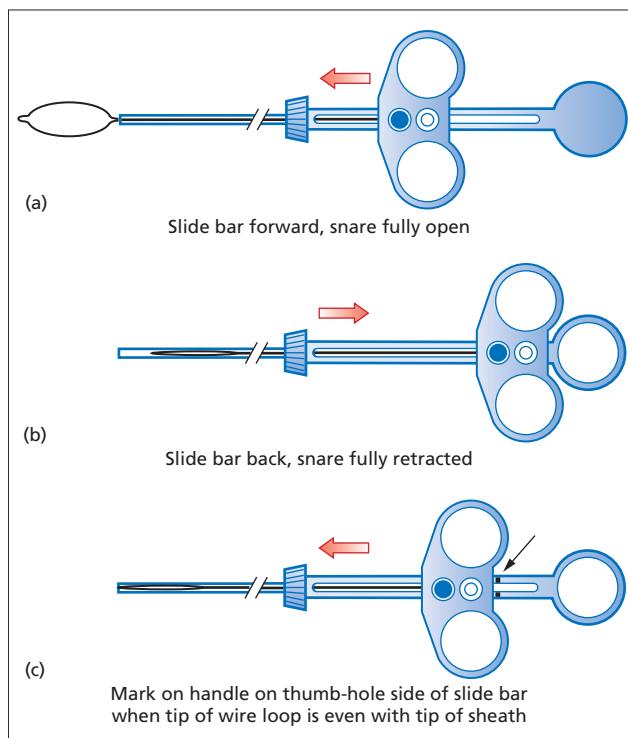


Fig. 35.1 Mark the snare handle. (a) With the slide bar forward, the snare is fully open. (b) With the slide bar back, the snare is completely retracted into the sheath. (c) The “information mark” is placed on the thumbhole side of the handle at the edge of the slide bar when the slide bar is at the position when the tip of the wire loop is even with the tip of the sheath.

line across the handle where the edge of the slide bar crosses it. The mark must be on the thumbhole side of the slide bar crossing, not toward the plastic sheath.

During snare closure, by observing the line on the handle and stopping there, even without any closure sensation, the assistant will be assured that a polyp is not sliced off unintentionally.

Estimate of tissue volume in the closed snare

The endoscopist may desire to know the approximate volume of tissue encircled by the snare. This would be useful whenever an extraordinarily large amount of tissue were captured. If the endoscopy assistant were to communicate to the endoscopist that the volume of tissue within the closed loop was greater than expected for the estimated size of the polyp, then several interpretations of that estimate would be available for consideration: that the snare is seated across a wide area of the polyp (instead of at the narrow base), that the polyp base is too wide for a single transection, or that excess surrounding mucosa is also included within the tightened loop.

Using the mark on the handle as noted previously, the amount of wire loop outside the sheath during snare closure can be estimated by the assistant who can see the distance from the side of the fully retracted slide bar (when spongy resistance is felt) to the previously drawn mark. If closure sensation has been noted, and the slide bar is at the mark, then there is little likelihood of excess tissue being caught within the snare or that the snare is improperly sited. It should be noted that some snares with stiff wires or a 2 : 1 ratchet wheel ratio (allowing full snare opening and closing with a shorter travel distance of the slide bar) may not permit the sensory perception of a “closure sensation.” On the other hand, if closure sensation is perceived, but the slide bar is not at the mark, the amount of tissue within the closed snare loop is directly proportional to the distance from the edge of the slide bar to the mark on the handle. If that distance is greater than 3 mm, there is a large volume of tissue within the loop (Fig. 35.2). Knowing that a substantial volume of tissue has been captured, the endoscopist must reassess the situation and decide whether to remove the snare by opening and repositioning the loop, or that placement is proper (for instance, that the snare is tangential across the polyp but is acceptable because piecemeal polypectomy will be necessary). Characteristically, larger portions of a polyp can be removed during the piecemeal technique than would ordinarily be resected by a single application of the wire loop around a single polyp. The decision as to whether large polyps should be removed piecemeal or with one transection is not necessarily related to the size of the polyp, but to the volume of tissue within the closed snare. Some large

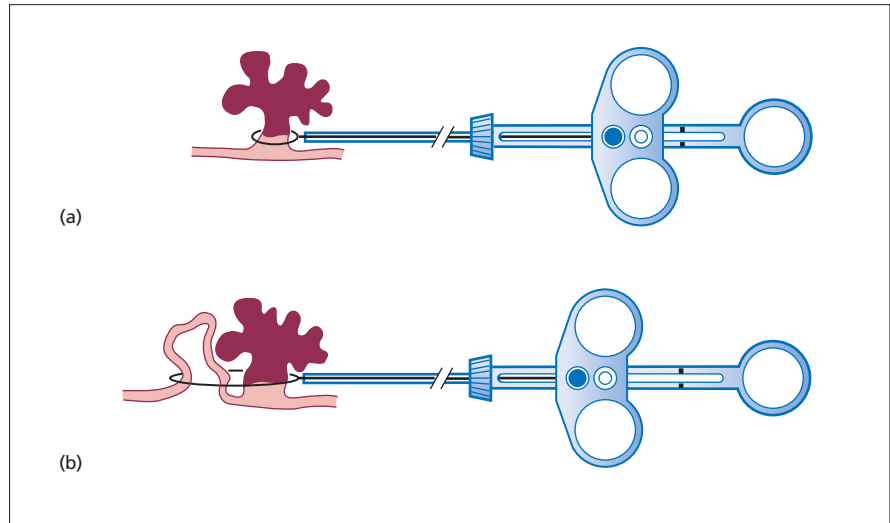


Fig. 35.2 The “information mark” used to estimate the volume of tissue captured within the closed wire loop. The amount of tissue within the loop is directly proportioned to the distance between the slide bar and the mark.

polyps may be soft and spongy, permitting a greater amount of slide bar retraction than is possible with a smaller but firmer polyp.

Use of the snare

When placing the snare sheath through the instrumentation channel of the colonoscope, the right lower portion of the scope tip should be directed toward the colon lumen rather than close to the wall. This is a safety measure that will prevent the sheath from piercing the wall as it exits the scope. The sheath enters the field of view at the 5 o’clock position, but if that portion of the scope tip touches the mucosa, the sheath will also contact the mucosa, and could, in spite of the blunt tip, be pushed through the wall. When opening the snare loop, it is again necessary to point the sheath toward the lumen. The request to open the snare should be made when there is sufficient clearance to permit the snare to open fully. It may be dangerous to have the sheath close to the polyp as the snare wire is protruded, since the sharp point of the wire tip is relatively stiff as it exits the sheath and could be advanced through the colon wall. On the other hand, the fully opened snare is quite flexible and can be pushed against the colon wall to anchor its tip position during placement over a polyp.

A useful safety measure is for the endoscopist to withdraw the sheath into the scope as the wire loop is being extended by the assistant. This maneuver starts with the sheath tip in the field of view and is accomplished in a simultaneous manner so as to keep only the tip of the wire snare in the field of view as the assistant opens the loop while the endoscopist pulls back the sheath. Once the loop is fully opened within the instrumentation channel, the endoscopist has complete control of the opened snare. The endoscopist can push the wire loop

toward the wall, extending the loop as needed by advancing the sheath without requiring further communication commands to the assistant to open the snare.

The tip of the sheath is the fixed point in the polyp–snare interaction, and remains stationary during snare closure. If the sheath tip is not against the polyp base, closure of the slide bar will move the far end of the wire loop closer to the sheath tip; as it closes, the wire will bend the polyp toward the sheath, and then slide over the polyp as it closes to the sheath tip, allowing the polyp to escape from the loop (Fig. 35.3a). If the open wire loop is placed over a polyp, and the polyp is in the middle of the open loop, the endoscopist must advance the sheath (not the tip of the colonoscope) as the loop is closed in order to prevent the polyp from escaping (Fig. 35.3b). The movements of the assistant in retraction of the slide bar and the endoscopist in advancing the sheath must be fully coordinated. For precise snare loop placement, it is most desirable to position the sheath tip (with the fully opened snare loop) at the margin of the polyp and mucosa. As the slide bar is closed, the wire loop will snug against the far edge of the polyp, ensuring total capture (Fig. 35.4). If the colonoscope and the extended wire and sheath are parallel to the colon wall, capture is relatively straightforward. When this ideal position cannot be accomplished, and the wire loop approaches the polyp as an angle, the endoscopist must advance the sheath to the mucosa as the slide bar is pulled back. If the polyp is on a convex fold, capture may be easier by placing the open loop over the polyp, and then withdrawing the sheath to hook the snare tip on the far wall of the polyp. The sheath must be advanced simultaneously with slide bar retraction to keep the polyp within the loop.

As the wire snare is electrically activated, the assistant should await the request of the endoscopist to close the

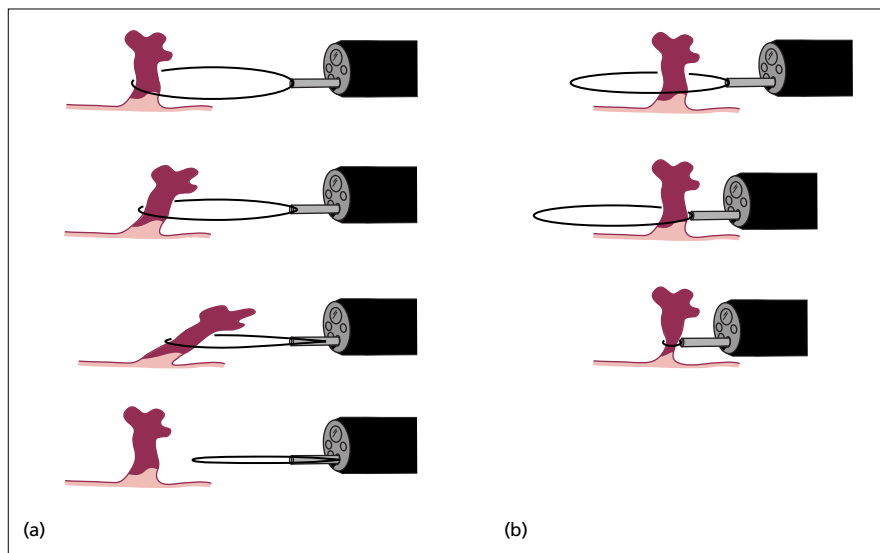


Fig. 35.3 The tip of the sheath must be advanced to the polyp edge since the wire loop closes toward the sheath. Pushing the sheath in during slide bar retraction will prevent escape of the polyp from the loop.

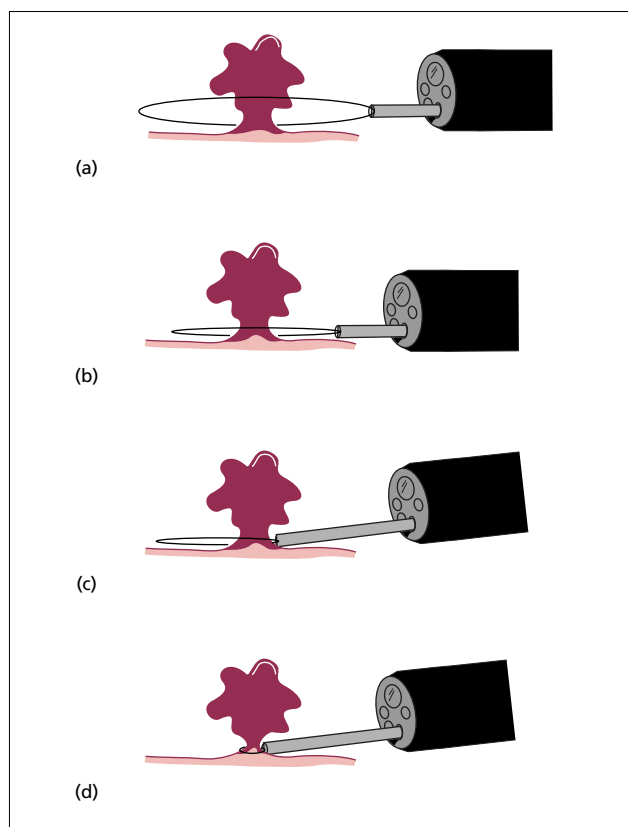


Fig. 35.4 The sheath tip must be placed at the junction of the polyp and the colon wall. With the wire loop parallel to the wall, it will close at that same plane on the far side of the polyp.

snare. Usually, there may be a 1–2 s delay while current is applied before the request for closure, to ensure that coaptive coagulation occurs. Slide bar closure should be smooth and continuous until severance.

Injector needles

The injector needle is an important component of polypectomy equipment. It must be of sufficient length to traverse the colonoscope, the sheath should be strong enough to prevent buckling when pressure is applied to force it through several loops and convolutions of the scope when in the right colon, and the needle should lock in position when extended to prevent excess play of the needle when attempting to push it into the mucosa. In addition, the bevel of the needle is an important but often overlooked component, since a long bevel may pierce two or more layers and permit simultaneous injection into the submucosa while also spilling fluid into the peritoneal cavity. The distended bowel wall is relatively thin, with the total thickness about 1.5 mm [13]; each layer (mucosa, submucosa, and muscularis propria) is about 0.5 mm thick, so the bevel must be rather obtusely angulated to allow precise submucosal injection. Even without a sharply angulated bevel, a smaller diameter needle is of benefit when it is desired to deliver fluid into the submucosal layer without extravasation into the colon lumen.

Hot biopsy forceps

The hot biopsy forceps is an electrically insulated forceps through which electrical current flows to direct electrical energy around the tissue held within the jaws, enabling simultaneous cautery of a polyp base while obtaining a biopsy specimen.

Types of polyps

There are two basic polyp configurations: pedunculated polyps are attached to the intestinal wall by a stalk,

and sessile polyps arise directly from the wall without a pedicle. Pedunculated polyps may be attached by a short, thick, or long, thin pedicle. All pedunculated polyps had their origin as a sessile polyp, but the action of peristalsis on the slightly protuberant polyp results in pulling and subsequent elongation of the normal mucosa and submucosa surrounding the polyp base. Most pedunculated polyps occur in the sigmoid colon in the area of strong muscular contractions, although some can be seen in the proximal colon.

Sessile polyps are more common than pedunculated polyps and are attached to the mucosal surface in a variety of configurations. Those that are less than 8 mm in diameter frequently have the shape of a split pea, with the base being the largest diameter of the polyp. Larger polyps can assume one of several configurations [12].

- **Marble:** spherical with a narrow base, attached to the colon wall by a small connection.
- **Mountain:** distinct edges and a broad base where the attachment is the widest part of the polyp. These are often multilobulated.
- **Ridge:** much longer than the width, attached along its entire length.
- **Clamshell:** wrapped around a colon fold. The proximal portion (away from the instrument) may be difficult to visualize completely because part of the mucosal attachment is on the opposite side of the fold.
- **Carpet polyp:** flat and can extend over a wide area.
- **Extended polyps:** a combination of attachments, with the major component usually being a mountain or clamshell type. The edges of this type of polyp usually extend diffusely into the mucosa.

The vast majority of polyps are sessile, with most of the pedunculated polyps located in the left colon where peristalsis is strong. Most sessile polyps are of the mountain and extended type, with the largest found in the rectum and right colon.

Precolonoscopic laboratory testing (see Chapter 20)

Routine testing for bleeding disorders prior to colonoscopic polypectomy is not necessary [14]. A history of a bleeding disorder should be obtained, including any tendency to bleed excessively following lacerations, a surgical procedure, or dental extraction. Patients do not need to be screened with a platelet count, prothrombin time, bleeding time, or clotting time.

Polypectomy technique

When to remove polyps

Large polyps in the distal portion of the colon should not be removed during the initial intubation. These often require special techniques and may result in deep

submucosal excavations. In addition, 50% of patients with one adenoma will have another, and it is important to perform total colonoscopy to seek and remove synchronous adenomas. In general, most colonoscopists do not remove large or difficult polyps during intubation since other unresectable polyps or a malignancy may be encountered further upstream which will require surgery. However, there is no contraindication to removing a polyp during intubation and then continuing the examination to the cecum, despite the probability that the scope will rub against the polypectomy site, and air will be pumped in to distend the colon, and loops in the shaft of the colonoscope will push on the freshly denuded submucosa and muscularis propria.

Small polyps in any position, when seen during intubation, should be removed at that time, since they may not be easily found during withdrawal. Medium sized polyps in good position for resection should be removed when visualized since they may not be well positioned during withdrawal.

Small polyps

Hot biopsy

There are several ways of removing small polyps. Hot biopsy forceps provide a histologically identifiable tissue specimen, while electrocoagulation current ablates the polyp base in most instances [15]. When cold biopsy forceps are used, fragments may remain and subsequently proliferate [16]. In order to prevent deep thermal injury to the colon wall during use of the hot biopsy forceps, the polyp head, once grasped wholly or in part, should be tented away from the wall toward the colon lumen. As current is applied, a zone of white thermal injury will become visible on the stretched normal mucosa surrounding the polyp base. When this injury zone is 1–2 mm, current should be discontinued and the specimen retrieved as with any biopsy technique. There is a high rate of residual adenoma when incomplete fulguration occurs [15,17]. Because of reported complications with the hot biopsy forceps [18], there has been some reluctance to use them, but many endoscopists employ them routinely to eradicate polyps in the range of 1–5 mm.

Snare and cautery

Small polyps may also be removed with a wire snare. The mini-snare is suitable (3 × 1 cm), for it can more easily be manipulated around the head of a polyp than the standard snare since the standard snare requires that the full 6 cm length of wire be extended before the two wires spread apart and form a loop (Fig. 35.5). Small polyps, less than 4 mm in diameter, can be safely removed by severing the polyp without employing electric

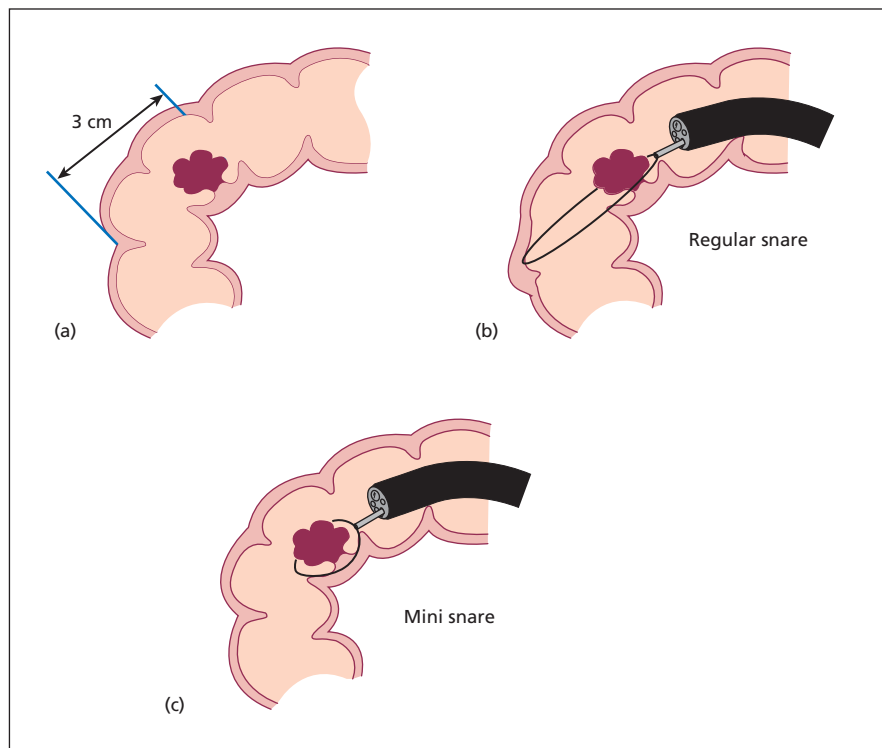


Fig. 35.5 A mini-snare can be used for most polyps since the majority are less than 1 cm in diameter. It is also useful in convoluted colons where there is not sufficient distance (6 cm) for the standard snare to open fully.

current. Since Tappero *et al.* [19] first described this technique, many endoscopists guillotine small polyps without cautery current. Bleeding is insignificant and stops spontaneously without the need for the application of hemostatic techniques [20]. Tiny polyps, in the range of 1–2 mm in diameter, can be totally extirpated with a biopsy forceps, but for polyps in the range of 3–4 mm fragments of adenoma may fill the cups of the forceps, requiring several passages of the forceps to ensure total removal. Polyps of this size can be totally removed with a “cold snare,” leaving a “tiny button” of denuded mucosa (Fig. 35.6). The specimen can be retrieved into a polyp trap (see Chapter 37).

Placement of the snare catheter tip

The most important step in polyp capture is to place the catheter tip at the precise site where transection is desired once the open snare loop has been placed over the polyp [21]. If the polyp is pedunculated, the tip of the sheath should be advanced to the midportion of the stalk. If sessile, the sheath should be advanced to the line of visible demarcation between adenoma and colon wall. Closure of the loop will result in seating the snare on the opposite side of the polyp, since the wire loop always concentrically closes toward the tip of the snare sheath, which is the fixed point in the polypectomy system. To assure proper seating of the wire loop, it is important to look for and observe the tip of the wire loop as it is being withdrawn behind the polyp. This will prevent inadvert-

ent capture of a portion of the wall behind the polyp by the snare tip as it slides across the wall (Fig. 35.2).

Pedunculated polyps

A pedunculated polyp of any size should be able to be removed by a single transection [12]. Attempts should be made to completely encircle the head of the polyp with the loop and to tighten it on the pedicle. This can usually be accomplished with any of the standard size commercially available polypectomy snares.

Sessile polyps

The polyp with a wide attachment to the colon wall may be transected with one application of the wire snare, providing that it is located in the left colon and the base is less than 1.5 cm in diameter. In the right colon, where the wall is somewhat thinner, the endoscopist should consider piecemeal polypectomy or submucosal injection technique for any polyp whose base is over 1 cm. The heat produced by snare activation is localized to the area immediately around the wire loop, but also spreads toward the submucosa and serosa of the colon wall. The larger the polyp, the greater will be the volume of tissue captured within the wire loop, and a greater amount of thermal energy will be required to sever the polyp. This may result in a full thickness burn of the colon wall, which can result in a perforation of the bowel. It is once again noted that once the polyp and mucosa has been

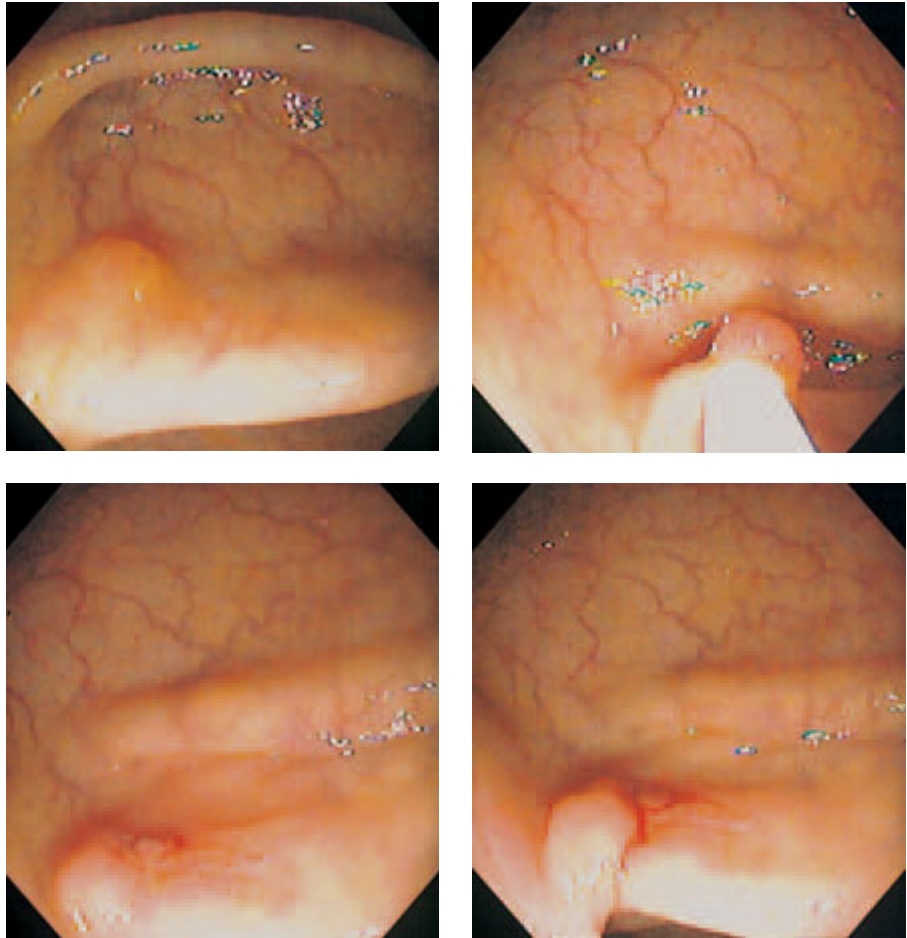


Fig. 35.6 Cold snare guillotine of small polyps (less than 5 mm in diameter) is safe with minimal bleeding.

captured in the loop, the submucosal layers and muscularis propria are in total about 1 mm thick [13].

Air aspiration

During the technique of sessile piecemeal polypectomy with or without saline injection, an attempt should be made to place one edge of the wire snare at the edge of the adenoma or the junction between adenoma and normal mucosal wall [21]. The other wire of the loop can then be sited over a portion of the polyp to encircle a large piece of tissue. Aspiration of air just prior to snare application will result in a decrease in the air-induced wall tension, resulting in a contracted segment of the wall. As the diameter decreases, the polyp becomes thicker and more pronounced, making it easier to ensnare (Fig. 35.7). Removal of air results in a decrease in the circumference of the cylindrical colon and also in a shortening of its length. This requires careful attention to the visual field as the initial relationships may be altered by deflation. If a fold is brought into view and obscures the snare and/or polyp, reinflation or moving the tip of the colonoscope closer to the polyp usually regains the view.

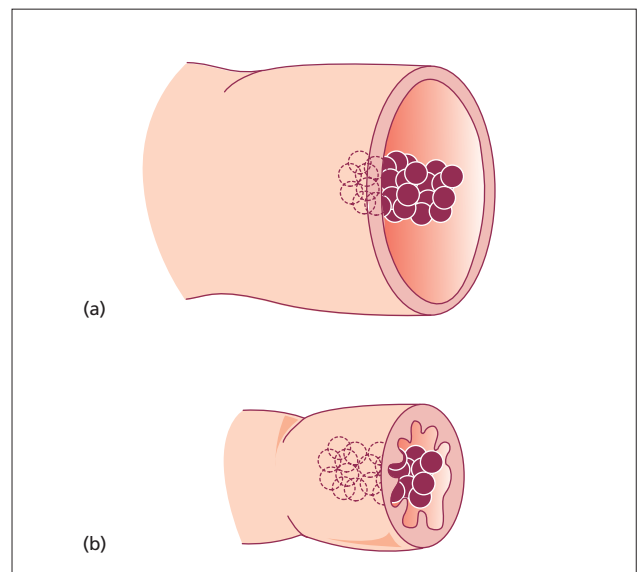


Fig. 35.7 Aspiration of air decreases both the length and cross-sectional diameter of the colon. This causes a decrease in the size of the polyp and increases its thickness and the thickness of the colon wall.

The tip of the snare

As the snare is closed slowly, the endoscopist's attention should be directed toward the tip of the loop as it slides over the mucosal surface behind the polyp. By so doing, it is often possible to see whether a portion of normal mucosa is caught and dragged up into the loop along with the polyp, or whether the tip slides over the mucosa and engages on the far margin of the polyp. This assessment is important, but in some instances of piecemeal polypectomy, the polyp itself may obscure direct vision. When this occurs, careful attention must be directed to the closure mark previously placed on the snare handle to assess the volume of tissue caught within the closed snare loop.

When full vision is obscured

When complete visualization is not possible as the loop is being closed, the assistant should close until resistance is met, or, if no closure sensation, then stop at the mark. Once closed, the catheter sheath should be jiggled to and fro at the biopsy port while observing the colon walls around the polyp. If extraneous portions of the mucosa are not caught in the loop, the polyp will be seen to move independently of the surrounding colon walls as the sheath is jiggled. If the polyp and the surrounding wall move simultaneously, there is a strong probability that a portion of adjacent mucosa has been captured within the snare loop. Complete removal of the snare or partially opening the loop for repositioning is then advisable before application of electrocautery current. Transection of a large fragment of inadvertently captured normal mucosa is not a desirable outcome of polypectomy and may lead to perforation. If extra tissue is captured, there is no assurance that it will only consist of mucosa, for submucosa may also be entrapped, and when electrocautery current is applied a deep burn may result.

Tent the polyp away from the base

After the wire is seated securely around the polyp, the sheath should be lifted slightly away from the wall, tenting it toward the lumen to separate the polyp from the submucosa [21]. This will limit the depth of thermal injury when current is applied because the local zone of heating has a lessened chance of damaging the muscularis propria and serosa because the layers are pulled away from each other. Tenting of the polyp can be accomplished by a variety of movements with the success of any one being judged by its result; often a combination of efforts will be necessary: pushing the snare in or withdrawal, elevation with the thumb on the up/down dial, or torque. Movements that are too vigorous may result in tearing the polyp away from its attachment.

Position of polyp

To capture a polyp, one of the most important factors is that it be in a proper position relative to the tip of the colonoscope. One of the most frustrating problems encountered during polypectomy is that the polyp is in a poor position. All colonoscopes have the suction/instrument channel situated at the 5 o'clock position in reference to the visual field. All accessories are obligated to enter the visual field in the lower right quadrant and progress toward the 11 o'clock position. This fixed reference point results in a relatively easy snare capture of a polyp located in the right lower portion of the field, and occasionally those in the 5 to 11 o'clock axis, but causes considerable difficulty in snaring a lesion which is not on that diagonal. A polyp located between 9 and 12 o'clock in the visual field is much more difficult to lasso than a polyp in the right lower quadrant, and those in the 3 or 8 o'clock position are impossible. An attempt should be made to bring all polyps into the 5 o'clock position to facilitate snare placement [21] (Fig. 35.8). This can usually be accomplished by rotation of the scope to reposition the face of the scope in relation to the adenoma.

Rotation of the scope may be difficult during intubation when the instrument shaft has loops and bends. Advantageous positioning may be best accomplished when the colonoscope shaft is straight, because a straight instrument transmits torque to the tip, whereas a loop in the shaft tends to absorb rotational motions applied to the scope. It is often difficult to capture a sigmoid polyp during intubation, when the obligatory sigmoid loop is present. It may not be possible to straighten the scope in the sigmoid because rotation and loop withdrawal results in losing the scope's position. With a loop in the scope, the angulation controls may no longer work effectively to turn the instrument tip because the cables which transmit motion are maximally stretched by the loop. These two negative forces, the inability to torque

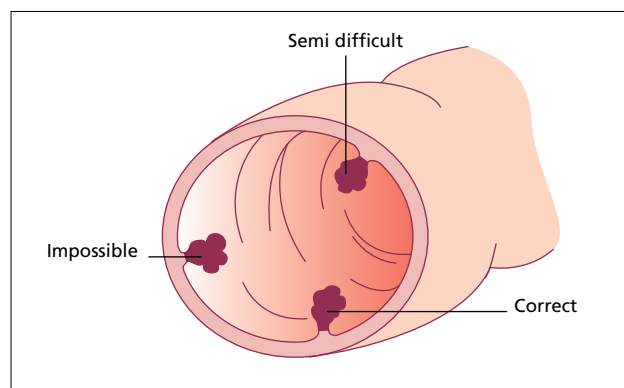


Fig. 35.8 Approach to a colon lesion for biopsy or polypectomy is easier when the lesion is placed at the 5 o'clock position by rotation of the colonoscope shaft.

effectively and the loss of cable-controlled tip deflection, combine to create an extremely difficult situation when attempting to maneuver the snare into position around a polyp. Maneuvering can be made considerably easier by passing the scope far beyond the polyp, even to the cecum (and thus visualize the rest of the colon), and attempting capture during the withdrawal phase of the examination. As the scope is withdrawn, the loops are removed and the polyp which proved difficult to position during intubation may be quite easily ensnared because both torque and tip deflection are responsive when the shaft is straight.

Positional changes and abdominal pressure

As noted previously, it is usually easier to properly position polyps for removal following total colonoscopy to the cecum. As the instrument straightens out by virtue of pulling the shaft out of the colon, clockwise or counterclockwise torque combined with angulation control manipulation can result in unimpeded rotation of the colonoscope tip so that a polyp encountered at the 10 o'clock position (which may be difficult to ensnare) can be moved to the 5 o'clock position even if it is located in the ascending colon. An additional consideration to shift a polyp into a more favorable position is to change the patient's position or apply abdominal pressure. Polyps partially hidden behind folds may come more prominently into view as the patient's position is altered. Polyps submerged in a pool of fluid can be rotated into a drier field by turning the patient so that fluid flows away from the base.

Summary

The removal of colon polyps is part of the performance of colonoscopy and should not be considered as an advanced procedure. The concept of colonoscopy embraces both diagnostic and therapeutic aspects; if a polyp is found, it should be removed at that time, and the endoscopist must know how to perform basic polypectomy but must also have the equipment available to accomplish polyp removal. Knowledge of the approach to polyps, basic polypectomy, and snare handling comprise the information base for polyp removal. The endoscopist and gastrointestinal assistant must work as a team to ensure a positive outcome. Sharing the same information base will make polypectomy easier and safer.

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Chapter 36

Difficult Polypectomy

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 Nib Soehendra and Jerome D. Waye

Introduction

This chapter describes various techniques that can be employed to assist in the removal of colon polyps that are considered to be large or “difficult.” Size alone is only one of the features that may cause some hesitation in making the decision to attempt polyp removal. Other factors that are related to the perceived level of difficulty are polyps that are flat and only slightly elevated above the mucosal surface, location on a wall of the colon that is not accessible to the snare, a polyp in a segment of severe diverticular disease or wrapped around a fold in clam-shell fashion. A polyp situated behind a fold can be difficult to approach, and those in the cecum hidden behind the ileocecal valve present a special challenge for resection. These and other problems will be addressed in this chapter, as will the localization of lesions or polypectomy sites for future surgery (in the case of malignant polyps) or for reevaluation following total or incomplete polyp removal. The impossible polyp is one which the endoscopist feels cannot be removed. The feeling of futility when faced with such a polyp is directly dependent on the training, experience and courage of the endoscopist. What may be “impossible” for one endoscopist may be a relatively “routine” polypectomy for another. In general, there are three criteria that make a polyp “impossible,” and when the three occur in the same lesion, then the polyp may be “really impossible.” The

three factors which by themselves or in combination with others may place the polyp into an “impossible” category are size, location of the polyp, and configuration.

Size

It is fortunate that polyps over 3 cm in diameter are not commonly found during colonoscopy. During the last 30 years, only a few publications [1–8] have reported on endoscopic removal of large colorectal polyps (Table 36.1). Christie [3] found in 1977 that only 58% of colorectal polyps measuring 20–60 mm were amenable to endoscopic polypectomy. Bedogni *et al.* [9] reported in 1986 that in their experience 75% of colorectal polyps larger than 30 mm were endoscopically removable (66% of the removed polyps were sessile). Lower malignancy rates of less than 15% in large colorectal polyps have been reported irrespective of their macroscopic and histologic growth pattern [2,10].

When a large sessile polyp is identified, several decisions will impact upon the probability of its removal. The first factor to consider is whether the polyp is benign or malignant. A question that arises is whether to perform a biopsy and then bring the patient back for polypectomy based on the subsequent results of biopsy or to depend on the visual impression of whether the polyp is benign. There are no studies on the visual criteria which can be applied to a polyp to determine the pres-

Table 36.1 Endoscopic resection of large colorectal polyps.

Study	Patients (no.)	Size (cm)	Sessile lesions (%)	Invasive CA (%)	Subsequent surgery (%)	Polypectomy complications	Malignant recurrence
Christie [3]	47	2–6	100	25	13	6% bleeding	0
Bardan <i>et al.</i> [1]	25	3–6	16	44	8	12% bleeding	1 patient
Walsh <i>et al.</i> [8]	108	1–8	100	23	27	3% bleeding 1% microperforation	1 patient
Binmoeller <i>et al.</i> [2]	170	> 3	73	12	9	3% bleeding	1 patient
Kanamori <i>et al.</i> [6]	32	3–8.5	100	15	0	10% minor bleeding	0
Nivatvongs <i>et al.</i> [7]	28	2–6	100	29	18	4% bleeding	0
Bedogni <i>et al.</i> [9]	66	3–11	68	15	11	3% bleeding	1 patient
Iishi <i>et al.</i> [5]	56	2–5	100	0	9	7% bleeding	0
Hintze <i>et al.</i> [4]	72	2–8	100	4	4	1% bleeding	0

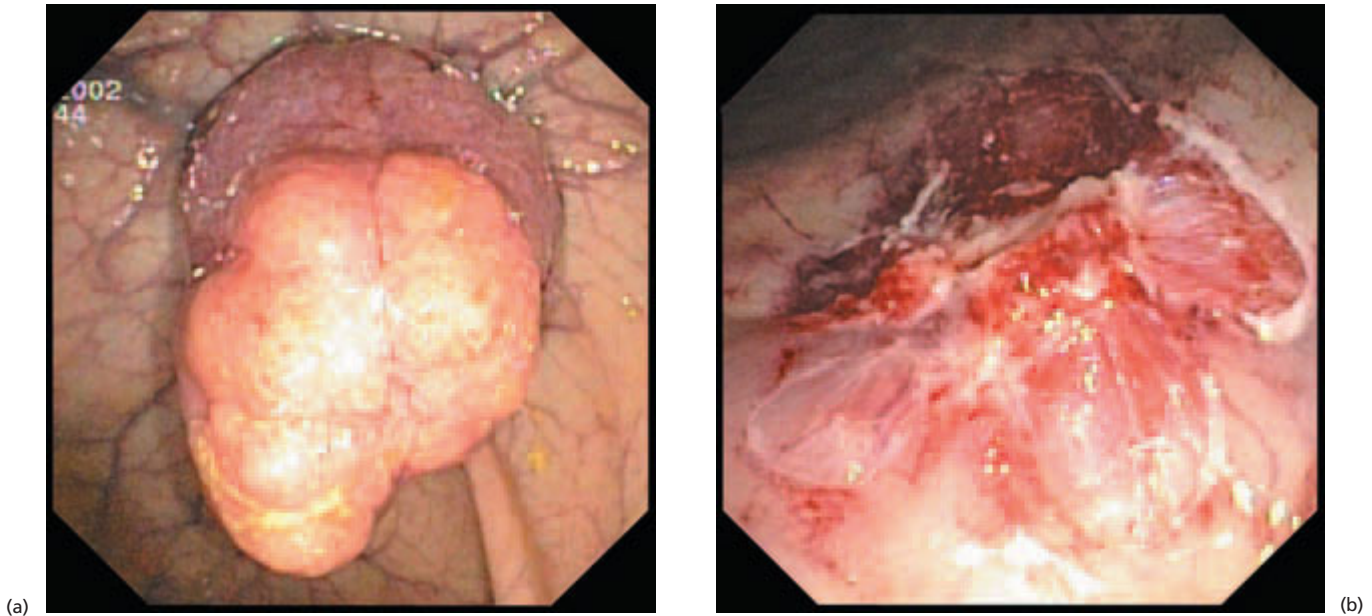


Fig. 36.1 Polyp with submucosal tissue remnants at the center of the resection site. (a) The polyp initially did not appear malignant and was resected in five pieces. (b) Indurated tissue in the middle of the resection site was suspicious for malignancy, but histology showed only moderate dysplasia.

ence of malignancy; however, endoscopists in a tertiary referral center in Hamburg, Germany [2] have stated that a benign polyp does not have any of the following features: ulceration, induration, or friability. Japanese endoscopists [6] who endeavored to remove large polyps noted that large flat polyps were usually benign, and that invasive carcinoma was only seen in elevated sessile polyps. These visual characteristics may not always be accurate but biopsies are notoriously erroneous for the diagnosis of invasive carcinoma within a polyp because the depth of tissue obtained is usually limited and because high-grade dysplasia on biopsy (which used to be called noninvasive carcinoma or carcinoma *in situ*) is histologically identical to invasive carcinoma. In addition, the amount of tissue sampled by biopsying a large polyp represents only a fragment of the total polyp volume submitted for histopathology. Most colonoscopists base the decision as to whether a large polyp is benign or malignant on the visual impression when it is identified. If the assessment is that the polyp is benign, the decision for removal should be based on other visual criteria; if it looks like it can be removed, an attempt should be made to resect it (Fig. 36.1). There is a general reluctance among endoscopists to remove large polyps because of the possibility of invasive carcinoma. One report stated a 40% incidence of invasive carcinoma in large polyps, but this finding was based on the pathologist's finding of carcinoma in surgical specimens

that were sent to the pathology laboratory, not polyps that were removed endoscopically [11]. Endoscopically resected polyps, which meet the visual criteria of being benign, will actually have an incidence of about 10–15% of invasive malignancy [2,6,9,10].

When the decision is made by the endoscopist to attempt removal of large polyps, it is necessary to obtain the patient's agreement to repeated endoscopy sessions and follow-up endoscopies. Complete resection of large sessile polyps may require several sessions and, since high rates of local recurrences are reported [4,8,9], it is mandatory to confirm complete removal by follow-up examinations.

If the polyp appears to be benign on endoscopic visual examination, the average endoscopist (as compared to experts) must then consider three criteria for its removal. If any of these are present, the endoscopist will have considerable difficulty in its removal. These three criteria [12] are:

- 1 the polyp occupies more than one-third the circumference of the colon wall;
- 2 the polyp crosses over two haustral folds;
- 3 the polyp encircles and actually involves the base of the appendix.

A polyp which extends more than one-third the circumference of the colon wall will create a large mucosal defect if it is removed. It is possible that polyps of this size could be removed by an expert endoscopist (Fig. 36.2), but even the expert may elect to send such a patient for surgical resection rather than face the possibility of multiple colonoscopic examinations, particularly if the colonoscopic approach to the polyp was extremely difficult and demanding. Polyps that cross over two haustral folds present another problem in their total

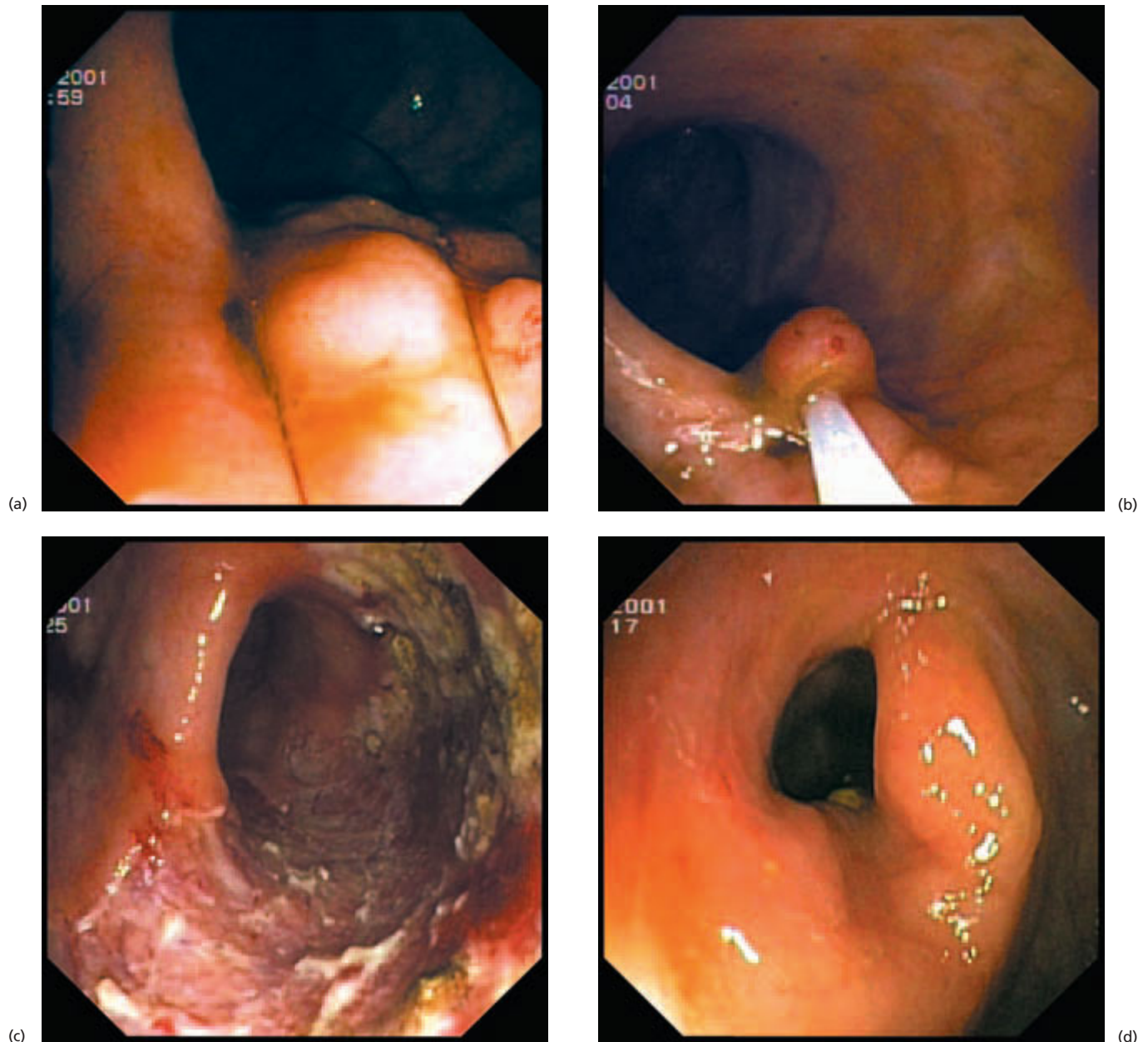


Fig. 36.2 Extensive laterally spreading flat polyp. (a) This polyp measures 7 cm in length and involves two-thirds of the luminal circumference. It is positioned at 6 o'clock and snare resection is started on one side of the polyp. (b) The ensnared part of the polyp is lifted from the bowel wall prior

to resection. (c) The flat lesion is resected completely by piecemeal technique. (d) Follow-up colonoscopy after 6 weeks did not show any remnant polyp tissue. A mild asymptomatic stricture has occurred.

removal, since it may be almost impossible to remove the entire polyp, especially the portion that lies in the valley between two haustral folds. Polyps that involve the appendiceal orifice may extend into the appendix, and, although this phenomenon is rare, total removal of this type of polyp is problematic (Fig. 36.3). Large pedunculated polyps have large nutrient arteries, and may bleed during or after polypectomy. Injection of epinephrine into the stalk may decrease the risk of

bleeding. Other measures are application of endoloops; or a technique of using one disposable snare to cut off the blood supply and another to perform the resection [13,14] (Fig. 36.4).

Ambulatory or inpatient polypectomy

Most diagnostic colonoscopies are performed on an ambulatory basis. When a large polyp is encountered

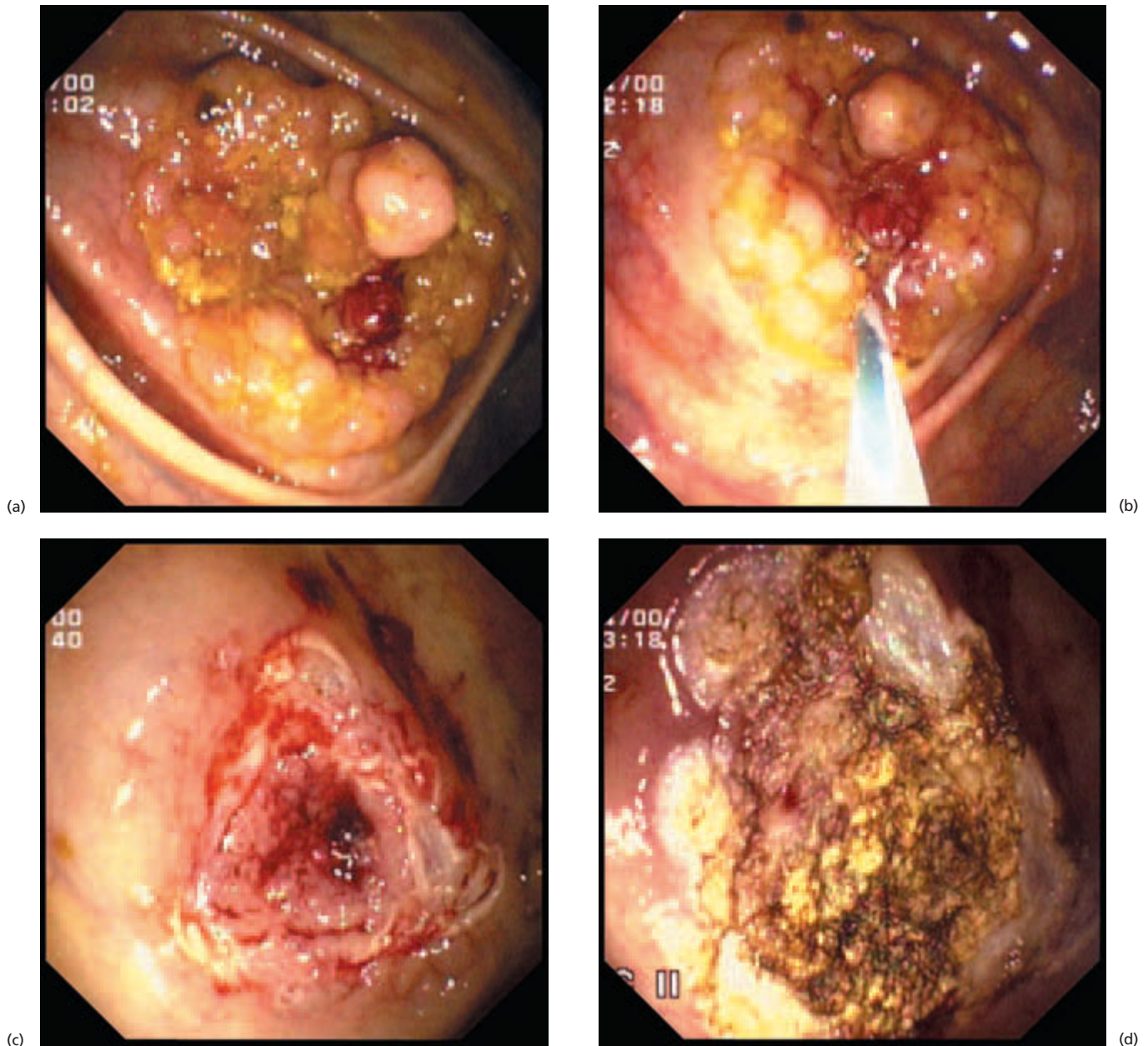


Fig. 36.3 Removal of large sessile polyp involving the appendiceal orifice. (a) Large sessile polyp at the cecal pole. (b) Injection of epinephrine (1 : 20 000) lifts the lesion from the muscle layer and allows for easier and safer ensnaring. (c) The appendiceal orifice is visible after piecemeal resection. (d) APC is performed to remove the remaining adenomatous tissue at the appendiceal orifice.

that meets the criteria for removal, the endoscopist must decide whether the patient should: (i) be admitted to hospital; (ii) have the polypectomy in a hospital outpatient setting; or (iii) have the procedure performed in an office facility remote from a hospital? Literature supports the safety of ambulatory polypectomy [15], and

only 1 of 170 patients who had large polyps removed required immediate hospitalization for suspected perforation [2].

Much of the reluctance to remove large polyps is related to the fear of complications. The actual incidence of perforation in removal of large polyps is low, with two series [2,6] of large polypectomies reporting that no patients required surgical intervention, there were no perforations, and when bleeding during polypectomy occurred in 10% [6] and 24% [2] of patients it was successfully handled. The published rate of complications indicates that bleeding occurs in 1.4% of polypectomies and perforation in 0.3% of patients [5] (see Chapter 15).

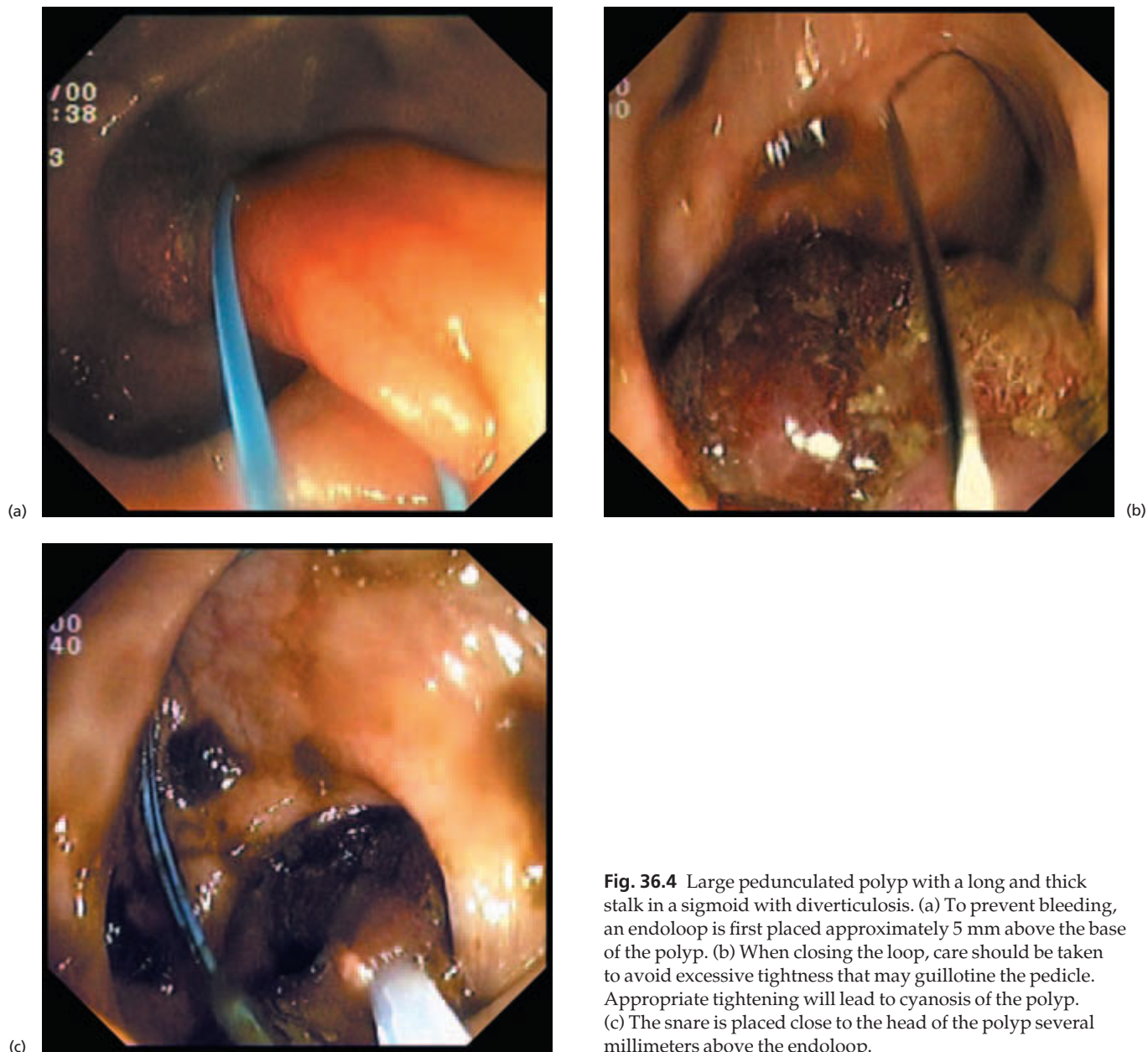


Fig. 36.4 Large pedunculated polyp with a long and thick stalk in a sigmoid with diverticulosis. (a) To prevent bleeding, an endoloop is first placed approximately 5 mm above the base of the polyp. (b) When closing the loop, care should be taken to avoid excessive tightness that may guillotine the pedicle. Appropriate tightening will lead to cyanosis of the polyp. (c) The snare is placed close to the head of the polyp several millimeters above the endoloop.

The colonoscope

For difficult polypectomy, a therapeutic colonoscope with a 4.2-mm working channel and an additional channel for a water pump is recommended. A large working channel allows for sufficient simultaneous suction during the procedure which is particularly helpful to control severe bleeding. An additional small-bore channel connected to a water pump provides a strong water jet for cleansing the mucosa surface, e.g. in case of oozing during endoscopic mucosal resection or piecemeal resection. However, many endoscopists use a standard colonoscope for removal of large polyps.

Endoscopic mucosal resection

Submucosal injection for polypectomy

The submucosal injection technique is often used for removal of large sessile adenomas [16,17]. Deyhle *et al.* first performed submucosal injection to raise flat mucosal lesions facilitating ensnaring in 1973. Saline or epinephrine solution (1 : 20 000) is injected from the margins of the polyp. Submucosal injection may be useful to lift parts of the polyp located in the appendiceal orifice or behind a haustral fold. However, submucosal injection even with large amounts of saline solution may

not avoid perforation if too large pieces of polyp are ensnared and resected [18]. Diluted epinephrine solution is used to prevent bleeding during polypectomy. However, a possible drawback of this precaution may be delayed bleeding due to the short-lasting vasoconstrictive effect of epinephrine.

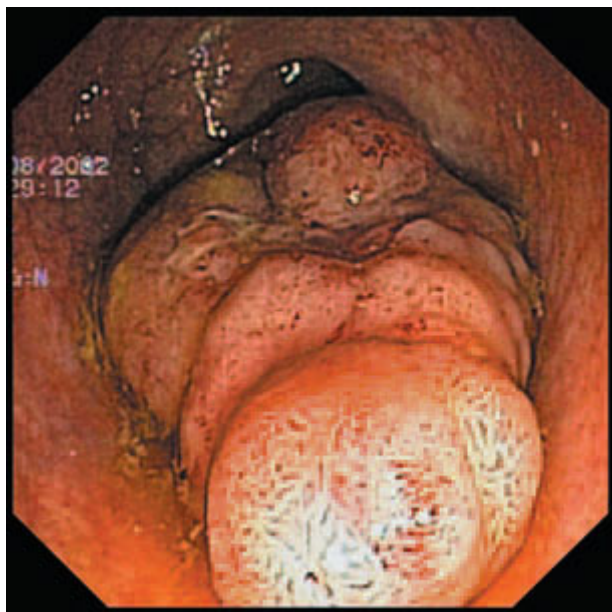
Endoscopic mucosal resection (EMR) using a double-channel endoscope was introduced by Tada *et al.* in 1993 [19] to remove large sessile and flat polyps. The lesion is lifted by using a forceps to enable ensnaring (“lift and cut” technique). Several modifications of EMR technique have been introduced in the management of early cancer of the stomach and esophagus [20].

In the colon and rectum, EMR is widely performed using the simple snare resection technique. The colon wall is 1.5–2.2 mm in total thickness, and thermal damage to deep layers of the colon is frequently encountered [21]. Injection of fluid into the submucosa beneath the polyp will increase the distance between the base of the polyp and the serosa. When current is then applied via a polypectomy snare, the lesion can be more safely removed because of a large submucosal “cushion” of fluid which lessens the likelihood of thermal injury to the serosal surface (see Chapter 34). The fluid, injected through a long and stiff sclerotherapy needle may be saline (normal or hypertonic) [22], with or without methylene blue to enhance visualization and with or without epinephrine [23]. Most endoscopists use normal

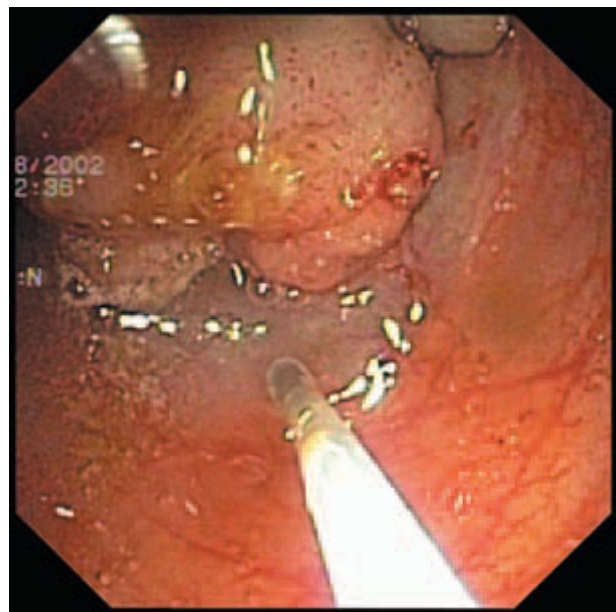
saline only. Hypertonic saline solution and epinephrine are used to retain the fluid at the site for a longer period, but submucosal saline lasts for 10–15 minutes, which is sufficient time for removal of most polyps. A viscous mucinous solution of 0.5% sodium hyaluronate has been used (via a 21 gauge needle) to elevate large flat polyps for endoscopic mucosal resection [24]. This solution is isotonic and remains at the injection site longer than saline. Further studies need to be performed to assess the practicability of various injection solutions. There is a theoretical advantage to the injection of dilute epinephrine, to prevent bleeding at the time of polypectomy or to prevent delayed bleeding (Fig. 36.5). However, the incidence of immediate bleeding is low (1 out of 100 procedures) [25] and the long-term effect is nil because the vasoconstrictive action is measured in hours, not days.

The injection needle may be placed into the submucosa just at the edge of a polyp, or if the polyp is large and flat, multiple injections may be given around the polyp or directly into the middle of the polyp. If a bleb does not form at the injection site when 1 mL of fluid has been given, the needle should be withdrawn since the tip may have penetrated the wall and pierced the serosal surface. When the needle is in the submucosal plane, continuous injection of saline will result in submucosal infiltration of fluid. A large localized fluid collection is the desired endpoint, with marked elevation of the polyp. When the tissues expand in response to fluid injection, the fluid is being deposited in the areolar tissue of the submucosal layer since neither the mucosa, muscularis propria or the serosa will accept injected substance. If the needle placement is too superficial, the fluid will leak out from the beveled edge and spill into the lumen. This

Fig. 36.5 Large sessile polyp extending over the rectosigmoid junction. (a) This 5-cm large polyp was found in the rectosigmoid junction. (b) Prior to resection, injection with epinephrine 1 : 20 000 is performed to lift the polyp from the muscle layer.



(a)



(b)

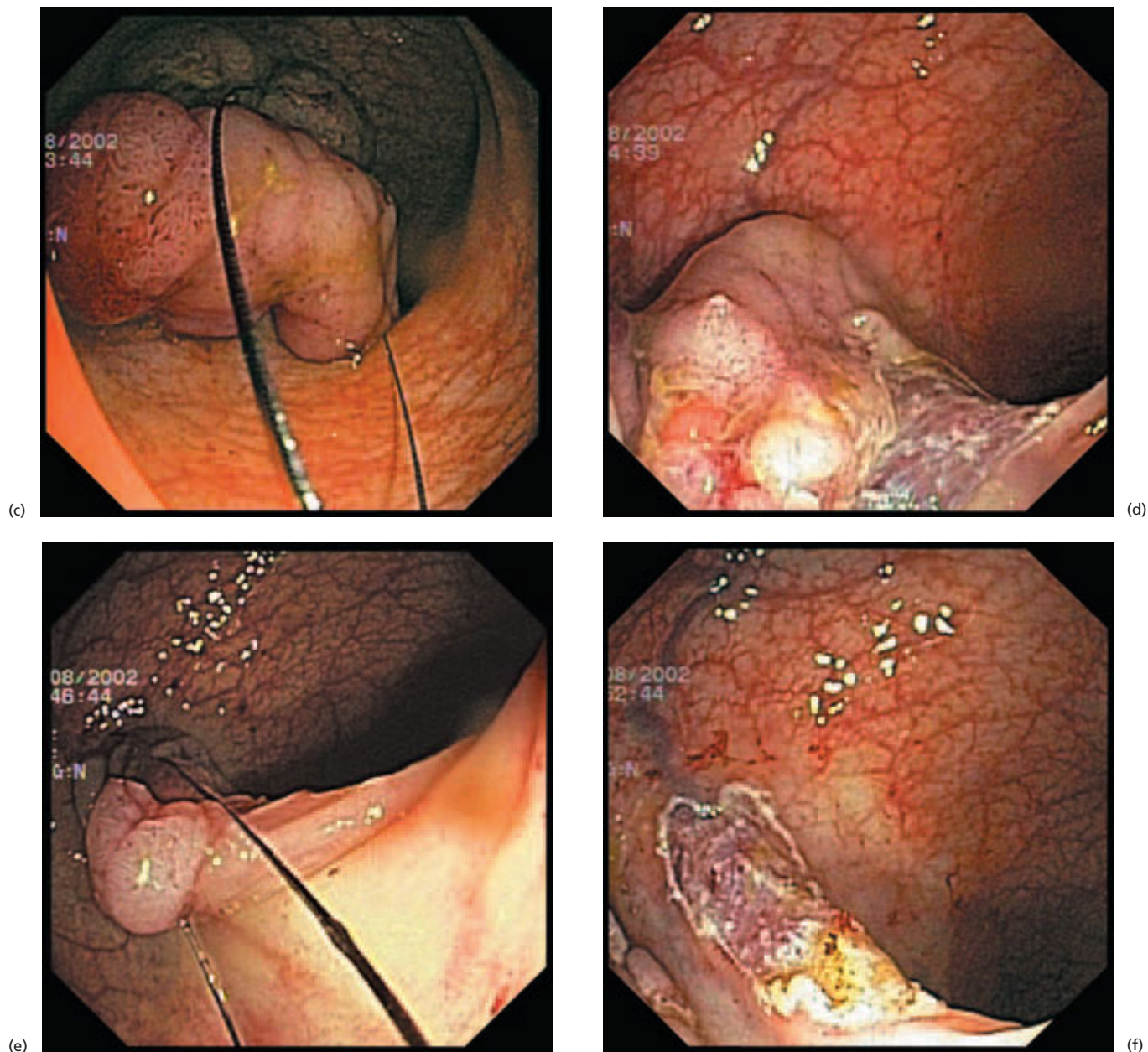


Fig. 36.5 (cont'd) (c) Initial piecemeal resection of small portions is performed to avoid perforation. (d) The exposed muscle layer will serve as a point of orientation for further resection. (e) Remaining parts of polyp behind the

fold are removed using the fulcrum technique. Tangential orientation of the snare to the muscle layer allows for safe ensnaring. (f) Minute remnants of adenomatous tissue can be removed by APC.

spilling is especially noticeable when a colored fluid is used, such as methylene blue or Indian ink. Multiple repeated needle placements and attempts at injection may be required to locate the correct plane for polyp elevation. If possible, the approach by the needle injection should be tangential and not perpendicular to the mucosal surface. Elevation of the polyp may take 3–4 mL of saline given in several places, although some authors use up to 30 mL of fluid [6]. Polyps up to 2 cm in

diameter may be removed with one application of the snare, but larger polyps may require several transections in piecemeal fashion [26].

It is permissible to remove a much larger piece with this technique than one would ordinarily snare when in the right colon without a “cushion” of fluid. The pieces should probably not be larger than 2 cm in diameter [6]. With the fluid as protection against deep thermal tissue injury, it is possible to fulgurate the base of the resection

site with devices such as a hot biopsy forceps, the tip of the snare, the argon plasma coagulator, or any other thermal device which delivers heat to the residual polyp site.

When attempting submucosal injection for polypectomy (SIP), there is not a specific volume of fluid which is used, but rather the desired end point is a large submucosal swelling beneath the polyp and adjacent portions of the mucosa. When part of the polyp is either hidden from view behind a fold or wrapped around a fold in clamshell fashion, injection of the part nearest to the colonoscope may elevate that portion, but can cause interference with polypectomy because the mound of saline will block vision. The solution to this problem when the proximal edge of the polyp is hidden is to inject the far side of the polyp. This is accomplished by passing the scope beyond the far edge of the polyp. While deflecting the tip toward the polyp, the injection should be made into the normal mucosa just at or near the edge of the polyp (or into the proximal edge of the polyp). Injection into the wall on the far side of the polyp will raise that portion up on the fluid mound, rendering snare application easier (Fig. 36.6). Depending on the polyp size, several injections may be required to elevate the polyp so that snare placement is more readily accomplished. After the back portion of the polyp has been removed, then saline may be injected into the area closest to the scope to assist in completing the polypectomy.

The nonlifting sign

In general, malignant tumors should not be removed by the submucosal injection technique. If a polyp fails to elevate (the “nonlifting sign”) [27], it may be an indication of infiltration by cancer into the submucosa, with fixation by tumor limiting the expansion of the submucosal layer [28]. Although deep or superficial needle placement may be the cause for failure to raise a bleb under a polyp, a submucosal bulging or bleb on one side of a polyp in response to injection without any visible elevation of the tumor itself is a clue that there is fixation into the submucosa. This phenomenon may also be caused by a prior attempt at polypectomy with healing and scarring of the mucosa and submucosa, preventing their separation by fluid injection.

Tumor tracking

There is a theoretic possibility that injection through a malignant tumor may cause tracking of cancer cells into and even through the bowel wall. The risk of this happening is minimal, with experience gained from direct percutaneous needle aspiration of malignant tumors in other sites throughout the body. The risk of tumor tracking is 1 in 10 000 to 1 in 20 000 cases [29].

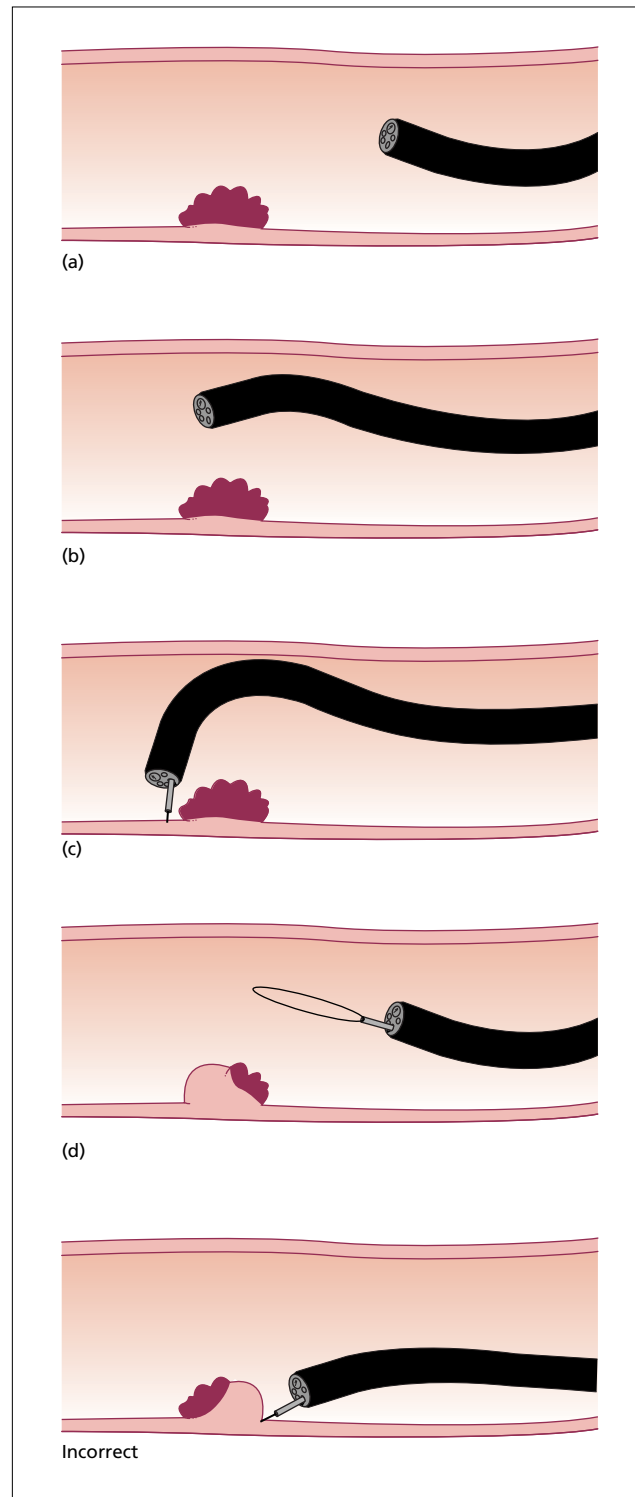


Fig. 36.6 The proper location for submucosal injection of saline is into the colon wall (or into the polyp) on the far side of the polyp. This will raise the polyp toward the instrument tip. An injection into the closest part of the polyp may hide the polyp behind the saline bleb.

Parenthetically, it seems that any tumor which can be elevated with submucosal injection of fluid can be totally removed by endoscopic resection, even if invasive cancer is found on tissue examination. The ability to elevate a tumor indicates that there is only a limited degree of fixation to the submucosal layer, with the possibility of complete removal.

Cap-assisted polypectomy (see Chapter 25)

A suction cap may be attached to the colonoscope tip, and a preloaded snare can be placed at the mouth of the cap. Once the polyp elevated with SIP has been aspirated into the cap, a sizable portion of the wall can be removed using coagulation current. Caution is urged for using this technique above the peritoneal reflection [30]. Endoluminal full-thickness resection using a rigid instrument was introduced by Buess *et al.* to remove sessile and/or malignant polyps in the rectum [31]. This technique may offer a better alternative to endoscopic piecemeal resection or resective surgery in selected cases. However, it does not allow for lymphadenectomy, and has therefore a limited use in malignant lesions that cannot be treated endoscopically.

Stop at the snare-handle mark

When complete visualization is not possible as the loop is being closed, the assistant should close until resistance is met, or, if there is no closure sensation, then stop at the line (see Chapter 35). Once closed, the snare sheath should be jiggled to and fro at the biopsy port while observing the colon walls around the polyp. If extraneous portions of the mucosa are not caught, the polyp will be seen to move independently of the surrounding colon walls as the sheath is jiggled. If the polyp and the surrounding wall move simultaneously, there is a strong probability that a portion of adjacent mucosa or bowel wall has been captured within the snare loop. Complete removal of the snare or partially opening the loop for repositioning is advisable before application of electrocautery current. Transection of a large fragment of inadvertently captured normal mucosa is not a desirable outcome of polypectomy and may lead to perforation. If extra tissue is captured, there is no assurance that it will only consist of mucosa, for submucosa may also be entrapped, and when electrocautery current is applied a deep burn may result.

Piecemeal polypectomy

When removing a sessile polyp, the characteristic whitening at the site of wire placement when electrocautery current is applied often cannot be observed because the wire is embedded in the polyp. After a few

seconds of current, the wire snare should be slowly closed until separation occurs. During piecemeal polypectomy, the next placement of the snare may be immediately adjacent to the first, with the edge of the wire positioned into the denuded area just created by removal of the previous piece (Fig. 36.7). In this fashion, multiple portions can be sequentially resected in an orderly fashion, with removal of each succeeding piece being facilitated by its predecessor. Several applications may be required, removing fragments until satisfactory polypectomy is achieved [7,32]. The polyp fragments may be removed by suction into a trap if they are small or retrieved with a Roth basket or, less effectively, with a dormia basket or a tripod grasper. One or two fragments may be captured in a snare loop for removal.

The fulcrum technique may be used for the endoscopic treatment of laterally spreading polyps. The tip of the opened snare is impacted against the colonic wall behind the polyp. By keeping the tip fixed, slightly advancing the snare, and bending the endoscope tip to left or right the snare is pivoted to either side (Figs 36.8, 36.9). If the tip of the opened snare is placed in front of the polyp, it can be flexed backwards along its long axis by advancing the snare and the tip of the endoscope (Fig. 36.10). To prevent perforation, the wire loop should be pressed flat against the bowel wall to ensnare the mucosal and submucosal layers only.

Position of polyp

Whenever a polyp is to be removed, snare placement is facilitated by rotation of the colonoscope to bring the polyp to the 5 o'clock position. Rotation of the scope is necessary to reposition the instrument tip in relation to the polyp.

Rotation of the scope may be difficult during intubation when the instrument shaft has loops and bends. Advantageous positioning may be best accomplished when the colonoscope shaft is straight, because a straight instrument transmits torque to the tip, whereas a loop in the shaft tends to absorb rotational motions applied to the scope. It is often difficult to capture a sigmoid polyp during intubation, when the obligatory sigmoid loop is present. It may not be possible to straighten the scope in the sigmoid during the intubation phase because rotation and loop withdrawal often results in losing the scope's position. With a loop in the scope, the dial controls may no longer work effectively to turn the instrument tip because the cables which transmit motion are maximally stretched by the loop. These two negative forces, the inability to torque effectively and the loss of cable-controlled tip deflection, combine to create a difficult situation when attempting to maneuver the snare into position around a polyp. Snare placement can be made considerably easier by passing the scope

far beyond the polyp, even to the cecum (and thus visualizing the rest of the colon), and attempting capture during the withdrawal phase of the examination. As the scope is withdrawn, the loops are removed and the polyp which proved difficult to position during intubation may be quite easily ensnared because both torque and tip deflection are responsive when the shaft is straight.

Polypectomy in a narrow diverticular segment

Types of snares (see Chapter 25)

For resection of difficult polyps there is probably no significant difference between snares made of braided or monofilament wire. A braided wire creates more

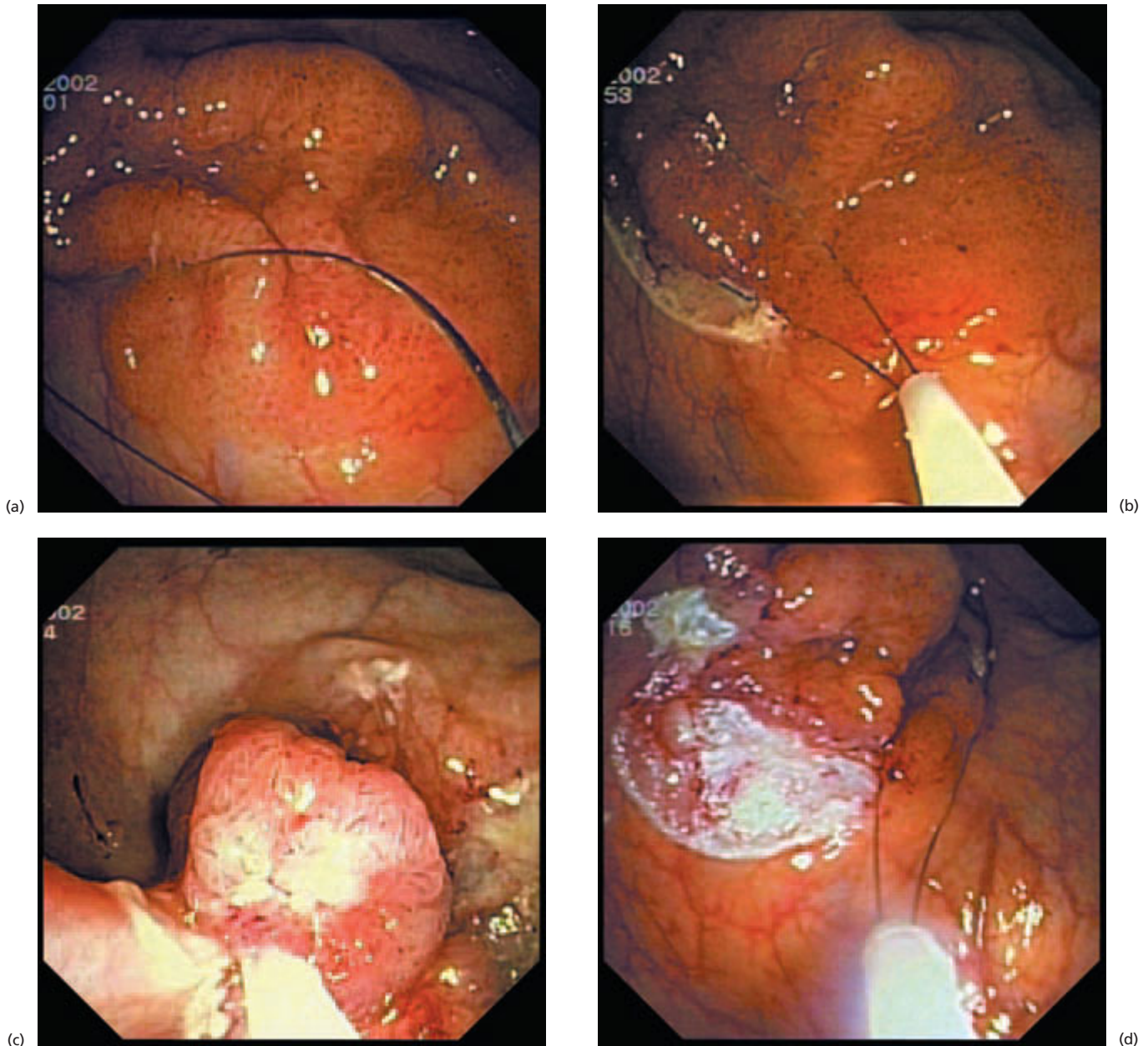


Fig. 36.7 Piecemeal resection of an adenoma with flat and elevated parts. (a) The front part of the polyp is ensnared first. The snare is pressed flat against the bowel wall. As the snare is closed the catheter is simultaneously advanced. While closing the snare suction should not be applied. (b) After the first piece

is resected, the exposed muscle layer provides orientation concerning the correct depth of further resections. (c) During application of current the ensnared portion is lifted from the bowel wall to avoid deep coagulation. (d) Piecemeal resection is continued on the other side.

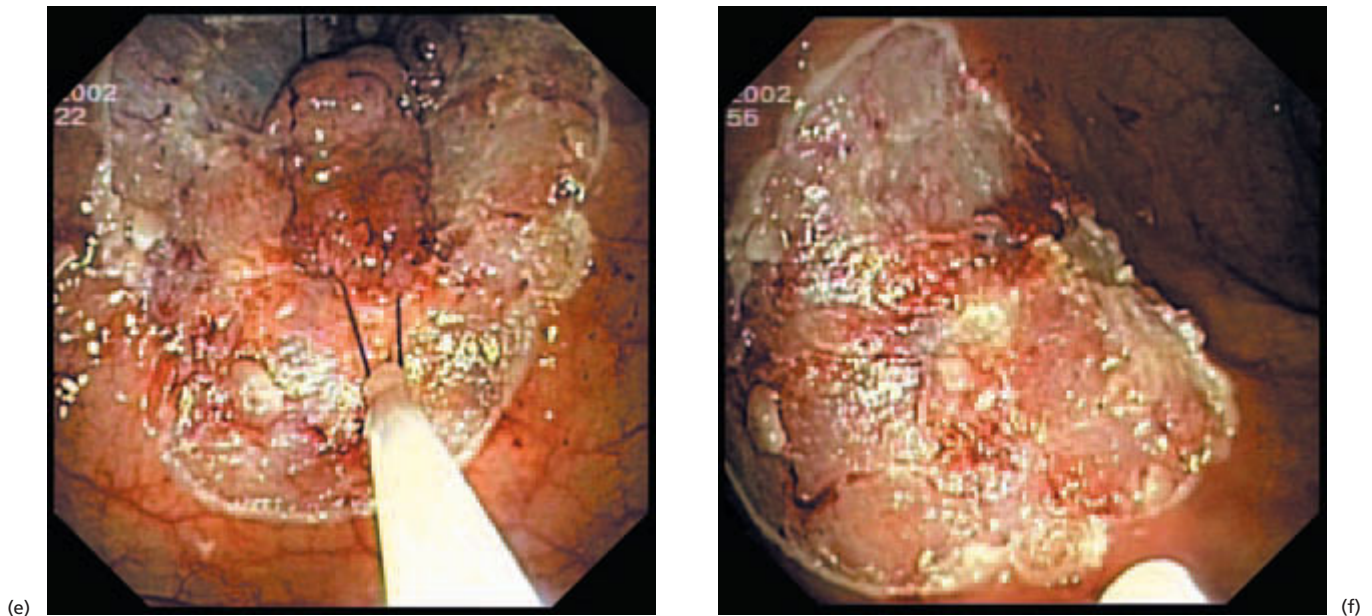


Fig. 36.7 (cont'd) (e) Finally the elevated middle part is resected. (f) Total piecemeal resection is accomplished.

coagulation effect than a monofilament wire. Bleeding may be less frequent with braided wire, but it may carry a higher risk of perforation due to greater thermal penetration depth. In our experience, a monofilament snare made of 0.5 mm steel wire is stiffer and provides greater stability for ensnaring flat polyps (Fig. 36.11). The standard Erlangen polypectomy snare (Grosse Co., Daldorf, Germany) is 5 × 3 cm in size. In a narrowed bowel lumen such as encountered in diverticulosis, a smaller floppy snare made of braided wire may be useful.

Use of the mini-snare

Even after total colonoscopy has been performed and the colonoscope has been straightened, there may still be

difficulty in the sigmoid colon when attempting to capture a polyp because of narrowing by diverticula and thickened hypertrophic folds. There are two maneuvers which may permit easier endoscopic polypectomy. The first is to use a mini-snare, which will allow a full extension of the snare within a short segment of the bowel. The standard regular-sized polypectomy snare may not be able to capture a small polyp in a difficult and “tight” location where there is not sufficient distance for the wire loop to open sufficiently wide to be placed over a polyp. A problem with the standard snare is that it must be completely extended to its full length of 6 cm in order for the loop to completely expand. During colonoscopy, it often occurs that the wire loop can only be extended a few centimeters beyond the scope because of a tight bend or because the tip of the loop impacts on an adjacent wall of the colon. When the snare loop cannot be fully extended, the two partially open parallel wires

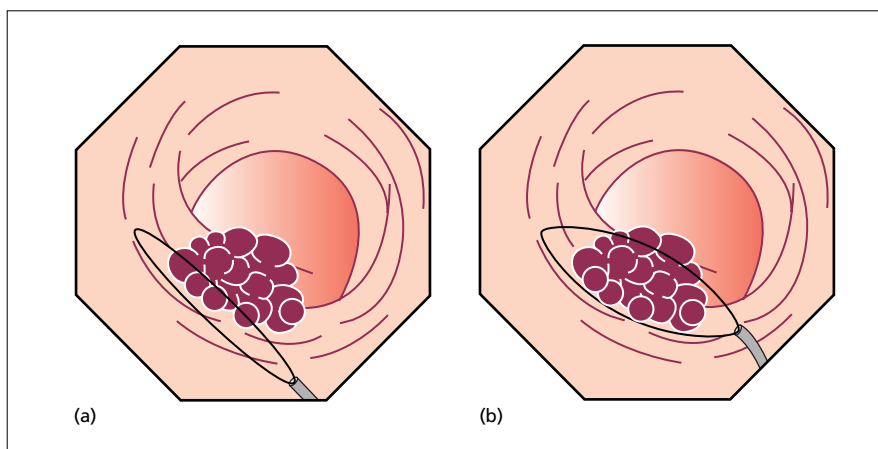


Fig. 36.8 The impacted tip of the snare acts as a fulcrum on the colonic wall. Bending the endoscope tip to the right allows for safe snaring of the polyp alongside the haustral fold.

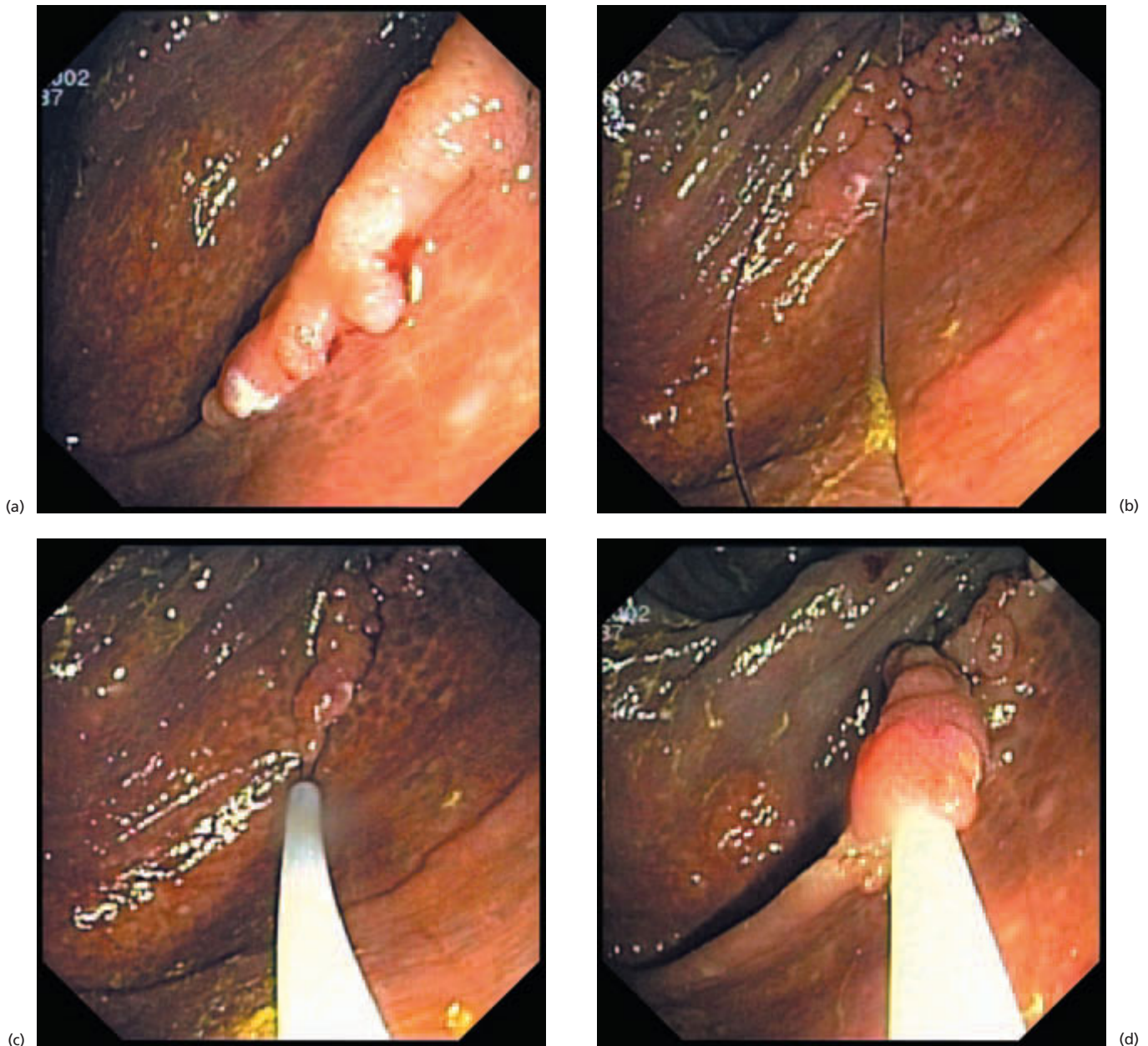


Fig. 36.9 Resection of a polyp along a fold. (a) Maximum air insufflation of the lumen shows that the polyp is on a fold. (b) The tip of the opened snare is placed behind the polyp. The snare is then pushed and firmly pressed against the bowel wall to spread out the fold exposing the entire loop. (c) Using the tip of the snare as a fulcrum the snare is pivoted to the left by

bending the tip of the endoscope. The left part of the polyp is engaged into the snare. (d) The ensnared polyp portion is lifted into the bowel lumen and resected under optimal endoscopic control. Complete polypectomy is accomplished with piecemeal technique from the left to the right.

may not sufficiently spread apart to enable polyp capture. In this circumstance, a mini-snare of 3 cm in length and 1.0 cm in width [33,34] is extremely valuable. This snare will open fully when extended only 3 cm beyond the sheath, making it useful in areas where multiple bends are present (such as in the sigmoid narrowed with diverticulosis), or when polyps are located in the depth of a haustra. Since the vast majority of colon polyps are

less than 1.0 cm in diameter, they are within the limits of this mini-snare.

Gastroscope for better tip reflection

The second maneuver is use of a narrow caliber scope to intubate the colon. A pediatric colonoscope is useful, but not generally available. A standard gastroscope has

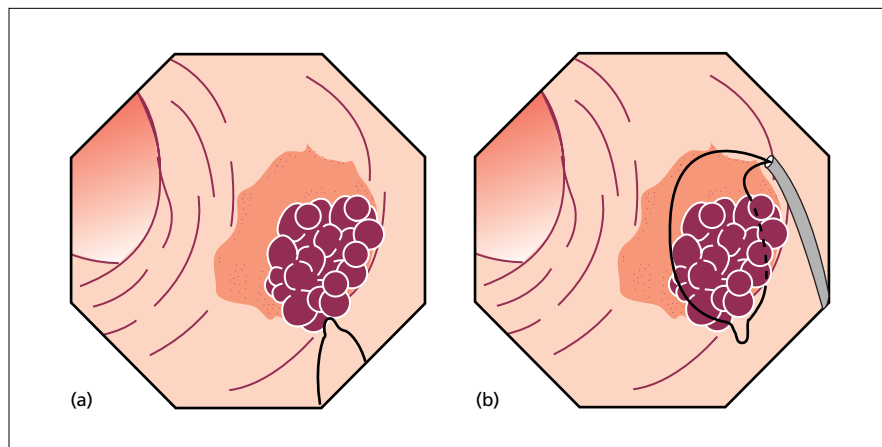


Fig. 36.10 Reverse lasso technique. After positioning the tip of the snare in front of the polyp the open snare is advanced and the tip of the endoscope slightly elevated. Thus the snare is pivoted back alongside its own axis.

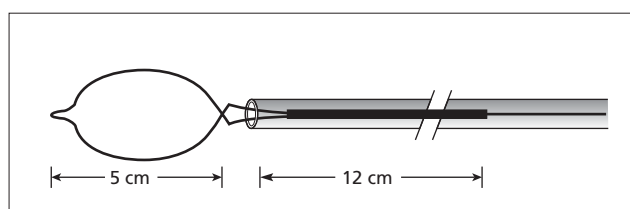


Fig. 36.11 Monofilament Erlangen snare. The snare measures 3 cm × 5 cm and is made of 0.5 mm monofilament stainless steel wire. A 12-cm-long flat wire is built in between the loop and traction wire in the same plane with the loop. It can only be flexed horizontally and the snare will always be adjusted automatically parallel to the mucosal surface when the endoscope is bent. The outer sheath is a 7Fr Teflon catheter.

been demonstrated to be of benefit [35]. The major attributes of the gastroscope is that it has a tighter bending radius of the tip than does a colonoscope and the tip beyond the bending portion is shorter in length. This will frequently allow easy snare positioning in the same location where the colonoscope was both cumbersome and difficult. There is a growing awareness among endoscopists that gastroscopes can easily and readily be used in the colon to intubate difficult and narrowed segments, to be passed through strictures, and to render a previously inaccessible polyp more readily manageable. The upper intestinal endoscope can be of use even in the rectum, where it may not be possible to snare a polyp on the proximal surface of one of the rectal valves. In this circumstance, the bending section of the colonoscope may be too long to permit a tight turn, whereas a gastroscope with its greater tip deflection capability and shorter “nose” (or straight portion beyond the bending section) may permit easy visualization and removal of polyps.

Clamshell polyps

Large sessile polyps wrapped around a fold in a

“clamshell” fashion usually permit the distal portion to be readily removed, but resection of the proximal portion on the far side of the fold may be considerably more difficult. This type of polyp is often located in the right colon and should be removed in piecemeal fashion (Fig. 36.12). The piecemeal technique usually requires rotation of the colonoscope to place the polyp at the 5–6 o’clock position. Although it would be ideal to resect the total polyp at one session, it may only be possible to remove the portion nearest to the scope, leaving some of the polyp on the far side of the fold for an interval resection. Subsequent scarring may flatten the polypectomy site, bringing the residual polyp into a favorable location for subsequent polypectomy. Often, an injection of fluid into the mucosa on the far side of the polyp will facilitate its removal, as previously described. If it is elected to attempt total polypectomy at the first session, the stiffness of the plastic snare catheter can be used as a probe. After endoscopic transection of the portion closest to the scope, and with the loop extended, the tip of the catheter can be positioned on the ridge of the fold in the polypectomy site where a portion of the polyp has just been removed. By a combination of torque and rotation of the large control knob, downward pressure on the ridge at the site of the polypectomy divot will often depress it sufficiently so that a portion of the residual adenoma will extend into the loop permitting capture under direct vision (Fig. 36.13). Several repeated snare applications and transections of this type will usually result in complete polypectomy. The tip of the instrument must be close to the polypectomy site for this technique to be effective, since the plastic polypectomy sheath becomes quite flexible when it is extended more than a few centimeters beyond the colonoscope. The sheath, with its tip barely protruded from the faceplate of the scope, is stiff and will depress a fold when torque or tip deflection is applied to the colonoscope shaft. A stiff monofilament snare may be used to flatten the fold exposing the entire polyp. Pushing on a fresh

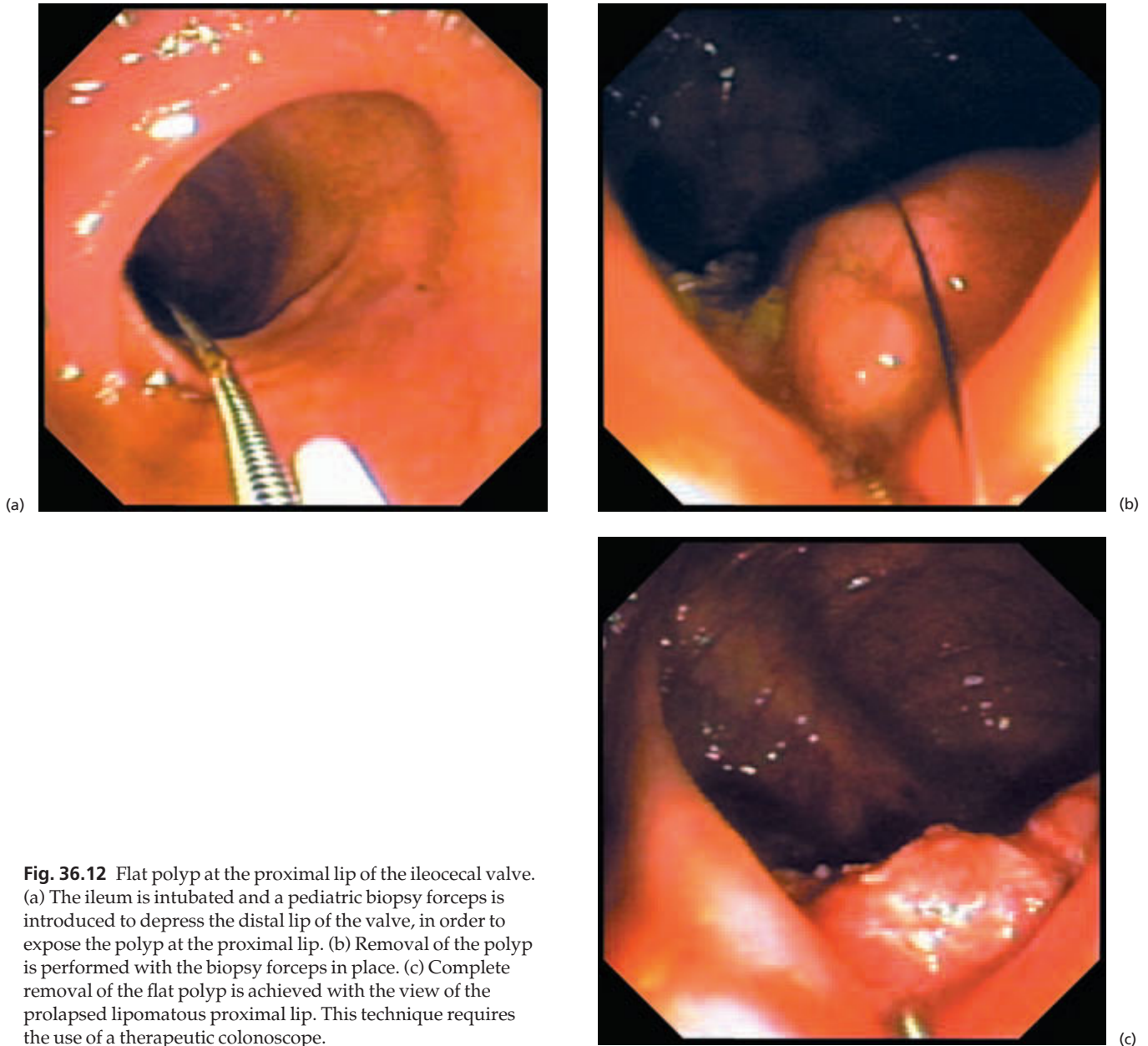


Fig. 36.12 Flat polyp at the proximal lip of the ileocecal valve. (a) The ileum is intubated and a pediatric biopsy forceps is introduced to depress the distal lip of the valve, in order to expose the polyp at the proximal lip. (b) Removal of the polyp is performed with the biopsy forceps in place. (c) Complete removal of the flat polyp is achieved with the view of the prolapsed lipomatous proximal lip. This technique requires the use of a therapeutic colonoscope.

polypectomy site in this manner is not associated with any adverse results.

Retroversion

An alternative technique for removal of a polyp located on the far side of a fold is to perform a U-turn maneuver. With standard instruments, this can only be accomplished in the cecum, ascending colon, descending colon and sometimes in the transverse colon, although it is somewhat easier with pediatric colonoscopes. It is difficult but not impossible to resect a polyp in a U-turn mode because the tip deflection responses are opposite to those usually expected (Fig. 36.14).

Flat polyps

In spite of the knowledge and skill of modern endoscopists, not all colon polyps can be successfully removed with a colonoscope. Among these are carpet-like polyps which extend over several centimeters. An attempt can be made to fulgurate the surface of such polyps with the shank of the monopolar biopsy forceps, a bipolar (BICAP) probe, a laser, or the argon plasma coagulator. A helpful maneuver to be considered when the lesion appears too flat to capture with the snare loop is to aspirate air from the colon with the snare device in place. This will collapse the distended colon, causing a decrease in the circumference of the colon wall and, as

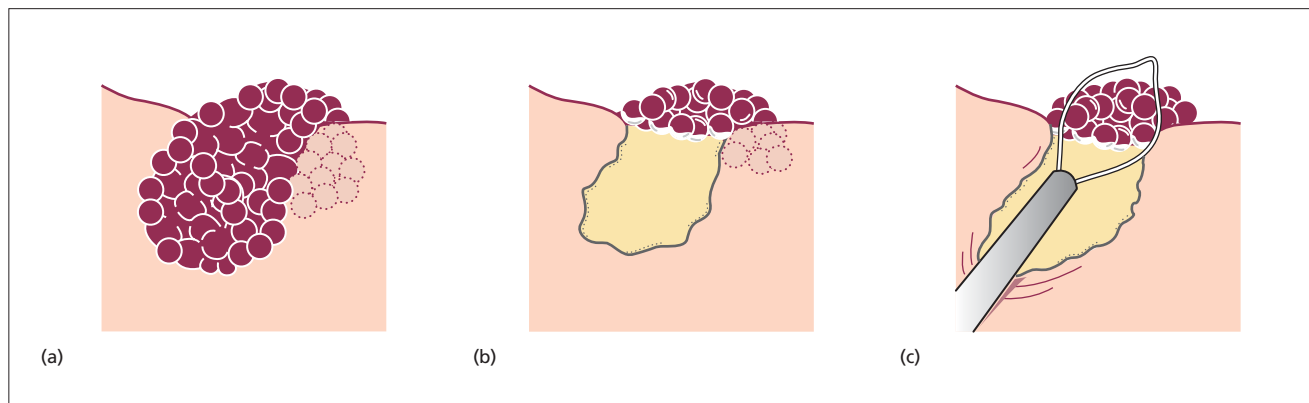
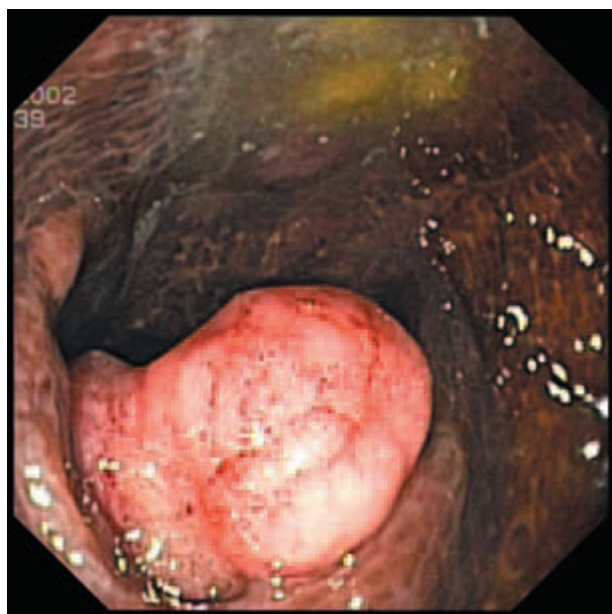


Fig. 36.13 The far portion of a clamshell polyp may be difficult to lasso with the snare. This can be accomplished by pushing on the freshly resected polyp base. Depressing this surface with the sheath may elevate the proximal portion into the opened snare.

that occurs, the polyp flattened against the stretched wall will become thicker and more elevated, rendering capture relatively easy so that piecemeal-type resection may be performed. Alternate possibilities include submucosal injection of fluid to elevate the polyp for safer transection and use of a two-channel colonoscope where a forceps can be passed through one channel to grasp the polyp over which the opened snare has been positioned. Once the forceps lifts up the polyp, the snare is tightened to capture the polyp.

Fig. 36.14 Retroflexed resection technique. (a) The polyp is in the upper rectum. (b) To achieve better access, epinephrine (1 : 20 000) is injected submucosally.



(a)

Residual fragments of adenoma after polypectomy

Often the base of a large polyp which was resected in piecemeal fashion has some residual adenomatous tissue at the edge or in the middle of the polypectomy site. If residual tissue is seen at the base, there will be adenomatous tissue at that site on follow-up colonoscopy. The site of polyp resection heals concentrically, from the edges toward the center, so that usually only one polypoid excrescence will be present upon complete healing of the site, whether or not several small islands of adenoma remained at the periphery of the initial resection base. If the polypectomy was adequate, the residual polyp will be smaller than the original size of the polyp, and can be easily removed. The application of thermal energy to the fragments of adenoma remaining at the base and edges of a fresh polypectomy site can reduce the incidence of residual polyp (Fig. 36.15). This has been studied with the argon plasma coagulator (APC), with reduction of adenoma on follow-



(b)

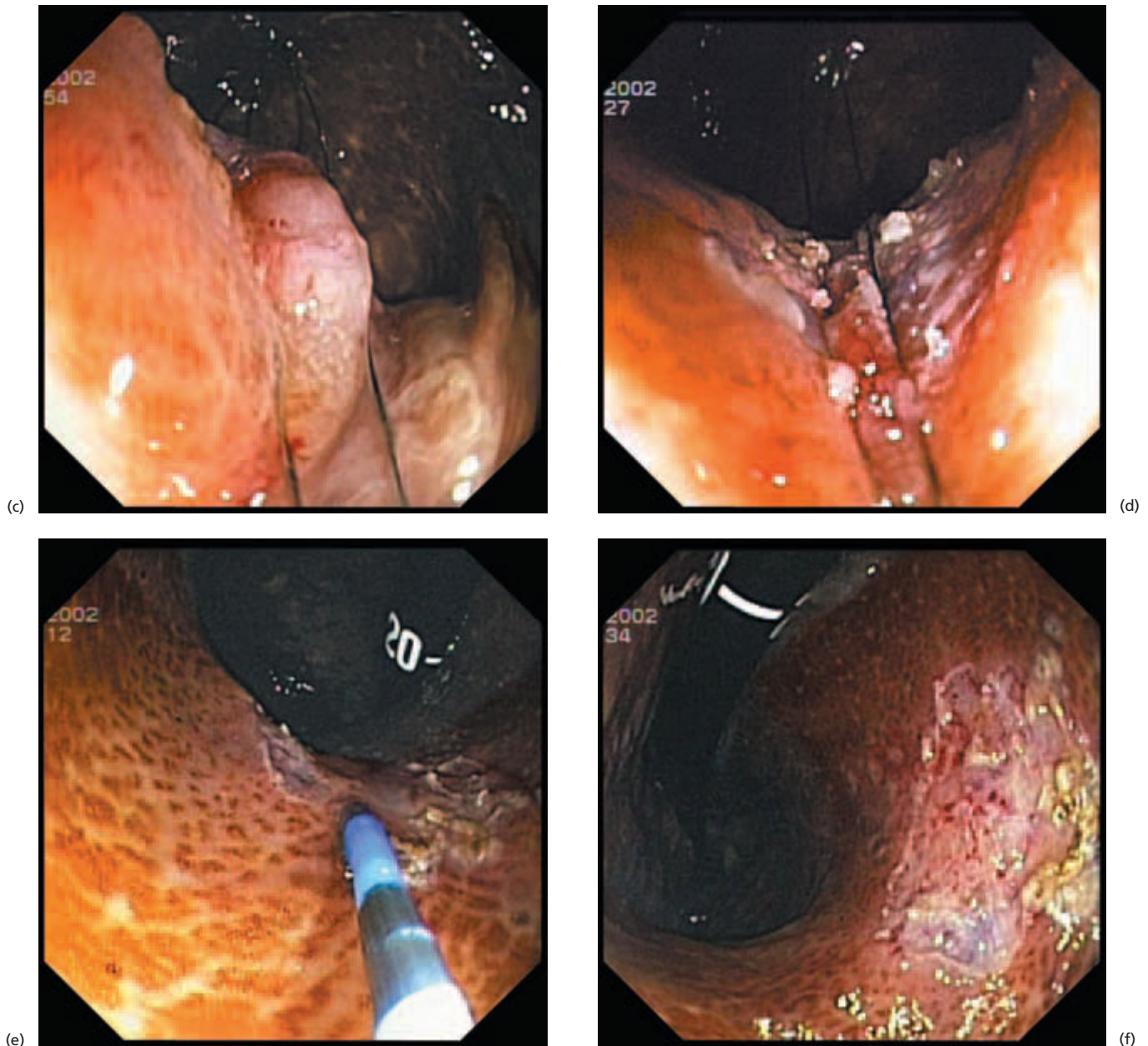


Fig. 36.14 (*cont'd*) (c) Piecemeal resection starts from the front part of the polyp. (d) Remaining parts of the polyp are removed in retroflexed position. (e) APC is used to remove the adenomatous remnants at the proximal margin. (f) Final result after polypectomy.

up from 100% to 50% when residual tissue at the fresh base is destroyed [36,37].

Location of lesion in the colon

There are several reasons to mark an area of the colon for future localization. Most of the time, the endoscopist desires to have a precise identification of the site where

a polyp was removed. When large polyps are resected in piecemeal fashion, even though the endoscopist considered that it was totally removed, there is a strong possibility that residual adenoma will be present at a follow-up examination. It may be difficult to find the exact place where a polyp was removed, as the initial placement of the site was wrong, the scar is behind a fold, or the residual is small. Of equal importance is the knowledge that the polyp was indeed completely resected at the original session, and the site can be declared free of residual adenoma.

Now that laparoscopic-assisted surgical colonic resection is becoming as well accepted as primary colonoscopy, there is even greater urgency to have precise

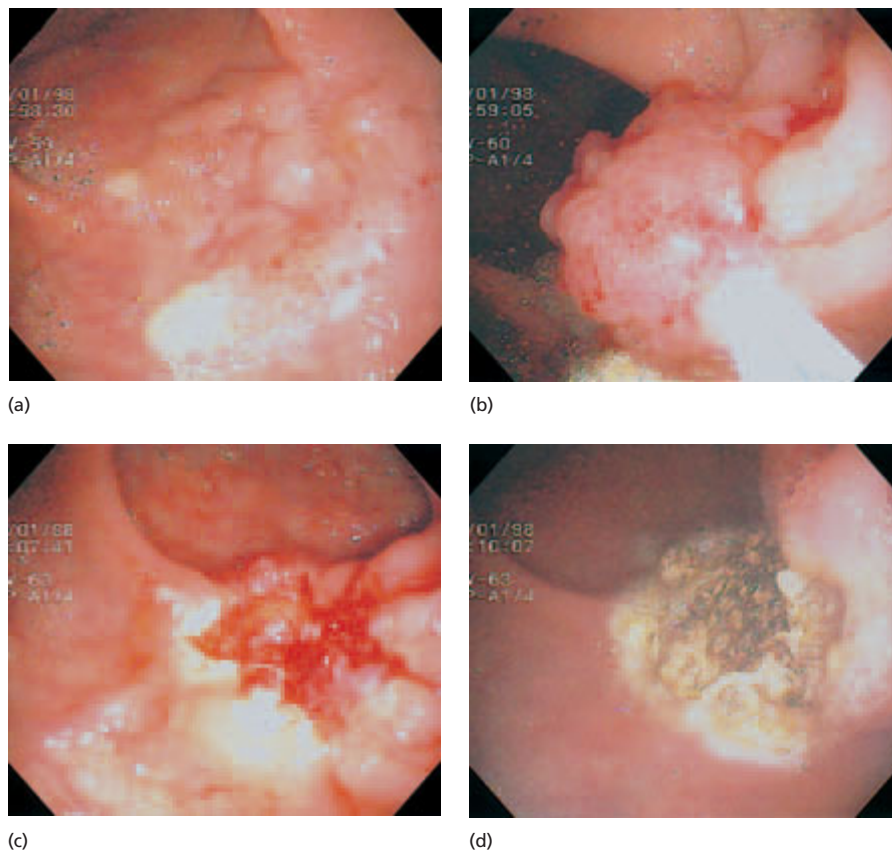


Fig. 36.15 (a) A “mountain” polyp with a broad base was elevated by the injection of saline and removed in one piece (b). The base had some residual adenomatous fragments (c) which were fulgurated with the argon plasma coagulator (d).

lesion location, since the laparoscopist does not have the capability of palpating the colon between the fingers at exploratory laparotomy [38]. For the laparoscopist, it is of great importance to have an easily visible marker which can be seen through the telescopic lens of the laparoscope. It is not acceptable for the endoscopist to state that “a lesion is in the transverse colon,” since a more specific localization is needed to avoid a subsequent open surgery to find the lesion.

Healing of polypectomy site

Even under circumstances when open laparotomy is to be performed, site identification becomes necessary when a specific portion of the large bowel requires resection and the lesion may not be readily apparent by visual or palpatory exploration. Following endoscopic removal of a malignant adenoma, the site may heal completely in 8 weeks, and a locator mark may assist both the surgeon and the pathologist in identifying the place where the lesion had been.

Localization by number of centimeters inserted

Localization by measurement of centimeters of instrument introduced into the rectum is an extremely poor method for tip localization [39]. During introduction of

the instrument, when loops are common, it is possible to advance the full length of a long colonoscope (180 cm) into the rectum, yet the tip may still be at the sigmoid/descending colon junction [40]. However, it is possible, by repositioning the instrument, removal of loops, and straightening, to reach the cecum in that same patient with a total length of only 60 cm of instrument. The actual number of centimeters inserted may bear no relationship with the actual tip location within the colon [41].

A report from a previous examiner that “a polyp was found at 100 cm” is meaningless for surgical localization. With the current knowledge of intraluminal landmarks—the splenic flexure, transverse colon, hepatic flexure—it is much better to identify the approximate area of the lesion. During withdrawal, there is usually a good correlation between length of scope inserted and tip localization since the loops are removed and the instrument is straightened. It is usual, on withdrawal, to have the splenic flexure at 40–50 cm and the upper sigmoid at 30–35 cm. Because of sigmoid looping, shaft measurements during withdrawal are not usually helpful until the splenic flexure has been reached.

Endoscopic landmarks

Landmarks are notoriously imprecise for exact localization of areas between the rectum and cecum. Even the

most experienced colonoscopists may err in their estimate of tip location [38,40,42]. Indeed, in a large tortuous sigmoid colon, it may be difficult to localize a lesion to even the mid- or upper-sigmoid colon. Similarly, a lesion estimated by the endoscopist to be near the splenic flexure may be under the diaphragm, could be either proximal or distal to the flexure, or may even be actually located at the sigmoid descending colon junction. Precise location may be impossible because of tortuosity and multiple bends in that area of the colon. The only invariable localizing landmarks are when a lesion is located within 15 cm of the anus, there is no doubt that it is close to or in the rectum, and a lesion near the endoscopically identified ileocecal valve can be easily found by the surgeon. The problem in the latter case revolves about the endoscopist's ability to recognize beyond a doubt that the cecum was indeed reached.

Clips

Clips may be placed through the colonoscope and onto the mucosa at any location. These will assist in radiographic or ultrasonographic location of the marked segment. However, clips tend to fall off at an average of approximately 10 days [43], with some falling off earlier and some maintaining their attachment for longer intervals. Although it has been suggested that clips may be a helpful marker for surgical localization, it has been found that the clip devices are quite small to be palpated easily. In addition, the surgeon cannot be assured that a palpable clip had not been spontaneously detached just prior to surgery and is at some distance from the original placement during endoscopy. If, indeed, a surgeon palpates a clip in the sigmoid colon and resects that segment, it is possible that the clip actually had been placed at a location near the splenic flexure, had become detached, and migrated distally. A report of eight patients with prelaparoscopic clip placement by colonoscopy stated that intraoperative ultrasound readily located the marked areas for surgical resection [44].

Barium enema

The barium enema is still an acceptable method for determining the location of polyps or cancers [41] but small lesions may not be readily identified on the barium enema X-ray examination. Certainly, if a malignant polyp were endoscopically resected, it may be extremely difficult to then try to locate the area where the polyp was removed, since only a small puckering may be present [41,45] or the site may be almost completely healed within 3 weeks.

During colonoscopy in a suite where radiographic imaging is possible, either fluoroscopy or an X-ray of the

abdomen during endoscopy may assist in locating the site of a lesion. Unfortunately, it may be difficult, with the instrument in a straightened configuration, to state that the tip of the colonoscope is in the distal descending colon or in the midportion of a long redundant sigmoid loop.

Magnetic imaging (see Chapter 24)

New methods of inductive sensing with a low-intensity magnetic field may aid in the moment-to-moment localization of the tip of the fiberoptic colonoscope as it progresses through the colon. The magnetic sensors are attracted to electromagnets within the sheath of the colonoscope (or on a wand-like device inserted into the biopsy channel) [46,47]. These methods have replaced such devices as metal detectors for localization of the instrument tip [48]. Unlike a fluoroscopic image which demonstrates both the scope and air in the colon as a contrast media, the electromagnetic field method only shows the colonoscope itself, but is capable of a three-dimensional format. This technique may be of benefit in localizing the site of a colonic tumor or polyp [49].

Intraoperative colonoscopy

It is possible to localize the site of a tumor, or a resected polypectomy site, by performing intraoperative colonoscopy [50,51]. This technique has been avoided by most endoscopists because of the need to perform an endoscopic examination in the operating room with all the constraints of positioning the patient, handling the scope, and trying to use maneuvers such as torque and straightening techniques with the abdomen open. The amount of air insufflated for colonoscopy can create problems with surgical techniques once the endoscopist has completed the necessary localization. Because the site of a polypectomy may heal within a few weeks, there is a possibility that a polypectomy site may not be seen during an intraoperative endoscopy. Lesion identification can also be accomplished by colonoscopy and submucosal injection of radioactive-labeled albumin microaggregates [52] just prior to surgery. The surgeon can localize the precise area with detection by a gamma probe during laparotomy or laparoscopy.

Marker injections into the colon wall

The ideal method for lesion localization is to have an easily identifiable marker which will immediately draw the attention of the surgeon or endoscopist [42]. This can be achieved with injection of dye solutions. An experimental study demonstrated that of eight different dyes injected into the colon wall in experimental animals, only two persisted for more than 24 h [53]. These

were indocyanine green and India ink. The indocyanine green was visible up to 7 days after injection, and it is known that India ink is a permanent marker which lasts for the life of the patient by virtue of submucosal injection of carbon particles. Other dyes, such as methylene blue, indigo carmine, toluidine blue, lymphazurine, and hematoxylin and eosin, were all absorbed within 24 h, leaving no residual stain at the injection site. Indocyanine green is approved by the Food and Drug Administration (FDA) for human use, but India ink has not been so approved. A new surgical marker has been FDA approved, and consists of pure carbon in suspension. It is marketed as a prediluted sterile compound in preloaded syringe [54].

Indocyanine green

Indocyanine green is not associated with any significant tissue reaction, and is relatively nontoxic, but ulceration of the injection sites have been reported in an animal model [53,55]. Clinical experience with indocyanine green tattoo in 12 patients demonstrated that the dye was easily visualized on the serosal surface of the colon at surgery within 36 h following injection [56] and may remain visible for up to 7 days [53]. Animal experimental models have shown that the dye was not visible after 1 day [55] or lasted up to 2 weeks [57]. The problem with a marker having such a relatively short visible span is that the decision to operate after removal of a malignant polyp may require a few weeks, with slide reviews and multiple consultations. An injection at the time of polypectomy will have disappeared whereas the site itself may become more difficult to localize with the passage of time.

India ink

Most experience with dye injection technique has been accumulated with India ink as a permanent marker [58,59]. The stain lasts for at least 10 years with no diminution in intensity at that duration. A permanent marker may be worthwhile for several reasons. A lesion requiring surgery may be injected and, for clinical reasons, surgery may be postponed for several weeks, at which time a vital dye such as indocyanine green will have been absorbed, leaving the operating surgeon with no visible evidence of its having been injected. Sometimes it is desirable to mark the site of a resected polyp for subsequent endoscopic localization when it is anticipated that the area will be difficult to find on a follow-up examination, especially when the lesion is located around a fold or behind a haustral septum. A stain with a permanent marker such as India ink will draw immediate attention to the site, enabling a more accurate and complete assessment. For the surgeon, a

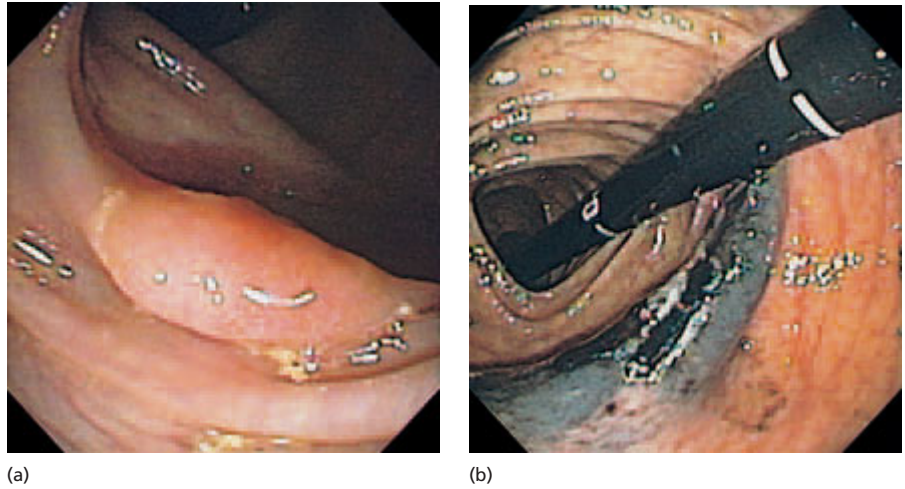
locator stain will aid immeasurably the efforts to seek and resect an area of the bowel containing the site of the lesion. When the lesion is relatively small, such as a flat cancer or a previously endoscopically resected malignant polyp which requires surgical resection, the site may not be evident from the serosal surface and may not even be palpable. If the area to be resected is in a redundant sigmoid colon or near the splenic flexure, it may be impossible to locate by either visual means or by palpation. Occasionally, even large lesions may not be palpable by the surgeon if they are soft and compressible [60]. As previously mentioned, visible marking can assist in precise surgical intervention for laparoscopic-assisted colon resections, or clips may be detected by an ultrasound probe.

There have been reported complications with India ink injection, but clinical symptoms resulting from the injection are relatively rare [61,62]. Tissue inflammation has been reported in an animal model [55]. The complications may in part be related to the wide variety of organic and inorganic compounds contained in the ink solution, such as carriers, stabilizers, binders, and fungicides [63]. It is possible that the toxic properties of India ink may be partially ameliorated by marked dilution of the ink. Ink diluted to 1 : 100 with saline produces as dark a spectrophotometric pattern as undiluted India ink, and in clinical tests, the tattoo made by 1 : 100 diluted India ink is readily visible by the endoscopist and by the operating surgeon. A small-volume injection (0.5 mL) may increase the safety of the procedure [55,64].

India ink is black drawing ink made with carbon particles. Permanent fountain pen ink is not an acceptable substitute. India ink is available from any stationery store, although it is supplied for medical use in non-sterile form as a stain to enhance the diagnosis of cryptococcosis in the cerebrospinal fluid. The India ink may be sterilized in an autoclave following dilution or can be rendered bacteriologically sterile by passing the diluted solution through a 0.22- μ m Millipore filter which is interposed between the syringe containing the dilute solution of India ink and the injection needle [65]. The preparation of India ink prior to injection is not required because of a new compound of sterile micronized carbon particles [54].

A standard sclerotherapy needle is utilized of sufficient length to traverse the accessory channel of a 168-cm colonoscope, and stiff enough so that the plastic sheath will not crinkle up as it is being forced through the biopsy port when the tip of the instrument is deep in the colon and the colonoscope shaft has several convolutions and loops. Ideally, the needle should enter the mucosa at an angle to permit injections into the submucosa, rather than to have the needle pierce the bowel wall. The edges of intrahaustral folds should be targeted (Fig. 36.16). If during an injection a submucosal bleb is

Fig. 36.16 The distal portion of a “clamshell” polyp (a) was resected, but total removal required retroversion (b), which also shows the injection of a permanent surgical marker so the site can be identified at the follow-up examination.



not immediately seen, the needle should be pulled back slightly, since the needle tip may have penetrated the full thickness of the wall and the ink may be squirting into the peritoneal cavity. An intracavity injection is not a clinical problem [45,46], but can scatter black carbon particles around the abdominal cavity, which may be somewhat disconcerting for the surgeon. A prior submucosal

injection of saline may aid the colonoscopist in depositing the carbon suspension in that layer, without risk of injecting either deep or superficial (Fig. 36.17) [66].

Since the colonoscopist cannot know which portion of the bowel is the superior aspect, multiple injections should be made circumferentially in the wall around a lesion to prevent a single injection site from being

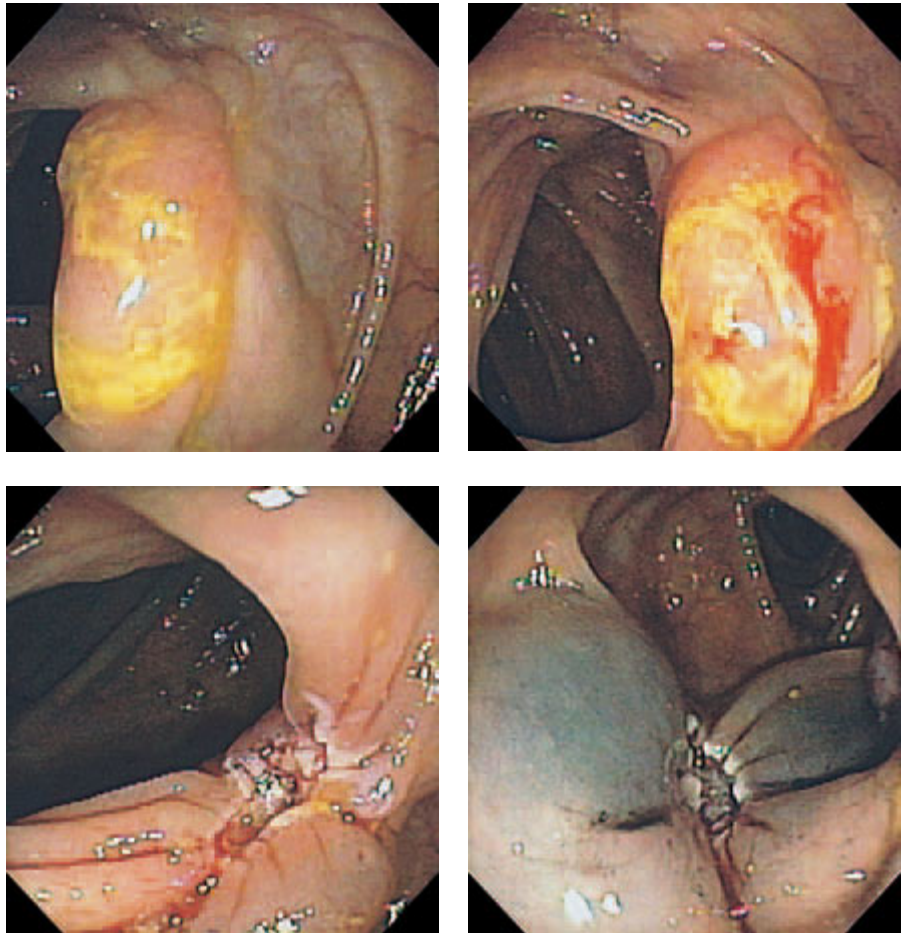


Fig. 36.17 Sessile polyp resected after submucosal injection of saline. The surgical marker was injected into the submucosal blebs to facilitate delivery into the correct plane.



Fig. 36.18 Stain of surgical marker at 8-year follow-up postpolypectomy. The scar is visible between two injection sites.

located in a “sanctuary” site, hidden from the surgeon as the abdomen is opened with the patient lying supine [67]. Each injection should be of sufficient volume to raise a bluish-black bleb within the submucosa at the injection site. The injection volume may vary from 0.1 to 0.5 mL. If injections are made a few centimeters from the lesion, the surgeon should be informed whether the injections are proximal or distal to the site. With the proper dilution of India ink, endoscopic visualization is still possible should some of the ink spill into the lumen, whereas with the more concentrated solutions, the endoscopic picture becomes totally black when ink covers the bowel walls [45].

Most endoscopists who use India ink to mark colonic lesions do not prescribe antibiotics prior to its use, although it has been suggested that prophylactic antibiotics be given before injections of indocyanine green [56].

Injection of carbon particles provides a permanent marker, with endoscopic visualization of the tattoo site being possible in every case on follow-up examination without diminution in color up to an interval of 10 years following initial injection (Fig. 36.18). Several reports have attested as to its safety as well as its efficacy [61,68,69].

The extremely difficult colonoscopy

If passage to the right colon has been arduous and prolonged, with the discovery of a large sessile polyp having a broad attachment that would require several attempts at piecemeal polypectomy, the wisest approach may be to suggest surgical resection to avoid the necessity for repeated difficult colonoscopies with repeated

difficult polypectomies. The risk–benefit ratio will depend on the location of the polyp: the right colon is somewhat thinner than the left, increasing the risk of colonoscopic removal. In patients with limited physiological reserves, there may be unacceptable risks associated with surgical laparotomy and colon resection.

The advent of laparoscopic-assisted partial colectomy may markedly change the attitude of adventurous colonoscopists who attempt removal of large polyps [70]. The ease of laparoscopic resection may make a significant difference in the willingness of the patient and endoscopist to embark on the repetitive number of colonoscopies required to ablate a right colon polyp. Both the risks and benefits of an aggressive endoscopic approach will need to be reevaluated.

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Chapter 37

Retrieval of Colonic Polyps

Bennett E. Roth

Introduction

The detection and removal of colon polyps is the most significant benefit colonoscopy provides toward the reduction of colorectal cancer mortality and morbidity [1]. All polyps encountered during colonoscopy should be removed and evaluated histologically. In so doing, those which are neoplastic and indicative of the need for further surveillance as well as those that may contain malignancy can be identified. In order to accomplish this, all removed polyps should be retrieved. The limited published data on polyp retrieval suggests failure rates ranging from 2.1 to 16.5% [2–4]. Difficulties are most often encountered when attempting to retrieve small polyps, those in the right colon, when performing piecemeal polypectomy, or in the presence of excessive quantities of stool and fluid in the colon. Portions of polyps as well as intact specimens may be lost in fluid or behind folds or significantly damaged in the act of retrieval. In an effort to enhance success rates, a variety of techniques and devices to enhance retrieval have been developed. The published literature is limited with regard to comparative studies. The two major factors that determine how polyps are retrieved are related to their size and the method used for resection. This chapter discusses retrieval techniques and describes available devices.

Small polyps

There are several options for removal of small polyps (< 6 mm). For those removed with hot or cold biopsy forceps, the tissue will be embedded within the device and is inherently retrieved when the device is removed from the colonoscope. However, when small polyps are removed with a snare they often drop into the colonic lumen and must be retrieved. One of the more frustrating experiences for an endoscopist is to have a small polyp disappear from sight and not be readily found. This can result from polyps lodging behind haustral folds or in fluid reservoirs. It is at times difficult to determine in what direction gravity will take such a polyp. A maneuver that will aid in directing the search employs the injection of water through the biopsy channel and observation of the flow of fluid from the colonoscope tip.

In so doing, one can anticipate where the polyps may have fallen [3]. If a jet of water is seen, the scope should be advanced to the first liquid pool. Conversely, if vision becomes blurred, water is flowing over the lens indicating that the tip is pointing toward the ceiling and water is cascading along the scope shaft. Withdrawal of the scope to the first pool of fluid will usually visualize the polyp. Other aids in locating the disappearing polyp include changing the patient's position and retroflexion of the instrument.

Small polyps may be recovered in a variety of ways. Probably the most common technique employs the use of suction into a retrieval reservoir. It is wise to attach a small specimen trap in the suction line to avoid losing the polyp in the larger fluid collection container. A simple collection bottle placed between the suction nipple (where the umbilicus is plugged into the light source) and the vacuum line enables quick and inexpensive specimen retrieval. Alternatively, a dedicated and purpose-designed specimen collection trap can be used. This has four separate chambers that can be accessed by rotation of the jar (Fig. 37.1), which permits identification of several polyps by site of extraction. However, if there are several small polyps within the same segment of the colon, the need for site localization is minimal. If polyps are retrieved into a single compartment bottle, they are separated from the fluid by emptying the container through a gauze or mesh strainer [5–7].

Another technique for suction retrieval of small polyps uses either cotton gauze or plastic mesh placed over the open end of the instrument suction port. By removal of the valve cap, the polyp will usually be suctioned through this access site and be trapped within the gauze or mesh. Polyps may adhere to the cotton gauze causing difficulty in removal, with resultant tissue damage. It is for this reason that mesh is superior for this technique [8,9]. Even with this makeshift filter, it is wise to attach a small suction container in the event the polyp passes through the filter and traverses the umbilical cable toward the large fluid reservoir. It is important to avoid excessive suction pressure when retrieving polyps. This might produce fragmentation and/or distortion of the tissue, hindering accurate histologic evaluation. While this admonition is important for all suction retrieval



Fig. 37.1 Multicompartment specimen retrieval jar.

attempts, it is obviously more vital with larger polyps where accurate histologic interpretation is of potentially greater importance. Polyps can be removed during the insertion of the instrument or subsequent to intubation of the cecum. If accomplished during insertion and the polyp is large, the scope may have to be removed and reinserted for its retrieval or a plan must be made to seek and remove the specimen during the withdrawal phase. When small polyps are retrieved via suctioning, the timing of polyp removal during the procedure is not an issue.

Large polyps

The retrieval of larger polyps (> 6 mm) is dependent upon size, location, and method of resection. Large polyps encountered in the rectosigmoid are often resected and removed during the insertion phase of the procedure. This is especially helpful if the polyp is encountered in an ideal position, is quite large, and subject to excessive trauma from the instrument shaft during the procedure. For polyps removed *in toto* following snare resection, the snare may be employed to regrasp the polyp with subsequent removal of the scope. The snare must be closed to maintain sufficient grip on the tissue so as not to lose it during retrieval. However, care must be taken not to close the snare too tightly, resulting in transection of the polyp. Alternatively, these polyps may be quickly removed by suctioning snugly to the scope tip. This

blinds the endoscopist's vision of the bowel as the scope is withdrawn, but is a reasonable option because the scope will be reinserted and that portion of the distal bowel will be seen subsequently. When suctioning polyps with a diameter less than 1–1.5 cm, a retrieval trap is recommended since they may be suctioned through the channel and into the larger suction container. To overcome this, stronger suctioning may be applied by removal of the valve over the suction port and covering the well with a finger. An alternative is to place the suction tube, which is usually applied to the nipple on the umbilical cord, directly over this well. If this is done with polyps less than 1.5 cm in size, the use of gauze or mesh over the port is recommended in the event the polyp is suctioned up by the strong negative pressure. For those instances in which a polyp is repeatedly dislodged during suction retrieval, the use of a snare or alternate retrieval device is recommended.

Most endoscopists prefer removing polyps after full insertion of the colonoscope. This permits evaluation of the entire colon so as to ascertain whether significant pathology is present beyond the sited polyp. However, since it is not uncommon for polyps to “appear” during removal of the instrument (i.e. were not identified during intubation), it is essential that the colonic mucosa be carefully inspected during withdrawal of the shaft (see Chapter 30). Since vision is limited or absent during suction retrieval of large polyps, this technique is not recommended when polyps are resected above the sigmoid colon unless the commitment is made to reinsert the scope. In most instances, retrieval devices or snares are recommended.

Retrieval devices

There are a variety of retrieval devices on the market (Fig. 37.2). These include pronged grasping forceps, baskets, and nets. Pronged forceps and baskets are manufactured by several companies and are produced both as single-use and reusable devices, with prices ranging from \$45 to \$430. Nets are currently available from only one manufacturer as single-use devices at a cost of \$75–95. All these devices are designed to facilitate the secure atraumatic removal of polypoid tissue without sacrificing visualization of the remaining colonic mucosa [10]. Many of these devices are used in both the colon and upper digestive tract for polyp retrieval as well as foreign body removal.

The essential rule to follow when using a retrieval device is to securely grasp the polyp while avoiding tissue injury or destruction. Following polyp resection, redeployment of the snare to grasp and retrieve the tissue is the most common maneuver used in most instances. It is both time and cost efficient. However, when retrieving tissue through angulated colons or around folds it

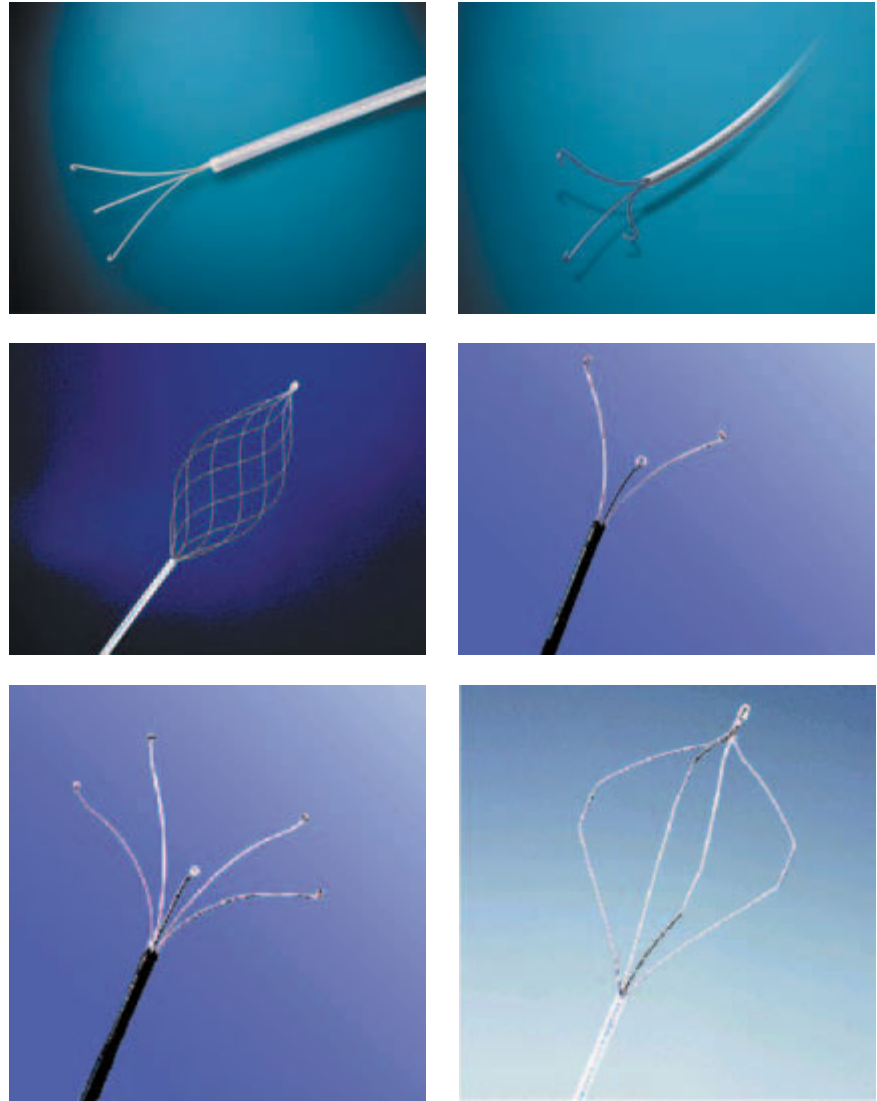


Fig. 37.2 Retrieval devices. (Courtesy of Olympus Corporation of America, Boston Scientific/Microvasive, Wilson Cook Medical, Inc.)

is not unusual for polyps to slip from the grasp of the snare or be transected by the snare wire during attempts to pull the polyp through the narrow and tortuous sigmoid colon. The snare with the captured polyp can be pushed forward to allow sufficient field of view for inspecting the remaining mucosa during withdrawal. This same technique is recommended for all retrieval devices. Multipronged grasping forceps are produced in three- and five-pronged versions. The tips of the prongs are curved inward, facilitating a firmer grasp on the tissue. Grasping forceps are effective for withdrawing polyps 1–1.5 cm in size. However, some difficulty may occur when retrieving these or larger polyps with this method due to insufficient grasping strength. A basket or net provides a more secure hold without risking damage to the tissue. The size of the polyp will determine whether a Dormia-type basket retriever can be used. Basket-retrieval devices come in varying designs:

they may be helical shaped with several wires or a simple four-strut device. While some baskets open to 3 cm diameter, the space between struts limits the size of polyp that can be grasped. By gently pressing the forward tip of the basket against the colonic wall, the struts can be flexed and separated permitting entrapment of larger polyps. However, difficulty may be encountered in retrieving polyps larger than 2 cm. The baskets can be opened and redeployed to regrasp several polyps or pieces of a large polyp without removal of the colonoscope. However, care must be taken to avoid dislodging of previously collected tissue when, during attempts to retrieve more tissue, the wires are flexed to increase the space between struts.

Mesh retrieval baskets

The Roth retrieval net has become a popular device for capturing large polyps or the fragments produced



Fig. 37.3 Roth retrieval net. (Courtesy of US Endoscopy, Mentor, Ohio.)

during piecemeal polypectomy. The net consists of a braided cotton filament mesh secured around a snare wire housed within a catheter sheath (Fig. 37.3). The net can open to a diameter of 2.5–3 cm and be easily reopened and used to grasp additional polyps or pieces without scope removal. It provides a secure grasp upon the tissue without risk of damage. When employing the net, the catheter should be advanced to the site of the resected polyp or fragment. Capture is easier if the specimen to be retrieved is at the lower portion of the visual field (6 o'clock). The net should be expanded slowly and placed over the tissue. With slight advancement of the catheter exerting gentle pressure toward the colonic wall, the net is slowly closed during which the tissue is trapped (Fig. 37.4). If additional tissue is to be captured, the procedure can be repeated without risk of losing the previous specimen since the surface of resected tissue becomes entrapped in the net material. Caution must be exercised when deploying the net to avoid turning the tip in the opposite direction, potentially everting the net and forcing the first specimen out [11]. Following withdrawal of the colonoscope and the polyp-laden net, the tissue is manually separated from the mesh.

The Nakao snare is an alternate version of the net, consisting of a combination polypectomy snare and retrieval

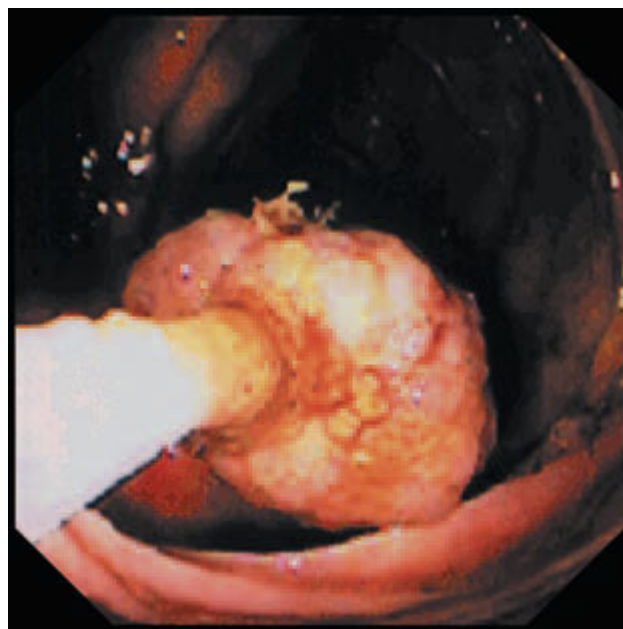


Fig. 37.4 Polyp in net. (Courtesy of US Endoscopy, Mentor, Ohio.)



Fig. 37.5 Nakao snare and retrieval net contained within one sheath. (Courtesy of US Endoscopy, Mentor, Ohio.)

net. This double-lumen device permits resection of a polyp and subsequent deployment of a retrieval net without removal of the catheter. It is twin-handled and has a catheter diameter of 3 mm (Fig. 37.5). Therefore, its use requires an instrument with a significant channel size [2].

Summary

Histologic tissue identification is the only accurate method by which an endoscopically removed polyp can be classified. The histopathologist will determine the degree of dysplasia, whether cancer is present and, if so, the criteria needed to decide if surgery is necessary or whether endoscopic follow-up is advised. The microscopic examination of tissue is based on retrieval of tissue fragments during the colonoscopic examination. Several methods are described, and the endoscopist must strive to collect all of the resected tissue, even if piecemeal techniques are employed.

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Chapter 38

Management of Malignant Polyps

Sidney J. Winawer and Michael J. O'Brien

Introduction

"Malignant polyp" is a term used when a polyp removed by colonoscopy appears grossly benign but has adenocarcinoma identified histologically (Fig. 38.1). The clinical issues in this setting are more difficult than in a patient who has had a surgical resection because of a large sessile polyp or suspected malignancy, where a surgical specimen and adjacent lymph nodes are available for staging. The management of patients with malignant polyps has assumed increased importance in recent years as a result of more widespread screening in the general population, and especially with the introduction of colonoscopy as a screening option [1,2]. A decision must be made in each of these patients whether to consider the colonoscopic polypectomy curative or refer the patient for surgery. This decision is compounded when an asymptomatic person has been induced to have a screening test that uncovers the unsuspected pathology. Management decisions require an

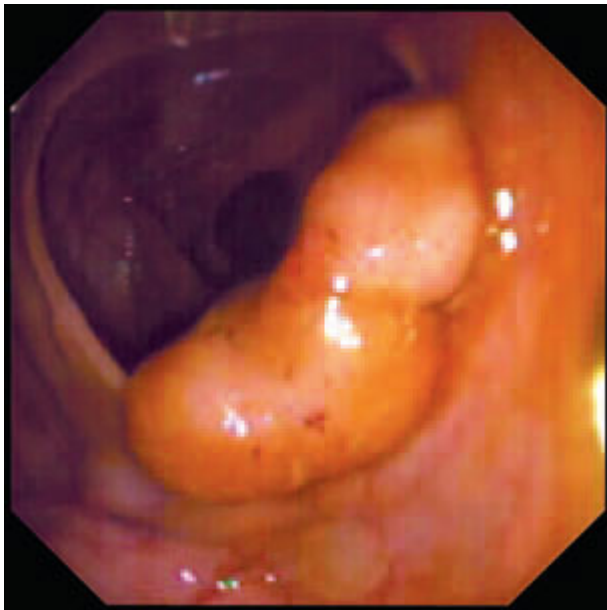


Fig. 38.1 Endoscopic photo of a large benign-appearing sessile polyp in the ascending colon that had early invasive cancer histologically.

assessment of the pathology, risk of adverse outcome, risk of surgery and colonoscopic follow-up, and the available surgical options. There are additional considerations in high-risk patients, e.g. those with a family history suggesting hereditary nonpolyposis colorectal cancer (HNPCC), long-standing inflammatory bowel disease, and familial polyposis. This chapter deals primarily with the average risk patient.

Pathology

Malignant polyps are adenomas with adenocarcinoma that has invaded beyond the muscularis mucosa (Fig. 38.2). The cancer cells have thus gained access to the submucosa, which contains lymphatics and blood vessels that can permit spread to adjacent lymph nodes and less commonly to distant organs. Spread to the deeper layers of the colonic wall can also occur by direct extension. In pedunculated adenomas, the submucosa is in continuity with the core of the stalk and head of the polyp. In sessile adenomas, invasive carcinoma is directly into the submucosa of the bowel wall. "Intramucosal carcinoma" is a term used to describe invasion of cells through the basement membrane of the crypts into the lamina propria of the surrounding mucosa but with no penetration into or through the muscularis mucosa into the submucosa. There is therefore no opportunity for regional or distant spread and there is no clinical significance regarding the initial management of the patient. The older term "carcinoma *in situ*" has now been replaced by the term "high-grade dysplasia," which also includes severe dysplasia. The pathologic diagnosis of high-grade dysplasia also has no clinical significance in terms of the initial management of the patient. All adenomatous polyps have at least low-grade dysplasia, which incorporates mild and moderate dysplasia [1,2].

Accurate assessment of the resected polyp is required for rational clinical decision-making. Every effort must be made to retrieve the entire specimen for examination and classification. This is easier for pedunculated polyps than for large sessile polyps that are removed in piecemeal fashion. Saline injection to provide a cushion of normal mucosa under a sessile polyp can greatly aid in the completeness of removal. An attempt should be

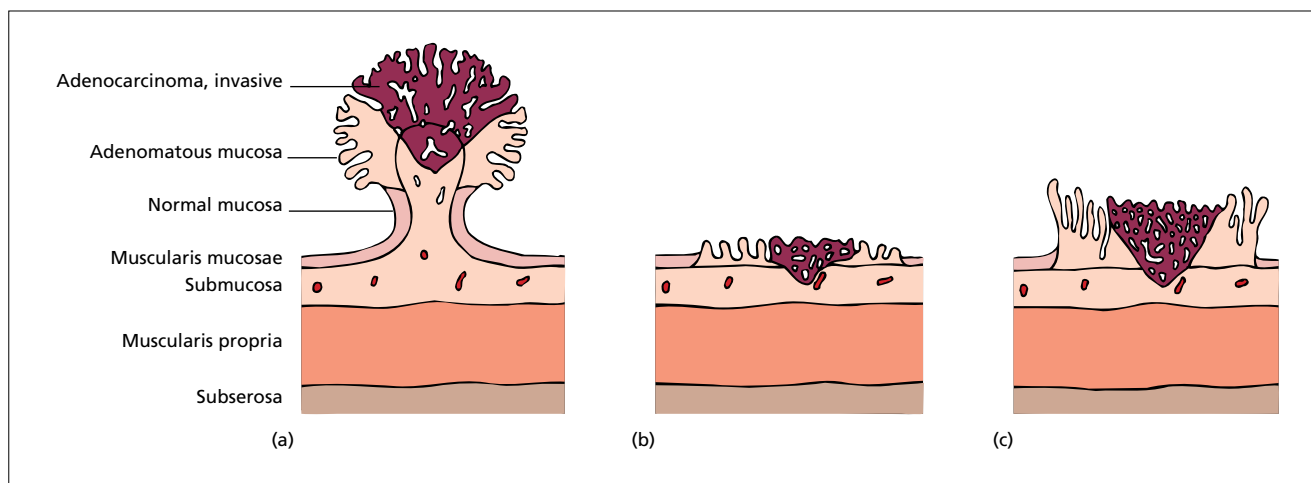


Fig. 38.2 Malignant polyp variants. (a) Pedunculated malignant polyp with invasion in the submucosa of the polypoid adenoma head. (b) Adenocarcinoma arising in a flat adenoma and invading the submucosa. (c) Sessile malignant polyp with adenocarcinoma invading the submucosa.

made to identify the base of the polyp. Contraction of the muscularis mucosa after resection may cause a specimen to curl into a ball, making subsequent identification of the resected site difficult. To avoid this, sessile polyps can be placed flat on a piece of cardboard or thick paper, on absorbable gelatin sponge (Gelfoam), or on a frosted glass slide before insertion into fixative. Histologic sections are made from stepwise sagittal blocks of the entire polyp, taking care to represent the stalk and polyp resection margin. When invasive adenocarcinoma is identified, the report should include the grade of differentiation of the carcinoma, lymphatic or vascular space invasion, volume of polyp replaced by carcinoma, depth of invasion, and proximity to resection margin. Pseudo-invasion with adenoma misplaced into the stalk or submucosa should be distinguished from true invasion (Fig. 38.3). Reporting should include whether there is adenomatous tissue at the resection margin and whether there is cancer at the margin to indicate the completeness of the removal histologically.

Risk factors for malignant polyps

The frequency of finding malignant polyps was 1.5% in the National Polyp Study, a multicenter study with a database of approximately 5000 polyps removed in 2000 patients [3] (Fig. 38.4). These patients were mostly average-risk men and women. In recently reported screening colonoscopy studies, approximately 10% of asymptomatic average-risk people had advanced neoplasia including 1% with malignant adenomas [4]. The vast majority of adenomas removed in these studies



Fig. 38.3 Pedunculated polyp showing pseudo-invasion of stalk. Glands are present in the submucosa of the polyp head and stalk deep to the muscularis mucosae. The glands are associated with stroma identical to adenoma mucosal stroma, and distinct from the fibrous stroma characteristic of invasive adenocarcinoma. The dysplasia of the glandular elements in the stalk in pseudo-invasion may be low or high grade (in this case, low grade). Other features that suggest pseudo-invasion include hemosiderin deposits and pools of acellular mucin. Pseudo-invasion is likely to represent a manifestation of polyp prolapse and is seldom if ever encountered in sessile or flat adenomas.

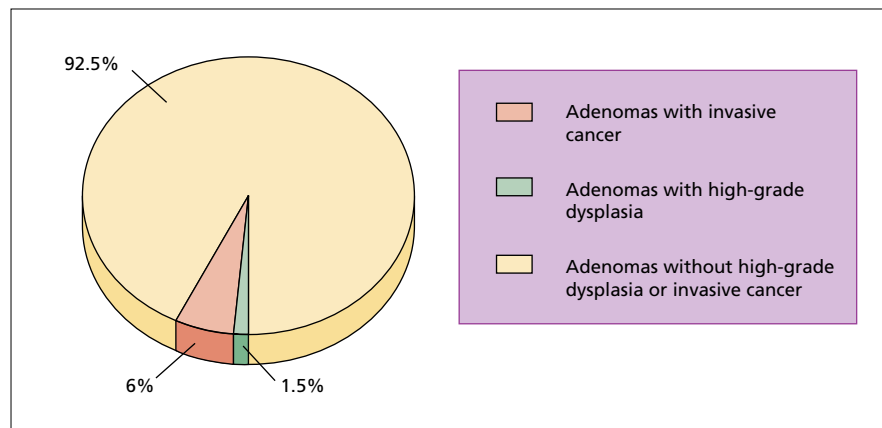


Fig. 38.4 Relative frequency of a finding of high-grade dysplasia or invasive carcinoma in an adenoma resected at colonoscopy.

were benign. It has been estimated that only 0.25% of adenomas will demonstrate conversion to malignancy each year [5].

Analysis of the National Polyp Study database has confirmed that polyp size is a major determinant of the likelihood that high-grade dysplasia will be found in a colorectal adenoma. The amount of villous growth in the adenoma is also an independent determinant of this risk, with an effect of comparable magnitude to that of size. Furthermore, the effects of size and villous component have been found to be multiplicative, i.e. their combined effect is greater than the sum of their individual effects. Frequency of high-grade dysplasia in adenomas is unrelated to gender of the patient, according to the National Polyp Study data analysis, but logically appears to increase significantly with advancing age. When a patient has multiple adenomas, which will

be the case in almost 50% of the adenoma-bearing population, the patient’s risk of harboring an adenoma with high-grade dysplasia is proportionately increased, although this increased risk from multiplicity appears to be dependent on the associated factors of size and villous component [3].

Increased polyp size, villous histology, and severe dysplasia are all associated with an increased risk of cancer in adenoma (Fig. 38.5). Reports from the pathology laboratory, in the years before colonoscopic polypectomy was introduced, also demonstrated (in surgically resected specimens) the relation of lesion size and dysplasia grade with the probability of malignancy [6–8]. The reported incidence of cancer in polypoid lesions pre and post the colonoscopy era are not comparable. The incidence of cancer in colonoscopically resected polyps reflects the histopathologic finding in lesions that

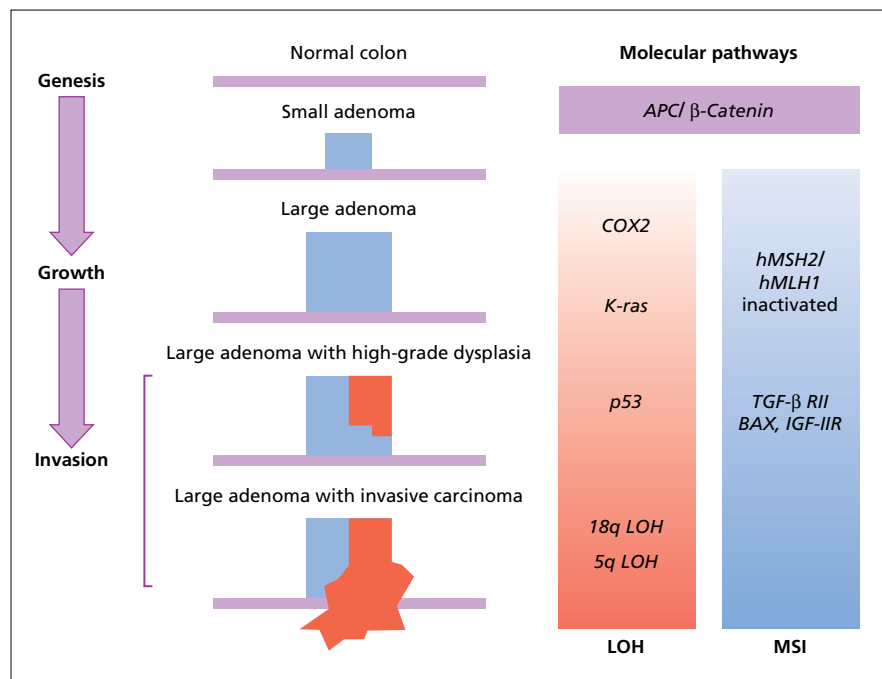


Fig. 38.5 Adenoma–carcinoma sequence. This schema summarizes the key molecular genetic events associated with the genesis of adenoma and its progression to invasive carcinoma. The key initiating event is a mutation of the APC or β-Catenin gene. The subsequent molecular changes can be grouped into two main categories. The predominant pathway is linked to LOH of key suppressor genes and chromosomal instability. The alternative pathway, which may account for up to 15% of colorectal cancers, is attributed to acquired microsatellite instability (MSI) leading to inactivating mutations of growth control genes such as TGF-β RII receptor and BAX gene.

the endoscopist considered to be endoscopically resectable (and most likely benign) as opposed to surgically resected lesions usually discovered on the barium enema.

Molecular changes parallel the histopathologic progression of the adenoma–carcinoma sequence.

The adenoma–carcinoma sequence may not always evolve within a polypoid lesion. Small flat invasive cancers have been described that are thought likely to have developed within a preceding flat adenoma [9,10]. Flat adenomas, originally described by Muto and colleagues [11], have been reported to have greater propensity to develop into cancer and invade the submucosa more readily than polypoid adenomas. An association between small flat adenomas and cancer has been reported in HNPCC. While these associations are controversial, it is accepted that cancer may develop in flat nonpolypoid adenomas and present particular problems for diagnosis and resection. These tumors may be difficult to identify endoscopically. Dye spraying with either topical spray of 0.2% indigo carmine on the colonic surface or by oral ingestion of dye during the preparation phase prior to colonoscopy may aid in their endoscopic visualization. Small flat adenomas, some of which contain invasive carcinoma, have been resected and cured by the submucosal injection of saline followed by removal with an endoscopic snare.

There are only a few reports of flat adenomas in the English literature, leading to speculation that they are not recognized and therefore “missed” during colonoscopy. The relative paucity of English-language reports may reflect either a difference in prevalence or the fact that they are seen and removed but not separately categorized by western endoscopists. Either of these two possibilities is more plausible than the theory that these small lesions are being repeatedly and systematically overlooked, since rigorous follow-up of patients by the National Polyp Study has demonstrated an extremely low incidence of subsequent cancer in colons from which all adenomas were removed by National Polyp Study endoscopists [12]. The latter of these two explanations would appear to be the “best fit” to available data because, when specifically sought, flat adenomas are found in North Americans. O’Brien and colleagues [13] reclassified as flat or polypoid all nonpedunculated adenomas detected at the initial colonoscopy in the National Polyp Study. Flat adenomas did not have an increased presence of high-grade dysplasia. In addition, patients with flat adenomas did not have an increased risk of subsequent advanced adenomas.

Initial endoscopic evaluation and treatment

The endoscopic appearance of a polyp may suggest a malignant component, although most malignant polyps

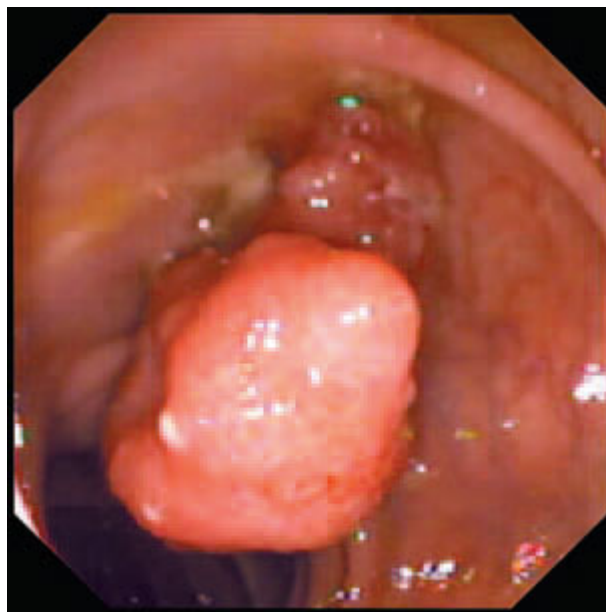


Fig. 38.6 Pedunculated polyp with irregularity of surface and nodularity of the stalk indicating the presence of deeply invasive cancer, which was demonstrated histologically.

have a benign appearance at endoscopy (see Fig. 38.1). Gross features of malignancy include an irregular surface contour, ulceration, firm (or hard) consistency when the head is pushed with a snare or forceps, and broadening of the stalk [1,2,14–18] (Fig. 38.6).

Although polyps with these features are not invariably malignant, the endoscopist should pay special attention to any lesion with malignant characteristics, since it may be desirable to resect these somewhat differently than the routine adenoma. If cancer is suspected by any of the above criteria, the snare should be placed more toward the wall when resecting a pedunculated polyp than toward the head, as is the usual practice. Special care must be directed to recovering all of the fragments for histopathologic evaluation and to localizing the polyp’s position in the colon precisely should subsequent surgery be a consideration by the endoscopist at the time of the polypectomy.

The initial evaluation by the endoscopist may be of great significance, since the morphology of the lesion may be difficult to assess accurately once the resection is completed. Following resection, it may not be possible to ascertain whether a polyp was sessile or pedunculated, because a short pedicle may retract completely into the polyp head. Polyps tend to curl up in formalin and the site of attachment of sessile polyps may not be recognizable in the pathology laboratory [19,20]. The endoscopist can usually tell, with some confidence, whether a complete polypectomy has been done when the polyp is pedunculated, since the stalk is readily identified and the absence of residual adenoma is easily discerned. The

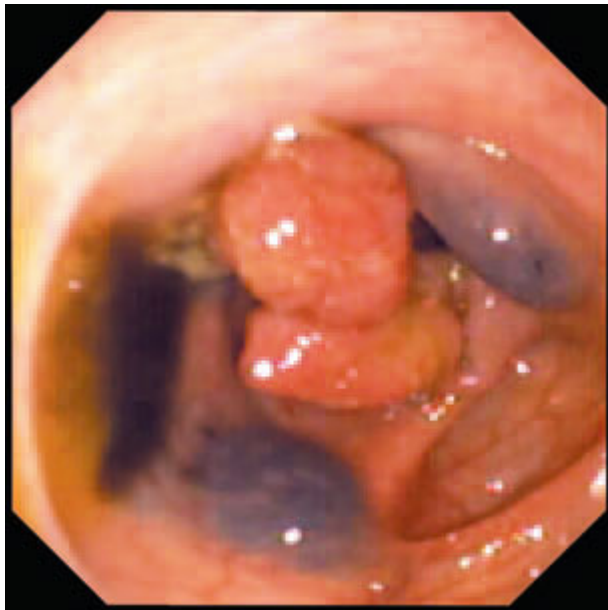


Fig. 38.7 India ink “tattoo” at time of polypectomy to localize polypectomy site because invasive cancer was strongly suspected.

determination is more difficult when a sessile polyp is resected, although a clean base without adjacent, evaluated, reddened tissue usually indicates completeness of resection. This assurance may be difficult to achieve when a polyp has been removed in piecemeal fashion, because fragments at the base could equally prove to be nonviable coagulum or residual adenomatous tissue.

Precise localization of the polypectomy site may be desirable even if surgery is not to be performed and the patient is to be followed endoscopically. Reliance on the distance of colonoscopy insertion (in centimeters) is unreliable, as are intraluminal landmarks. The best method for localizing the polypectomy site is by injection of a surgical marker such as India ink or a suspension of pure carbon particles, whereby a dilute suspension of sterile black carbon particles is injected at the site (Fig. 38.7). The area is stained forever and can be readily detected by the surgeon or the endoscopist on repeat examination. The injection, or tattoo, should be made circumferentially around the polypectomy site using 10 mL of solution in 2–3 mL fractions. Precise localization of the polypectomy site is critical since a resection may be done by laparoscopic technique.

Evidence for surgery vs. endoscopic follow-up

Pedunculated adenomas

The pedunculated malignant polyp has by long convention been placed in a different category from the sessile

malignant polyp by many clinicians. When polyps are pedunculated, the submucosa of the polyp is separated from the submucosa of the colon wall by a thin tubular segment of submucosa, whereas in sessile polyps the submucosa of the polyp is directly contiguous with the submucosa of the colon wall. The literature on malignant polyps is inconsistent, with several authors using their own classification system for depth of invasion, rendering it difficult to compare extent of tumor invasion and its significance from one paper to another. Some reports mix the results from surgically resected specimens with those removed colonoscopically, which tends to skew the outcomes unfavorably by including cases that would not have been considered for endoscopic resection.

However, guidelines for endoscopic polypectomy are fairly well accepted when discussing pedunculated polyps. When certain favorable clinical and histologic criteria are met following removal of pedunculated malignant polyps, it is the general consensus of the literature on this subject that surgery should not be performed since the risk of having residual cancer at the site or nodal metastasis is extremely low and less than the mortality from surgical resection. These favorable criteria are that the tumor be well or moderately differentiated, the resection margin be clear of malignant cells, and the cancer not invade lymphatic channels or vascular spaces within the polyp (Fig. 38.8).

Poorly differentiated carcinoma is rare in malignant polyps but is seen in 15% of surgical resection specimens for colorectal carcinoma [21]. Poor differentiation appears to be a feature that can be correlated with tumor mass and with vascular space invasion. Its presence in malignant polyps is an ominous prognostic sign and mandates surgical resection if the patient’s clinical condition does not preclude it (Fig. 38.9).

Invasion of lymphatics or veins within the submucosa of the polyp head or stalk is also a relatively rare phenomenon and is thought to be a poor prognostic sign, although there have not been enough cases reported to constitute a series that would bear a statistical analysis of its impact, independent of other negative factors. A recent report indicates that this type of vessel invasion is found more frequently if a combination of hematoxylin/eosin and elastin stains is used [22].

The acceptable distance from invasive carcinoma to the endoscopic diathermy burn is variable among many reports in the literature. Some authors insist that the margin must be “healthy,” while others permit a minimum of a 1-mm, 2-mm, or 3-mm margin [15,16,23,24]. Lipper and colleagues [25] state that the presence of malignant cells at the resection margin is the only criterion that reliably predicts a poor outcome. Morson [26] has found good long-standing results in cases with a tumor at the resection margin that was deemed to be safe

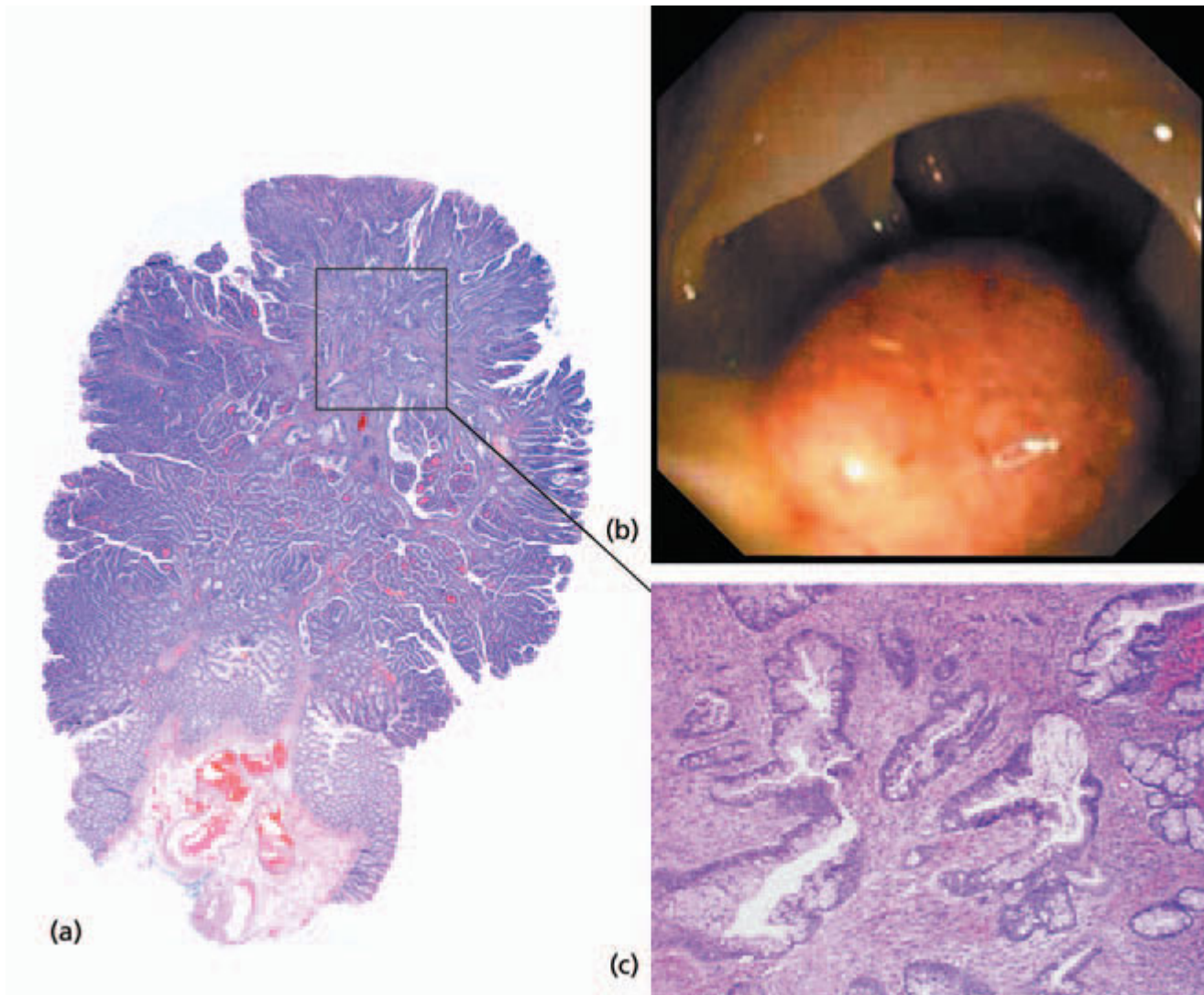


Fig. 38.8 Pedunculated adenoma with favorable histologic features. This pedunculated tubulovillous adenoma has focal well-differentiated adenocarcinoma in the head of the polyp. The short pedicle is free of tumor. The appearance of the polyp head at endoscopy (b) suggests slight surface erosion but is otherwise unremarkable. The invasive component (c) shows characteristic fibrous stroma.

because the endoscopist considered that all abnormal tissue had been removed during colonoscopy. Morson felt that in such cases the diathermy burn caused sufficient cell necrosis to eradicate all residual malignant cells at the margin of the tumor.

Sessile adenomas

Sessile malignant polyps are often considered separately by both clinicians and pathologists. The concern is that malignant cells that cross the muscularis mucosa of

a sessile polyp are actually invading into the portion of the submucosa that is directly contiguous with the rest of the bowel wall submucosa and are not protected by a “buffer zone” of submucosa as in pedunculated polyps. Many authors feel, however, that there is no sound basis for this assertion and that malignant polyps, which are sessile, should not be considered any differently from those that are pedunculated [15,25–27]. A review of the literature in 1988 [23] drew the conclusion that sessile and pedunculated malignant polyps did not differ in their risk for residual or metastatic disease if favorable criteria were applicable (Figs 38.10 & 38.11). However, a paper on decision analysis and the therapeutic options in malignant polyps concluded that all sessile malignant polyps should have an operative resection if the patient is a good-risk candidate. Other authors have also expressed the view that sessile malignant polyps should be treated by further surgical resection [28–32]. In one report [33], sessile malignant polyps had a high

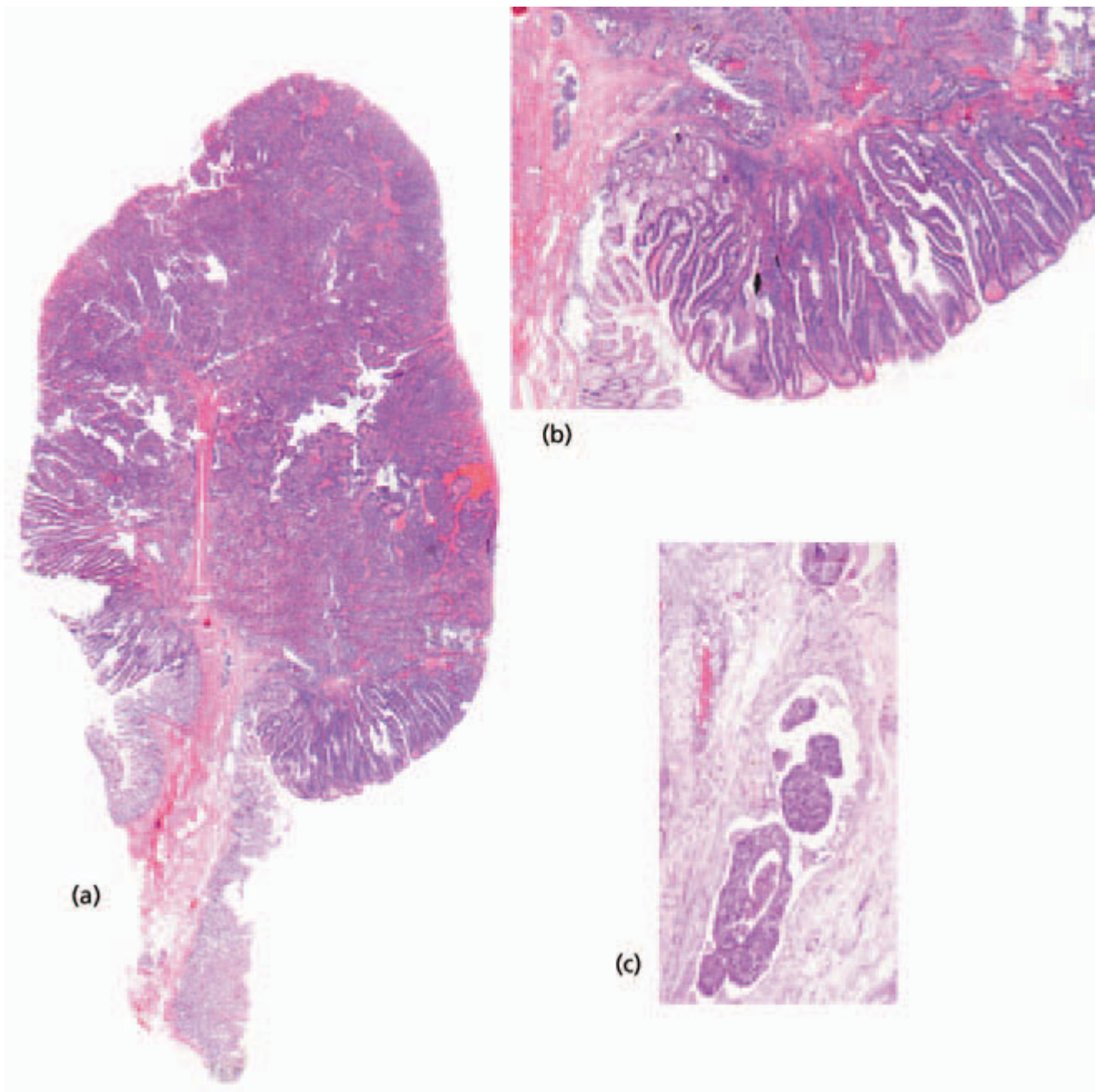


Fig. 38.9 Malignant pedunculated polyp with unfavorable histologic features. The head of this pedunculated villous adenoma is extensively replaced by poorly differentiated adenocarcinoma (a, b). In addition, invasion of lymphatics in the pedicle by invasive adenocarcinoma is present (detail in c).

frequency of residual or nodal cancer, but all eight of the cases in this series found to have residual disease also had positive resection margins. It has been suggested that only sessile malignant polyps resected in a piecemeal fashion should be subjected to surgery because of

the possibility of error in orienting tissue received by the pathologist [27].

Role of the clinician

There is a consensus that if no unfavorable criteria are present in pedunculated malignant polyps, there is a low or nonexistent risk of residual tumor or lymph node metastases and therefore surgery is not indicated [16,18,34,35]. Many also contend that this equally applies even if the polyp is sessile, but it is reasonable to consider a resection in these patients if their surgical risk is low

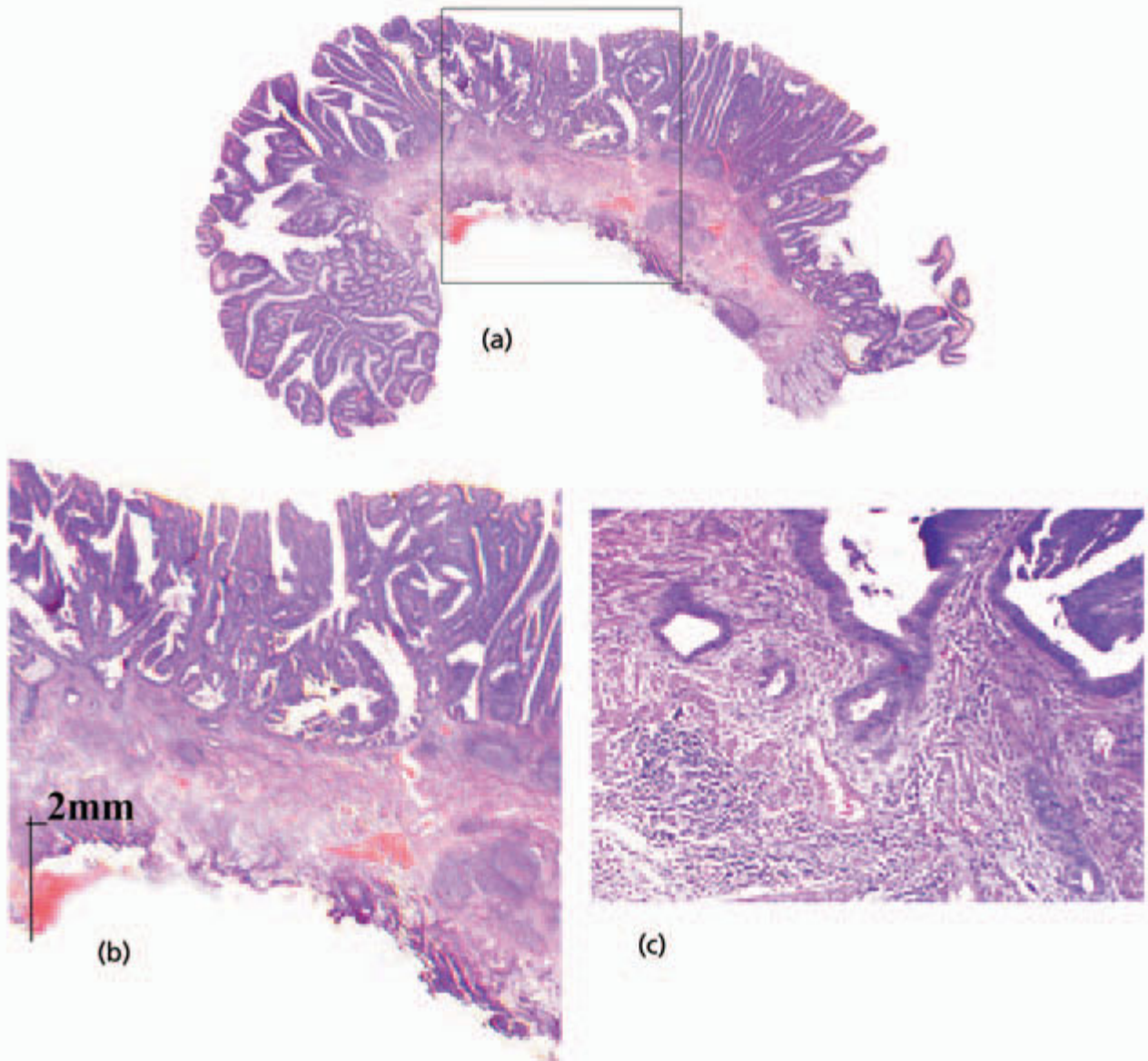


Fig. 38.10 Sessile malignant polyp with favorable histologic features. This sessile tubulo-villous adenoma shows a focus of well-to-moderately differentiated adenocarcinoma that superficially infiltrates the submucosa, barely extending beyond the boundary muscularis mucosae. The invasive edge is 2 mm from the resection cauterly margin, indicating an adequate excision.

[26,27,36]. Some authors have attempted to add other risk factors to the above-mentioned criteria, such as deep stalk invasion [36] or extensive tumor invasion of over one-third of the polyp's submucosa [16].

After colonoscopic removal of a malignant polyp with favorable risk criteria, a follow-up colonoscopy is generally performed in about 3–6 months to assess the polypectomy site for completeness of removal, particularly if the polyp was sessile [1,2]. If residual cancer is

found, the individual is referred for surgical resection, providing that the patient is a good surgical candidate. If there is no residual cancer, a 1-year follow-up colonoscopy may be performed, and if this examination is negative it may be repeated again in 3 years. Additional clinical follow-up with computed tomography and other tests such as carcinoembryonic antigen may be appropriate in select patients. Endoscopic ultrasound is usually not helpful after polypectomy because of the inflammatory reaction at the polypectomy site and possible reactive changes in regional lymph nodes [37,38].

In order to achieve the best outcome, the decision to operate on a patient who has had an endoscopically resected malignant polyp involves balancing the risk of residual cancer at the excision site and regional lymph node metastases against that of mortality from abdominal surgery. In general, the risk of death from elective

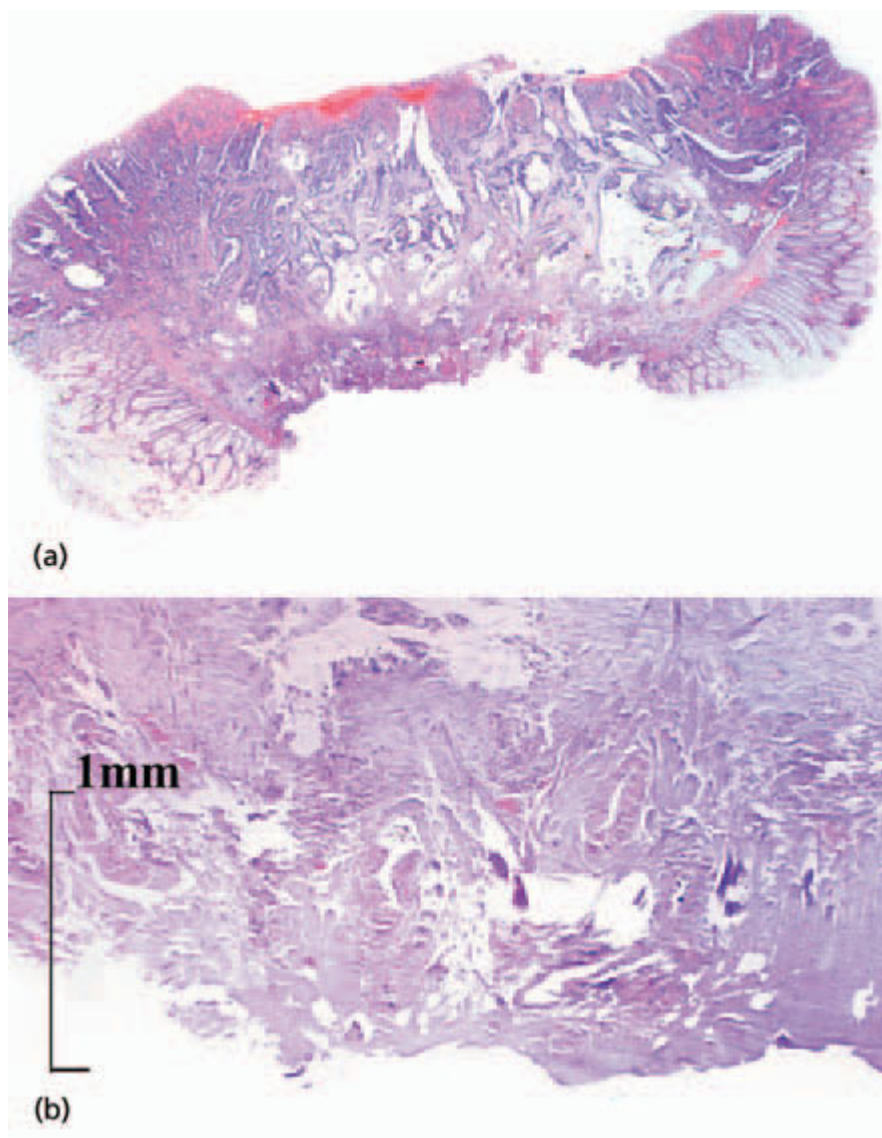


Fig. 38.11 Malignant sessile polyp with unfavorable histologic features. This sessile polyp is totally replaced by invasive moderately differentiated adenocarcinoma, partially mucinous, (polypoid carcinoma). The carcinoma extends to the cautery margin. A segmental resection performed revealed no residual carcinoma at the excision site but metastatic adenocarcinoma was present in several of the regional lymph nodes.

colonic surgery varies from 0.2 to 2%, with the patient below age 50 years being at lowest risk [39,40]. A summary analysis of the recent literature yields an estimate of the risk of residual tumor or nodal cancer in colonoscopically resected pedunculated malignant polyps with favorable criteria as 0.3% and for sessile malignant polyps as 1.5% [2] (Table 38.1).

Patients of any age with favorable resection criteria who have pedunculated malignant polyps resected

Table 38.1 Adverse outcome (residual cancer in colon or nodes) in malignant adenomas with favorable pathology*.

Pedunculated adenomas	0.3%
Sessile adenomas	1.5%

* Well differentiated, no vascular or lymphatic invasion, clear margins.

endoscopically should not have a subsequent surgical resection, nor normally should patients over 50 years of age with sessile malignant polyps with favorable resection criteria [41]. Among healthy patients under age 50 with sessile malignant polyps with favorable criteria, the risk of residual tumor or nodal disease is similar to or slightly higher than the risk of death from surgery, and the argument can be made that this group of patients should have surgical resection of that segment of bowel. Subsequent cancer surgery with bowel resection and node dissection will result in a cure of residual cancer in only about 50% of the patients with nodal metastases. Malignant polyps in the distal rectum require special consideration because permanent colostomy is an issue. Malignant polyps in this location are also unique in that they are amenable to proctologic surgical techniques that permit deep excisions, which are not applicable in the colon. In patients who have a positive margin at

colonoscopic polypectomy, a transanal surgical excision may reverse the situation to a favorable margin-free tumor. A low anterior or abdomino-perianal resection can thus be avoided. If the decision is made to refer the patient for surgery, the endoscopist should perform another endoscopy as soon as possible and tattoo the polypectomy site if this had not been done previously. This is critical because often there is a delay in the final decision until multiple consultations have been sought by the patient and the precise polypectomy site may not be identifiable. Patients who have a family history of HNPCC should be considered separately from the above considerations. The presence of a malignant polyp regardless of "safe" margins or other adverse pathology mandates a surgical resection. They may have an accelerated adenoma-carcinoma progression and have a high synchronous and metachronous rate of additional adenomas. For these reasons, surgery in these patients should be a subtotal colectomy [42].

Summary

The clinician's role is to take into account the many factors relevant to each patient with a malignant polyp. The first step is to examine the histologic slides with the pathologist in order to gain an accurate understanding of the pathologic characteristics of the cancer. Other factors that need to be considered by the clinician include the completeness of the polypectomy, ease or difficulties of the colonoscopy, anatomic location of the polyp, its configuration, and the patient's comorbidity. If a decision is made to refer the patient for surgery, there should be a discussion with the surgeon regarding the above factors as well as the surgical options, including transanal excision, and standard resection vs. subtotal colectomy. The surgery needs to be a cancer operation that will include an adequate number of regional lymph nodes as well as adequate lateral and deep margins, and the clinician needs to assist the surgeon by placing a tattoo at the polypectomy site. Effective management of patients with malignant polyps therefore requires a team approach that involves the pathologist, the clinician, and possibly the surgeon. Following this, the final decision must be made jointly with the patient, who because of comorbidity, age, personal philosophy, and other reasons will influence the final decision and ultimate outcome.

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Chapter 39

Postpolypectomy Surveillance

John H. Bond

Introduction

Patients who have undergone resection of one or more colorectal adenomatous polyps may have an increased risk for recurrent adenomas and subsequent cancer, and therefore may benefit from long-term follow-up surveillance. Lacking reliable scientific data, physicians in the past often performed this surveillance incorrectly, too frequently, or for the wrong patients. Many physicians still adhere strictly to a routine surveillance program that they learned in the past for all their postpolypectomy patients, rather than trying to use current data to assess risk and tailor follow-up to the specific features of each case. Inappropriate surveillance can result in enormous costs of time, resources, and patient inconvenience or risk. Rex and Lieberman [1] reported that in 1999 4.4 million colonoscopies were performed in the USA. An analysis using the large CORI national endoscopic database indicated that at least 17%, or about 750 000 of these examinations, are performed annually for follow-up surveillance after resection of colorectal polyps [2]. Obviously if we miscalculate the type and frequency of follow-up surveillance, we will either put many patients at unnecessary risk for developing colorectal cancer or waste considerable scarce healthcare resources.

It is now generally accepted that in western countries over 95% of colorectal cancers arise in benign adenomatous polyps that develop and grow slowly in the colon over many years before they turn cancerous [3]. Pathologic correlations indicate that malignancy does not occur in hyperplastic polyps, rarely occurs in small tubular adenomas, and is more common in tubulovillous and villous adenomas as they increase in size. A patient with one known adenoma in the large bowel has a 30–50% likelihood of harboring a second synchronous adenoma elsewhere in the colon at that time, and a 30–50% likelihood of developing a metachronous adenoma sometime in the future [4].

For these reasons (the adenoma to cancer relationship and the appreciable incidence of synchronous and metachronous adenomas), most endoscopists practice some form of follow-up surveillance for their polyp patients. The ultimate objective of this surveillance is to detect and resect clinically significant missed syn-

chronous adenomas and new metachronous adenomas before they can turn cancerous and harm the patient. The key questions that need to be addressed in designing appropriate follow-up strategies are: What is each patient's risk of colorectal cancer after resection of one or more benign adenomatous polyps, and will postpolypectomy surveillance eliminate or substantially reduce that risk? This chapter reviews the rationale and current recommendations for postpolypectomy surveillance, emphasizing the need to tailor surveillance strategies to the carefully considered individualized assessment of risk for each patient.

Colonoscopy is the procedure of choice for postpolypectomy surveillance

Colonoscopy is clearly the preferred method for postpolypectomy surveillance for most patients. It is substantially more accurate than double-contrast barium enema for the detection of polypoid lesions of all sizes. An earlier, carefully controlled, single-blinded study comparing the accuracy of the two examinations performed in the same patients demonstrated a sensitivity for detecting polyps of 67% and 94% for double-contrast barium enema and colonoscopy respectively [5]. More recently, the National Polyp Study reported the results of a similarly controlled comparison of both methods in a large cohort of patients actually undergoing postpolypectomy surveillance [6]. A total of 862 back-to-back double-contrast barium enema examinations and colonoscopies were performed in 680 patients. Expert radiologists or colonoscopists who were blinded to the result of the alternative examination performed all examinations. Barium enema studies were positive in only 39% of patients found to have adenomatous polyps at colonoscopy. Even when patients had adenomas that were 1 cm or more in diameter, the barium enema was negative in 52%. False-positive barium enemas occurred in 14% of cases. A retrospective analysis of cancer cases in 20 medical centers in Indiana showed an accuracy of colonoscopy and barium enema for detecting cancers of 95% and 83% respectively [7]. In a subset of colonoscopies in this study that were performed by gastroenterologists, who presumably had more training

and experience, the sensitivity for detecting cancer was 97%.

The entire colon and rectum can be thoroughly examined by colonoscopy performed by experienced endoscopists, with minimal discomfort in over 95% of cases. Most importantly, colonoscopy is both diagnostic and therapeutic, allowing resection of most detected polyps at a single sitting with a single bowel-cleansing preparation. Although the alternative strategy of performing barium enema plus flexible sigmoidoscopy initially may be less costly, the need to do subsequent colonoscopy for those with positive findings makes this approach, on average, equally expensive. The complication rate for colonoscopy is appreciably higher than that of barium enema; however, major complications including perforation are rare provided the examination is performed by a well-trained experienced endoscopist [8].

Computed tomography (CT) colonography ("virtual colonoscopy") is now being studied for follow-up surveillance of patients with colorectal cancer or polyps. CT colonography has already been shown to be more accurate than double-contrast barium enema for detecting polyps. In addition, some but not all studies indicate that this method is nearly as accurate as colonoscopy for detecting large (≥ 1 cm) polypoid adenomas, although accuracy rapidly drops off for medium-sized and small polyps. The published sensitivity of CT colonography for detecting large adenomas (≥ 1 cm) in three experienced centers in the USA was 75.2–91% [9–11]. However, not all centers currently performing virtual colonoscopy can achieve this level of accuracy. For example, a recent multicenter study in the USA reported that the sensitivity for detecting 1-cm polyps in over 500 patients in nine centers ranged from about 8 to 83% [12]. In the best US studies, the sensitivity of virtual colonoscopy for detecting medium-sized polyps (5–10 mm) was only 47.2–82%. A major limitation of virtual colonoscopy compared with conventional colonoscopy is that, as with barium enema, the study is only diagnostic. Whenever a suspicious lesion or a clinically significant neoplasm is found, the patient must undergo a subsequent colonoscopy to confirm and/or resect the lesion. The need to do two expensive tests would make surveillance costly and inconvenient. The follow-up endoscopy must usually be scheduled on a different day and therefore the patient must undergo a second bowel-cleansing preparation.

Risk of cancer following polypectomy

Two earlier studies from the Mayo Clinic estimated the risk of cancer after polypectomy. In 1984, Spencer and colleagues [13] reported the results of 10 000 person-years of follow-up of 751 patients who had undergone resection of a single small (≤ 1 cm) polyp from the distal colon during rigid proctosigmoidoscopy. There was no

apparent increased incidence of subsequent cancer in this group compared with that of the local age-matched population. In contrast, the same group of investigators reported 2 years later that patients with larger adenomas (> 1 cm) had a risk of developing metachronous cancer that was 2.7 times greater than expected, and those with multiple index adenomas had a relative risk that was five times greater than expected [14].

Another study of the risk of cancer after removal of rectosigmoid adenomas was reported in 1992 from St Mark's Hospital, London, by Atkin and colleagues [15]. A group of 1618 patients who had rectosigmoid adenomas resected during proctosigmoidoscopy with no further colonic surveillance were followed for a mean of 14 years (22 462 person-years). Patients with index adenomas that were tubulovillous, villous, or large (≥ 1 cm) had a 3.6-fold increased subsequent incidence of colorectal cancer. However, those with only small tubular adenomas (< 1 cm), whether single or multiple, had a subsequent incidence of cancer that was less than that of the age-matched general population. These investigators concluded that follow-up surveillance may be warranted in patients with tubulovillous, villous, or large adenomas, particularly if these adenomas were multiple. However, in patients with small tubular adenomas, surveillance may not be of value because the risk of subsequent cancer is so low.

Lastly, an important prospective postpolypectomy colonoscopy study was performed by Grossman and colleagues [16] on 544 asymptomatic subjects with a past history of adenomas found at screening proctosigmoidoscopy. In 142 patients whose worst index lesion was a single small (< 10 mm) tubular adenoma and who had no first-degree relatives with colorectal cancer, the prevalence of advanced neoplasia (defined as tubular adenomas ≥ 1 cm, tubulovillous or villous adenomas, or adenomas with high-grade dysplasia or invasive cancer) was only 3%, no greater than would be expected in the general population. In contrast, subgroups with advanced or multiple index lesions had prevalences of advanced adenomas ranging from 8 to 18%.

Concept of the advanced adenoma

These follow-up experiences, as well as a large and increasing volume of information about the molecular genetic basis for the adenoma–carcinoma sequence, are increasingly shifting the emphasis away from simply finding and harvesting large numbers of clinically insignificant small tubular adenomas toward strategies that focus on ways to reliably detect and resect the less common, but clinically much more dangerous, advanced adenoma (Table 39.1). Defined by both the National Polyp Study and several earlier studies such as that of Grossman and colleagues [16], an advanced adenoma

Table 39.1 Advanced adenoma.

<i>Size</i>
1 cm or larger in diameter
<i>Histology</i>
Villous change
High-grade dysplasia
Invasive carcinoma

is one that is either large (≥ 1 cm) or contains the advanced histologic features of villous change, high-grade dysplasia, or invasive carcinoma [17]. Large numbers of small simple tubular adenomas develop in large numbers of people: over 30% of the population over age 50 years have these lesions, yet only a small fraction will ever develop colorectal cancer. While it is obvious that all large adenomas were small at some time, most small tubular adenomas never grow, advance, and turn malignant. Colonic carcinogenesis is a complex, non-linear, multistep process occurring over many years that results from the progressive accumulation of genetic mutations and chromosomal deletions [18]. As neoplasia proceeds from normal-appearing mucosa, through small, medium and large benign adenomas, and finally to invasive cancer and metastases, genetic changes are found in increasing number. An adenomatous polyp is a monoclonal derivative of a single epithelial stem cell that either inherits (familial neoplasia) or acquires (sporadic neoplasia) the first of these many genetic alterations. Each additional genetic “hit,” probably caused by noxious environmental carcinogenic factors, leads to a new clone of daughter cells with a growth advantage that allows the clone to take over the developing polyp. The reason most small simple tubular adenomas stay small and clinically benign is because they never develop the additional genetic alterations (i.e. oncogene mutations and tumor-suppressor gene alterations) needed to make them advance. A large volume of high-quality scientific evidence published during the past decade indicates that colonoscopic resection of an advanced adenoma is both predictive of recurrent metachronous advanced adenomas during postpolypectomy follow-up surveillance and is a highly effective way of preventing colorectal cancer [19]. Thus, our postpolypectomy efforts need to increasingly focus on ways to reliably find and resect advanced adenomas before they turn to cancer.

Outcomes and observational studies underscore the different behavior of small tubular adenomas and advanced adenomas. In an earlier study by Hoff and colleagues [20], 215 polyps less than 5 mm in diameter were left *in situ* in 112 individuals for a 2-year follow-up period to ascertain their growth rate. At the end of the 2 years, 49% of adenomas had increased in size and 14% had regressed. Although total adenoma mass had

increased by 136%, none had grown to a size greater than 5 mm and none had developed high-grade dysplasia or carcinoma. In a more recent study from Japan, Obata and colleagues [21] marked 139 small polyps (3–10 mm) with India ink and followed them with yearly colonoscopy. During a mean follow-up period of 33 months, 135 (97%) did not change in form or size. These workers also concluded that small polyps do not appreciably change over 3 years and they advance very slowly if at all.

In contrast to these observational studies of the natural history of small polyps, there is considerable evidence that large polyps behave more aggressively. Eide [22] reported that the risk of developing carcinoma in a 1-cm adenoma was 3% per year in a Norwegian population. The National Polyp Study found a strong relationship between adenoma size and the prevalence of high-grade dysplasia: the odds ratio for high-grade dysplasia in a large polyp (≥ 1 cm) was 20.3 compared with that of a diminutive polyp (≤ 5 mm) [23]. Likewise, many reported series of polyp cases indicate a strong linear correlation between adenoma size, more extensive villous configuration, more severe dysplasia, and the presence of invasive carcinoma [24]. Such advanced adenomas also contain a larger fraction of the genetic mutations and chromosomal changes commonly found in the fully developed cancer phenotype [18].

Lastly, the classic study by Stryker and colleagues [25] clearly showed the considerable malignant potential of large adenomas. Before the availability of colonoscopy, 226 patients who had large (> 1 cm) polyps detected on barium enema but refused their removal by surgery were followed for up to 20 years. Follow-up of these untreated patients showed that 37% of the polyps enlarged, 21 invasive carcinomas developed at a polyp site, and 11 carcinomas developed at another site. The cumulative risk of cancer at 5, 10, and 20 years was 2.5, 8, and 24%, respectively. This study supports the need to find and excise all large colorectal polyps and the need for periodic surveillance of these patients to identify metachronous adenomas at a site in the colon remote from the index polyp.

Missed synchronous vs. metachronous polyps

Adenomas found by colonoscopy in virtually all reported postpolypectomy surveillance series are generally smaller than those resected at the initial colonoscopy examination [26]. While it is impossible to reliably differentiate between true recurrent adenomas and missed synchronous ones during follow-up colonoscopy, many undoubtedly were missed by the index examination. Direct determination of the colonoscopy miss rate for polyps was evaluated in two prospective “tandem”

colonoscopy studies. Hixson and colleagues [27] performed a study in which two colonoscopists performed same-day back-to-back colonoscopies in 90 subjects after a single bowel-cleansing preparation. The investigators alternated the endoscopist who would perform the first examination, during which detected lesions were documented but not removed. The study reported a miss rate for small (≤ 5 mm) and medium-sized (6–9 mm) polyps of 16 and 12% respectively; however, no large polyps (≥ 1 cm) went undetected. A similarly designed tandem colonoscopy study by Rex and colleagues [28] reported a miss rate for small (≤ 5 mm), medium (6–9 mm), and large (≥ 1 cm) polyps of 27, 13, and 6%, respectively, in 183 patients.

In order to differentiate between true recurrent and missed synchronous adenomas following surveillance colonoscopy, Hixson and colleagues [29] performed 2-year follow-up examinations in 58 of the original 90 patients who had undergone tandem colonoscopies. In 38% of these 58 patients 56 adenomas were detected, 31 of which were judged to be new metachronous lesions, defined as a follow-up polyp found in a colonic segment in which a prior lesion of the same histologic classification had not been previously detected during the tandem colonoscopies. Three of these adenomas were large (≥ 1 cm), and therefore the authors concluded that, while most metachronous adenomas found at 2 years of follow-up are small tubular adenomas, large ones can develop in normal-appearing mucosa in that time period. The miss rate and true 1-year recurrence rate of colorectal adenomas was also determined in a population of patients reflecting a broad spectrum of different gastroenterology practice settings within the context of two large prospective chemoprevention studies carried out by the Polyp Prevention Study Group [30]. The miss rate was determined by comparing findings for patients who had repeat colonoscopies within 120 days, both of which had good preparation and were complete to the cecum. The true 1-year recurrence rate was determined by subtracting this miss rate from the rate of adenoma detection at colonoscopy performed 1 year later as per the study protocol. The adenoma miss rate per patient was 8% and the 1-year recurrence rate was 28%. The authors concluded that there is a significant colonoscopic miss rate for neoplastic polyps at initial colonoscopy as well as a substantial postpolypectomy recurrence rate within 1 year of a clearing colonoscopy.

Frequency of postpolypectomy colonoscopic surveillance

The decision about who needs surveillance influences the cost of a surveillance program more than the decision about how often to do follow-up surveillance colonoscopy. When colonoscopic polypectomy was introduced

Table 39.2 National Polyp Study design (seven participating centers, 1418 patients).

Patient eligibility

No personal or family history of colorectal polyps or cancer
One or more adenomas removed on initial colonoscopy

(a) Less than 3 cm in diameter

(b) No invasive cancer

All polyps removed at that time

Patients randomized into two follow-up arms

Colonoscopy at 1 year and 3 years

Colonoscopy at 3 years only

in the early 1970s, performing yearly follow-up examinations became the standard even though its yield appeared to be small and was not supported by scientific evidence. For this reason the National Polyp Study (Table 39.2) was designed by a joint committee of the American Gastroenterology Association, the American Society for Gastrointestinal Endoscopy, and the American College of Gastroenterology [31]. Many of the current recommendations for postpolypectomy surveillance are based on this 10-year prospective, multicenter, landmark study funded by the National Cancer Institute and directed by Winawer. The main objective of the study was to determine if follow-up colonoscopic examinations performed at 3 years after initial polypectomy were as effective in detecting clinically important colonic neoplasia as follow-up evaluations at 1 and 3 years. Patients undergoing colonoscopy in each of the seven participating centers were eligible for the study if they had no personal or family history of colorectal polyps or cancer. From this group, patients were invited to enroll in the investigation if they had one or more adenomas resected that were less than 3 cm in diameter and did not contain invasive carcinoma, and if the colonoscopist believed that all polyps had been resected at the time of the index colonoscopy. A total of 1418 patients were randomly assigned to have either follow-up colonoscopy at 1 and 3 years and then every 3 years, or just a follow-up colonoscopy every 3 years after the initial polypectomy. The percentage of patients who had adenomas found by 3 years in the group examined at 1 and 3 years was 41.7% compared with 32% for the group examined only at 3 years [32]. However, the number of patients who had advanced adenomas by 3 years was the same in each group (3.3%) (Table 39.3). The study therefore concluded that an interval of at least 3 years is recommended before the first surveillance colonoscopy is performed after resection of colorectal adenomas. The further follow-up of both groups at 3-year intervals also showed that if the first 3-year follow-up revealed no new adenomas, subsequent follow-up could be safely extended to 5-year intervals.

Table 39.3 National Polyp Study results.

Group	Total adenomas at 3 years (%)	Advanced adenomas (%)
Follow-up at 1 year and 3 years	41.7	3.3
Follow-up at 3 years	32	3.3

Repeat clearing colonoscopy after polypectomy

Before embarking on a postpolypectomy surveillance program that prescribes follow-up colonoscopy in 3–5 years, the entire large bowel should first be thoroughly examined to clear it of all detectable synchronous lesions. A repeat clearing examination may be indicated for patients with an incomplete initial colonoscopy or for one done with a suboptimal bowel preparation. A second clearing examination should also be considered for selected patients with multiple polyps when the colonoscopist is concerned that clinically significant lesions may have been missed.

Repeat clearing colonoscopy to insure complete polypectomy is essential after piecemeal resection of large sessile polyps. Such polyps often contain appreciable amounts of villous tissue with a high malignant potential, and they tend to recur locally after colonoscopic resection even in cases where the initial polypectomy appeared to be complete. A second clearing colonoscopy should be performed in 3–6 months to confirm that resection was complete. Residual neoplastic tissue has been reported in up to one-third of cases after piecemeal snare resection of sessile polyps greater than 2 cm in diameter [33]. If polyp tissue persists after two or three examinations, good-risk patients should usually be referred for surgical resection. When patients are found to have these large sessile polyps, they need to be educated at the time of initial diagnosis about the importance of complying with the entire course of management and follow-up. Most experienced colonoscopists have witnessed tragic cases in which a patient was partially treated by piecemeal snare polypectomy, was then lost to follow-up, and returned later with an advanced cancer at the polyp site.

Effect of polypectomy on cancer incidence and mortality

It is difficult to assess the effect of postpolypectomy surveillance on the subsequent incidence and mortality of colorectal cancer because it is nearly impossible to separate the effect of the initial polypectomy from the effect of follow-up colonoscopic surveillance. It is now clear, however, that resecting advanced adenomatous polyps, both initially and during postpolypectomy

follow-up, is a powerful way to prevent cancer. Cohort and case-control studies of the effect of large bowel endoscopy have strongly indicated that polypectomy reduces the subsequent incidence and mortality of colorectal cancer located in the examined segment. Many years ago, Gilbertsen and Nelms at the University of Minnesota [34] reported that annual rigid proctoscopic screening and removal of rectal polyps performed in 21 000 volunteers over a 20-year period reduced the incidence of rectal cancer by 85%. Case-control studies of the effect of screening proctosigmoidoscopy by Selby and colleagues [35] and Newcomb and colleagues [36] suggested a reduction in mortality from distal cancer of 60 and 80% respectively. Lastly, a large case-control study involving over 32 000 veterans by Muller and Sonnenberg [37] indicated that patients who had flexible sigmoidoscopy, colonoscopy, and polypectomy had a 50% reduced risk of developing colorectal cancer.

Most convincing is the landmark analysis by Winawer and colleagues [38] from the National Polyp Study. All 1418 subjects enrolled in the study were pooled to determine the effect of initial polypectomy plus follow-up surveillance colonoscopies performed every 3 years. Only five new cancers were detected during an average follow-up of about 7 years (8400 person-years), which was 76–90% lower than expected by comparison with three reference populations. Thus, for the first time, a well-designed prospective trial showed that colonoscopic removal of all adenomas in the colon and rectum successfully interrupted the adenoma-cancer sequence, preventing most cancers from developing. Two recent reports from Europe confirm the findings and conclusions of the National Polyp Study. The Telemark Polyp Study from Norway [39] showed in a randomized controlled trial that colonoscopy and polypectomy for those with a positive screening flexible sigmoidoscopy reduced the subsequent incidence of colorectal cancer by 80%. A multicenter Italian study followed 1693 patients who had undergone resection of at least one adenoma greater than 5 mm in diameter [40]. The incidence of metachronous cancer was compared with that of a reference population. After a mean follow-up of 10.5 years (14 211 person-years), only six colorectal cancers were detected, indicating a reduction in incidence due to polypectomy of 76%.

Investigators from the National Polyp Study recently performed a Micro-Simulation Screening Modeling Analysis (MISCAN) to predict the incidence of colorectal cancer using data from the study [41]. The model demonstrated a dramatic reduction in expected colorectal cancer incidence and indicated that the initial polypectomy accounted for the major component of this incidence reduction. The model predicted a modest benefit from postpolypectomy surveillance after 6 years. This conclusion is consistent with the fact that many

more advanced adenomas were resected in the study at the index colonoscopy compared with the number found and resected during follow-up.

Further stratification of postpolypectomy cancer risk

Estimates by pathologists as well as an analysis of all patients undergoing colonoscopy in the seven centers of the National Polyp Study indicate that it takes, on average, 10–12 years for an adenoma to develop, advance, and turn to cancer [42,43]. The cumulative recurrence rate of advanced adenomas in this trial was low: 4% at 3 years and 8% at 6 years [44]. Because of the long natural history of the adenoma–carcinoma sequence and the overall low recurrence rate of advanced adenomas in follow-up studies, recent analyses have focused on ways to safely lengthen postpolypectomy intervals for most patients. Further analysis of follow-up data from the National Polyp Study and data from more recent outcome studies of postpolypectomy surveillance now indicate that it is possible to stratify risk of recurrent advanced adenomas based on patient characteristics and the findings at initial polypectomy [45]. In the National Polyp Study, patients with a relatively high risk of developing advanced adenomas during follow-up included those with multiple adenomas (three or more), large adenomas (> 1 cm), or age over 60 years at initial adenoma diagnosis plus a parent with colorectal cancer. Patients with a low risk of metachronous advanced adenomas included those with only one or two small adenomas and no family history of colorectal cancer.

Other studies suggest other predictors for recurrence of adenomas. The Polyp Prevention Study Group determined predictors for metachronous adenomas in 479 patients who had one or more polyps detected at their index colonoscopy and then had repeat colonoscopies 1 and 4 years later in a negative chemoprevention trial of antioxidant vitamins [46]. Multivariate analysis showed that multiple adenomas (three or more) or at least one tubulovillous adenoma at initial colonoscopy was associated with an increased incidence of multiple adenomas at follow-up. In this study, no factors predicted an increased incidence of advanced metachronous adenomas. Another follow-up analysis was performed using the Cleveland Clinic Adenoma registry of 697 patients who had an adenoma recurrence within 3 years of a positive baseline colonoscopy [47]. Having three or more adenomas on initial colonoscopy, with at least one measuring 1 cm or larger, greatly increased the chance of finding an advanced adenoma at the first 3-year follow-up surveillance colonoscopy. Conversely, patients with only one or two adenomas, all measuring less than 1 cm, were at extremely low risk of having an important adenoma

within 3 years. More recently, the Polyp Prevention Trial, a negative randomized trial of the effect of diet on the recurrence of colorectal adenomas, reported a recurrence rate of advanced adenomas at 4 years of 16% [48]. Baseline predictors of a higher risk of metachronous advanced adenomas included age over 65 years, proximal location of baseline adenomas, and villous histology.

Current colorectal cancer screening and surveillance guidelines recommend that clinicians assess each patient's risk of developing metachronous advanced adenomas and tailor postpolypectomy surveillance strategies accordingly [49,50]. Based on the available clinical and pathologic data reviewed in this chapter, patients with colorectal adenomas can now be stratified into high- and low-risk groups. After the colon has been satisfactorily cleared of all synchronous adenomas, repeat colonoscopy is recommended in 3 years for patients who are at high risk. These include those who at baseline colonoscopy have (i) large (≥ 1 cm) or multiple (three or more) adenomas, (ii) an adenoma with the advanced pathologic features of villous change, high-grade dysplasia, or invasive carcinoma, and (iii) those over age 60 years with a parent with colorectal cancer. Patients with a low risk of metachronous advanced adenomas include those who initially have only one or two small (< 1 cm) tubular adenomas without high-grade dysplasia or cancer, and no significant family history of colorectal cancer. For these low-risk patients, the first postpolypectomy follow-up colonoscopy can be safely delayed for at least 5 years or, in the case of advanced age or significant comorbidity, no follow-up may be indicated. Surveillance for this low-risk group is controversial. Some argue that since their risk of subsequent colorectal cancer does not appear to measurably exceed that of the average-risk population, no surveillance is indicated. Many, however, noting the discrepant findings in the different follow-up studies, are uncomfortable eliminating all surveillance for these patients.

Postpolypectomy surveillance recommendations

A comprehensive evidence-based polyp guideline was recently prepared by the Practice Parameters Committee of the American College of Gastroenterology entitled "Polyp guideline: diagnosis, treatment, and surveillance for patients with colorectal polyps" [50]. This guideline was also endorsed by the American Society for Gastrointestinal Endoscopy and the American Gastroenterology Association. The following are this guideline's recommendations for postpolypectomy surveillance.

1 Complete colonoscopy should be done at the time of initial polypectomy to detect and resect all synchronous adenomas.

2 Additional clearing examinations may be required after resection of a large sessile adenoma, or if (because of multiple adenomas or other technical reasons) the colonoscopist is not reasonably confident that all adenomas have been found and removed.

3 After a complete clearing colonoscopy has been accomplished following an initial polypectomy, repeat colonoscopy to check for metachronous adenomas should be performed in 3 years for patients at high risk for developing metachronous advanced adenomas. This includes those who at baseline examination have multiple (more than two) adenomas, a large (≥ 1 cm) adenoma, an adenoma with villous histology or high-grade dysplasia, or a family history of colorectal cancer.

4 Repeat colonoscopy to check for metachronous adenomas should be performed in 5 years for most patients at low risk for developing advanced adenomas. This includes those who at baseline examination have only one or two small tubular adenomas (< 1 cm) and no family history of colorectal cancer.

5 Selected patients at low risk for metachronous advanced adenomas may not require follow-up surveillance.

6 After one negative follow-up surveillance colonoscopy, subsequent surveillance intervals may be increased to 5 years.

7 If doing surveillance colonoscopy is not feasible, flexible sigmoidoscopy followed by a double-contrast barium enema is an acceptable alternative.

8 Follow-up surveillance should be individualized according to the age and comorbidity of the patient, and should be discontinued when it seems unlikely that follow-up is capable of prolonging quality of life.

Cost and cost-effectiveness of postpolypectomy surveillance

Adoption of these recommendations would substantially reduce the cost of postpolypectomy surveillance because many clinicians still perform surveillance more frequently than is necessary. For example, Ransohoff and colleagues [51] estimated that postpolypectomy surveillance that leads only to the detection and resection of small tubular adenomas is unlikely to appreciably reduce colorectal cancer incidence or mortality. They performed a cost-effectiveness analysis of available data and concluded that the cost of surveillance of those with a low subsequent risk of colorectal cancer, such as those with a single small tubular adenoma, is prohibitive. Based on their assumptions in 1991, it would cost \$80 000–300 000 per life saved for a surveillance program of colonoscopy every 3 years for all 50-year-old patients with small adenomas followed for 30 years. In another cost-effectiveness mathematical modeling analysis, Lieberman [52] concluded that conventional

postpolypectomy surveillance comprises 19–34% of the total cost of a colorectal cancer screening program. According to his calculations, if postpolypectomy surveillance focused solely on the detection of advanced adenomas, this cost could be reduced by over 40%. In 1996, a large practice in Minneapolis consisting of 19 gastroenterologists analyzed the economic impact of adopting the postpolypectomy recommendations of the National Polyp Study [53]. A survey of 500 prior cases indicated that this group of physicians had deviated from these recommendations in 45% of their cases (range 15–80%); most were performing more frequent follow-up examinations than were needed. After implementing a practice guideline based on the National Polyp Study findings, follow-up practice in the next 500 polypectomy cases deviated by only 12% (mostly a result of physicians' deciding against any follow-up when polyps were found in elderly or ill patients). During the next 12 months, this group documented savings of more than \$600 000 in facility and professional charges for colonoscopy that were directly attributable to adopting a rational evidence-based guideline for postpolypectomy surveillance.

Rex and Lieberman [1] recently analyzed the feasibility of performing direct colonoscopy screening in the USA. They concluded that some of the capacity currently unavailable to carry out this screening could be created by shifting resources away from unnecessary postpolypectomy surveillance to colonoscopy screening. If postpolypectomy surveillance were designed to detect only advanced adenomas, two-thirds of the colonoscopies currently being done annually for surveillance could instead be used for screening. Another important cost-saving strategy is to eliminate screening for patients who are already participating in a postpolypectomy colonoscopy surveillance program. No additional colorectal cancer screening of any type is needed when a patient is asymptomatic and has had normal results on surveillance colonoscopy within 3–5 years.

Summary

Following removal of benign adenomatous polyps, there is a 30–50% likelihood of developing a metachronous adenoma in the future. Removal of colon polyps will, to a large extent, interrupt the adenoma–carcinoma sequence and protect the patient from developing carcinoma. Not all patients have the same likelihood of developing metachronous adenomas. The timing of follow-up colonoscopic examinations needs to take into account each patient's risk for developing metachronous advanced adenomas and tailor postpolypectomy surveillance strategies accordingly. Patients with colorectal adenomas should be stratified into high- and low-risk groups. Interval colonoscopic examination is

recommended in 3 years for patients who are at high risk. These high-risk patients are those who have had the removal of large or multiple adenomas, an adenoma with the advanced pathologic features of villous change, high-grade dysplasia, or invasive carcinoma, and those aged over 60 years with a parent with colorectal cancer. Patients with a low risk of metachronous advanced adenomas can safely have their first follow-up colonoscopy at 5 years. This group of low-risk patients includes those who initially have only one or two small tubular adenomas without high-grade dysplasia or cancer and no significant family history of colorectal cancer. Stratification of patients into various colonoscopic follow-up strategies will permit the medical profession to conserve precious resources while providing the best and most efficient protection against the possibility of developing colon cancer.

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Chapter 40

Colonoscopy after Colon Cancer Resection

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Introduction

After curative operative resection for colon cancer, colonoscopy follow-up examinations are frequently performed with the intention of detecting recurrence of cancer, and to remove new adenomas in the attempt to prevent metachronous cancers from developing [1] (Table 40.1). The most important question to be addressed is whether interval repeat colonoscopy following colon cancer resection will indeed detect recurrence of colon cancer at a stage when a salvage operation can be successfully performed, and if so, what should be the optimum time for the colon examination. A second question is: can colonoscopy prevent metachronous carcinomas, and if so, at what intervals should follow-up colonoscopy be performed?

In order to answer the first question, it is necessary to assess the probability of an intraluminal recurrence of cancer at the suture line (Fig. 40.1). As reported in a systematic review and metaanalysis of randomized controlled trials and follow-up, intraluminal recurrence of cancer at the anastomosis (Fig. 40.2) accounts for only a small percentage of patients who develop recurrent carcinomas [2] (Table 40.2). Makela *et al.* [3] found intraluminal recurrences in only 3 of 106 patients who had tumor recurrence following surgical resection, while Ohlsson *et al.* [4] reported four anastomotic recurrences in 107 patients. Schoemaker *et al.* [5] discovered eight intraluminal recurrences out of 325 patients with recurrent cancers, and Pietra *et al.* [6] reported only two intraluminal recurrences out of 207 patients with recurrent tumor previously operated upon for colorectal cancer. Kjeldsen *et al.* [7], on the other hand, reported that 16 out of 283 patients with recurrent cancer were found to have intraluminal recurrences. The overall rate of reported intraluminal recurrences in the Renahan *et al.* review [2]

was 3.2% of all patients operated upon for colon cancer. Because of the low incidence of recurrent cancer of the anastomosis, the conclusion was that colonoscopy was not the procedure of choice for the follow-up search for recurrent cancer. This is also reflected in Chapter 11, concerning colonoscopy and the incidence of anastomotic cancer and metachronous adenomas (Figs 40.3, 40.4) following colon cancer resection. The data in this chapter (Table 40.3) reports a combined 7.6% incidence of recurrent cancer at the anastomosis and metachronous cancer at other sites.

As for the frequency of follow-up examinations, there was little difference in any of the studies between recurrent colon cancer in patients who had an intensive follow-up after curative surgery versus those whose follow-up was "conventional" as a control population [1]. During follow-up examinations, metachronous cancers were relatively low in prevalence (Tables 40.2, 40.3). The overall rate of detection of metachronous carcinoma in the Renahan *et al.* review was 1.3% [2].

Overall, the rate of recurrent cancer between patients that are followed with "intensive" follow-up regimens versus a control group showed no difference, with a 33% recurrence rate in the intensive group and 33% in those having regular follow-up examinations. However, it may be important that recurrences were detected 8.5 months earlier in the group that had intensive follow-up examinations. The intensive follow-up regimens often consisted of clinic visits and tests every 3 months for 2 years then every 6 months. These tests usually included liver function studies, complete blood count, chest X-ray, carcinoembryonic antigen (CEA) levels, and liver ultrasound every 6 months, CT scan every year, colonoscopy at intervals of 6 months for 3 years and then less frequent. The control groups had less frequent examinations.

Even with "intensive" follow-up, the symptomatology of the patient is an important parameter in heralding the recurrence of colonic cancer. In spite of intensive surveillance, symptoms will be the first sign of tumor recurrence in 27–50% of patients who have recurrence of colon cancer [24]. Of all of the tests that can be performed for the follow-up of patients after curative resection for colon cancer, Kievit [25], in an extensive literature

Table 40.1 Aims of colonoscopic surveillance after resection for colorectal cancer.

-
- 1 Detect synchronous neoplasia
 - 2 Diagnose and treat metachronous neoplasia
 - 3 Evaluate the anastomosis
-

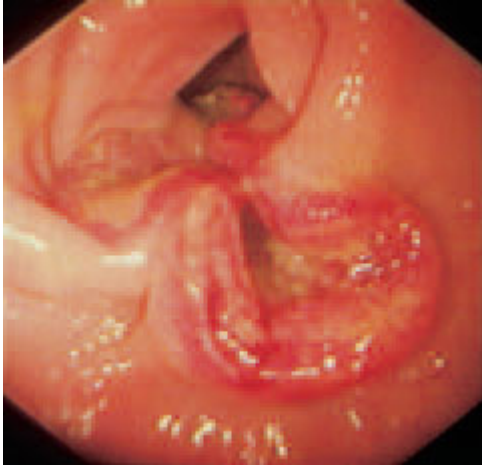


Fig. 40.1 Intraluminal local recurrence at anastomotic site, 1 year after resection for cancer.



Fig. 40.3 Anastomotic metachronous growth of villous adenomatous tissue.



Fig. 40.2 Anastomotic ulcer 6 months after resection for cancer (local recurrence of adenocarcinoma at histology).



Fig. 40.4 Anastomotic metachronous adenoma.

analysis, observed that only computer tomography and the CEA are reasonably sensitive for the detection of either hepatic metastases or local recurrences, an observation also reported in the Renahan *et al.* review [2].

There have been many review articles and analyses of literature on the subject of follow-up after curative-intent surgery for colorectal cancer, and many individual case series have been reported. The conclusions of some authors were that intensive follow-up after curative-intent colorectal cancer surgery provided no survival benefit. Others felt the opposite. Most reports that dealt

Table 40.2 Incidence of suture line recurrence and metachronous cancer after curative resection for colon cancer. (From Renahan *et al.* [2].)

Study	Total recurrent tumors (no.)	Anastomotic recurrence		Metachronous cancer
		No.	% of total	
Makela <i>et al.</i> [3]	106	3	2.8	2
Ohlsson <i>et al.</i> [4]	107	4	3.7	2
Shoemaker <i>et al.</i> [5]	325	8	2.4	2
Pietra <i>et al.</i> [6]	207	2	1.0	1
Kjeldsen <i>et al.</i> [7]	283	16	5.6	2
Total	1026	33	3.2	9

Table 40.3 Diagnostic yield of surveillance colonoscopy after colorectal cancer resection. (Data from Table 11.5, courtesy of F. Froehlich & J.-J. Gonvers)

Author	Comment	Patients (no.)	Colonoscopies (no.)	Cancer (anastomotic recurrence and metachronous)* (%)	Adenoma* (%)
Berkowitz & Kaplan [8]		52		2	17
Brady [9]	Prospective follow-up 2–8 years	207	445	7	NC
Brenna [10]	Prospective	51	51	3.9	40
Carlsson [11]	At least two postoperative colonoscopies	129	358	0.8	33
De Bosset [12]	Prospective	66	66	3	4.5
EPAGE study	Prospective. Unpublished results	284	284	3.3	19.1
Hall [13]	Prospective	54	54	2	6
Jahn [14]		539	1244	4	NC
Juhl [15]	Prospective	133	316	10	38
Kjeldsen [7]	Prospective randomized trial. Follow-up: intensive vs. no follow-up Examination at 5 and 10 years	290		19	NS
		307		15	NS
Kronborg [16]	Prospective	239	710	3.8	13
Larson [17]		68	135	7.4	35
McFarland [18]	Prospective mean follow-up 4.3 year	74	237	2.7	34
Morini [19]	Prospective. Personal communication	97	97	1	17.5
Nava & Pagana [20]	Follow-up 4 years	240	304	11.6	21.3
Patchett [21]	Prospective. Mean follow-up 5.5 year	132		6.1	11.4
Pietra [6]	Prospective. Follow-up: conventional vs intensive	103		20%	NS
		104		25%	NS
Shoemaker [5]	Prospective. Follow-up: standard vs. intensive	158	154	3.3% (5 out of 13 diagnosed by colonoscopy)	14.5%
		167	577	1.8% (3 out of 10 diagnosed by colonoscopy)	20%
Unger & Wanebo [22]	Prospective	56	56	1.8%	21%
Weber [23]	Prospective	75	197	4%	17%
Total		3698		7.6%	17.2%

* Number of patients with given findings at one or more examination. NC, not clear; NS, not stated.

with colonoscopy, in spite of the rigorously studied metaanalyses, claimed some benefit from colonoscopy as a follow-up tool.

Review of selected literature

Intensive postoperative follow-up gives no survival benefit

There are numerous reports, analyses, and metaanalyses on the rate of recurrence of colorectal cancer following curative intent surgery. Many attempts have been made to find the right follow-up regimen to seek the recurrent

cancer at a stage when a repeat operative resection could be curative. Some of the recent literature is extracted in this and the following sections to show aspects of cancer recurrence and the different results reported.

Makela *et al.* [3] followed 106 patients who had a radical resection for colorectal cancer, randomized into an intensive follow-up group and a control group. The best test for discovery of recurrence in both groups was the CEA determination. Four patients in the intensive control group had a radical resection as compared to the conventional group, and the cumulative 5-year survival was 59% versus 54%, respectively. The conclusion was that the overall recurrence rate was 41% in a conven-

tional group and 42% in the intensively followed group, but that earlier detection of colorectal cancer in intensive follow-up does not lead to either significantly increased resectability or improved 5-year survival. In this group, only three intraluminal recurrences were found in 52 patients of the intensive follow-up group. In the overall group, the CEA detected 20 of 43 recurrences, both ultrasound and endoscopy detected 4 of 43 recurrences, fecal occult blood test was responsible for detecting recurrent carcinoma in 3 of 43, and the CT examination was responsible for detecting recurrences in 2 of 43 patients.

Ohlsson *et al.* [4] found a recurrent rate of carcinoma in 33% of all patients and 33% of 107 patients that were randomized to no follow-up or intensive follow-up after surgery and early postoperative colonoscopy. These authors found no increased survival attributed to intensive follow-up after resection for colorectal cancer.

In 1998, Schoemaker *et al.* [5] reported that of 325 patients who underwent curative resection for colon cancer and were randomized into intensive or standard follow-up, yearly colonoscopy failed to detect any asymptomatic local recurrences. On completion of 5-year follow-ups, there was no significant difference in survival between the two groups, although the intensive group had follow-up consisting of yearly colonoscopy, CT of the liver, chest radiography, and clinical review and simple screening. Their conclusion was that yearly colonoscopy, liver CT, and chest radiography will not improve survival from colorectal cancer when added to symptoms and simple screening review.

Camunas *et al.* [26] found that endoscopy was useful in the diagnosis of local recurrences; however, they thought that there was no follow-up test that was capable of detecting recurrent colorectal cancer at a time when it could have been curable. These authors concluded that there was no value in an intensive postoperative follow-up program.

Intensive postoperative follow-up increases patient survival

Rosen *et al.* [27] reported that, in 2005 patients evaluated in a metaanalysis, patients who had an intensive follow-up had a cumulative 5-year survival 1.16 times higher than in the routine follow-up group, and the patients in the intensive follow-up group who had a recurrence and were operated upon had a 3.6 times higher survival rate than the control group. These authors concluded that an intensive follow-up detects more recurrent cancers that are stage amenable to curative resection resulting in improvement in survival after recurrence and an increase in the overall 5-year cumulative rate of survival. This report mirrored a previous report [28] where another metaanalysis of 3283 patients concluded that intensive follow-up using CEA blood testing can iden-

tify treatable recurrences at a relatively early stage. They concluded that treatment appears to be associated with an improved 5-year survival rate.

The Cochrane group [29] published their metaanalysis and concluded that there was an overall survival benefit for patients undergoing more intensive follow-up as opposed to less intensive. They concluded that there was a mortality benefit in performing more tests rather than fewer tests, but because of the wide variation in regimens in all of the studies that they examined, it was not possible to infer from the data the best combination or frequency of routine visits, blood tests, endoscopic procedures, or radiologic investigations.

Bergamischi and Arnaud [30] concluded that regular follow-up examinations could detect recurrences at an earlier time so that curative surgery could be performed as compared to patients whose follow-up program consisted of undergoing nonscheduled visits for symptoms.

Secco *et al.* [31] found a significant improvement in overall survival of patients who had intensive follow-up as compared to minimal surveillance. However, in this group of patients, 52.6% of patients in the intensive follow-up group had recurrent carcinoma as did 57.2% of those undergoing minimal follow-up.

Pietra *et al.* [6] randomized 207 patients who had curative resection for colon cancer into a conventional and an intensive follow-up group. The conventional group was seen twice in the first year, and yearly thereafter. Patients in the intensive follow-up group were seen every 3 months during the first 2 years, at 6-month intervals for the next 3 years, and then had an annual visit. Local recurrence was detected in 20 of 103 patients in the conventional group and 12 of 104 patients in the intensive group. Twenty of the 103 patients in the conventional follow-up group had recurrent tumors, and 26 of the 104 patients in the intensive follow-up group had local recurrence. Sixty per cent (12 cases) of local recurrences in the conventional group and 92% (24 cases) in the intensive group were detected during scheduled visits. Local recurrences were detected earlier in patients in the intensive follow-up group (10 months vs. 20 months) and curative reresection was possible in 10% of patients in the conventional group, compared to 65% of patients in the intensive follow-up group. The 5-year survival rate for patients in the conventional follow-up group was approximately 60% and in the intensive follow-up group 73%. These data support the use of an intensive follow-up plan after primary resection of large bowel cancer.

Colonoscopy follow-up is worthwhile

In a study of 460 patients who had a primary resection for colorectal carcinoma, 31 patients were prospectively followed by colonoscopy [32]. Twenty per cent had a synchronous adenoma at the time of the initial resection

for carcinoma, and three-quarters of these patients also developed metachronous adenomas. Of the 183 patients who did not have a synchronous adenoma, about half developed metachronous adenomas so that overall, 56% of patients developed a metachronous adenoma. Four patients developed metachronous carcinoma, all found after a mean interval of 7.7 years. These four patients had metachronous adenomas on multiple occasions prior to the development of metachronous carcinoma. The conclusion was the presence of synchronous adenomas and recurring metachronous adenomas is significant and warrants a more intensive follow-up program to ensure the early diagnosis and cure of any metachronous carcinoma.

Castells *et al.* [33], in a randomized follow-up of 199 patients who had undergone radical primary surgery for colon cancer, found that there were no differences in the overall recurrence rate (38% vs. 41%) and that a curative-intent reoperation was possible in 34% of those in the intensive cohort, but only 12% in the noncompliant cohort. Patients were offered a surveillance program consisting of laboratory investigation including CEA every 3 months, physical examination and abdominal ultrasound or CT every 6 months, and chest X-ray and colonoscopy yearly. The overall probability of survival was 63 versus 37% at 5 years. The conclusion was that systematic postoperative surveillance increases both the rate of tumor recurrence amenable to curative intent surgery and the rate of survival.

Staib *et al.* [34] analyzed 1044 colorectal cancer patients who had intensive follow-up consisting of endoscopy, chest X-ray, abdominal ultrasound, and pelvic CT scans. Thirty-three per cent of patients (350/1054) had a recurrence of carcinoma, and 56 of 350 had an attempt at curative resection. His conclusion was that abdominal ultrasound, endoscopy and CEA determination at 6-month intervals for 2 years and annual intervals for the next 3 years best served to identify patients whose recurrence could be amenable to curative resection.

Barillari *et al.* [35] evaluated the effectiveness of routine colonoscopy along with blood studies for tumor markers for the diagnosis of recurrent cancer. Four hundred and eighty-one patients were followed with clinic visits and CEA every 3 months with colonoscopy preoperatively, at intervals of approximately 1 year after surgical treatment, and then every 1–2 years or when symptoms appeared. About 10% of all the patients developed an intraluminal recurrence, and more than half of these lesions arose in the first 24 months following surgery. Patients with left-sided tumors had a higher risk of developing recurrent intraluminal disease. Twenty-nine patients had a second surgical operation with a 5-year survival of 70.6%. Twenty-two patients were asymptomatic when the recurrence was diagnosed and 12 of these had radical resection; of the 24

symptomatic patients, only five were amenable to radical resection surgery. CEA was the first sign of recurrence in eight cases. The authors thought that colonoscopy should be performed within the first 12–15 months after operation and that intervals of 2 years between examinations seemed sufficient to guarantee early detection of metachronous lesions.

Eckhardt *et al.* [36] followed 212 patients. Eighty-eight patients adhered to an endoscopic surveillance program and 124 did not. Tumor recurrences occurred in 10% of those in the endoscopic surveillance group and in 14% of the noncompliant patients. Patients with asymptomatic tumor recurrences survived longer than those who were symptomatic at the time of resection. The overall survival rate was significantly higher in compliant patients (80% 5-year survival) than in noncompliant patients (59% 5-year survival). Noncompliance increased the risk of early death by a factor of 2.5. They concluded that postoperative endoscopic surveillance leads to early tumor detection and is associated with an improvement in survival in patients with colorectal cancer.

Houry *et al.* [37] reported that curative resection was attempted in 32 patients who had local recurrence following a resection for carcinoma of the colon and rectum. The previous anastomosis was involved in 25 of these patients. At laparotomy, 12 patients had disseminated lesions, and five of these had complete resection of lesions. Twenty patients had local recurrence without metastasis; five of them were unresectable but 15 were amenable to curative secondary resection. After curative resection, the median survival time was 34 months, 5-year survival was 26%. After palliative surgery, the median survival time was 5 months, however, one patient is still alive 12 years after radiation therapy.

Lautenbach *et al.* [38] reviewed charts in 290 patients who had curative resection. Colonoscopy was performed every 6 months during the first year then every 1–2 years or when symptoms appeared. Overall, 31 (10.7%) developed recurrent disease with a median time to diagnosis of 20 months. Of these 31 recurrences, 14 (45.2%) were local (12 were asymptomatic). Nine of the local recurrent patients were able to undergo curative secondary resection. Of 19 symptomatic patients, only three (15.8%) were amenable to curative resection. Because of surveillance colonoscopy, 13 asymptomatic patients (4.5%) had curative resection for localized recurrent disease.

Buhler *et al.* [39] followed 188 patients operated on for carcinoma and all had colonoscopy follow-up. Twenty patients (10.6%) had local recurrence of cancer. Eleven of these patients had symptoms that triggered colonoscopy but nine were asymptomatic and had routine colonoscopy. In six of nine asymptomatic patients, a curative resection was performed, but this was not possible in any of the 11 symptomatic patients. Their conclusion

was that long-term survival may be expected in patients with local recurrences detected at an asymptomatic stage by regular colonoscopic examinations rather than waiting for symptoms to occur.

Stulc *et al.* [40] reviewed 158 patients with local recurrent carcinoma. Eighteen patients (11.4%) had a recurrent lesion at the site of anastomosis. All recurrences were found within 27 months of the primary surgery.

Pihl *et al.* [41] reported that 2.7% of patients who had a potentially curative resection for colon cancer had recurrence at the site of anastomosis. Fourteen of 35 were treated by further operation with curative intent.

Togashi *et al.* [42] studied the yield of postoperative colonoscopy in 341 patients who had colorectal cancer surgery, and found that two groups of patients have an increased risk of metachronous colorectal cancer: those with concurrent adenoma, and patients who had a history of an additional noncolonic malignancy.

In an extensive analysis of literature, Kievit [25] reported that 53 articles contained meaningful data about follow-up strategies concerning cancer recurrence, including 24 305 patients where the mean follow-up time varied from 1.9 to 10 years with an overall cumulative cancer recurrence varying from 11.3 to 84%. In this systematic literature review, approximately one-third of patients (37.5%) who had curative surgery for colorectal cancer had a recurrence within 5 years of the initial surgery, while two-thirds were still cancer-free 5 years after initial surgery: "Approximately 1 out of every 8 patients will experience local recurrence, approximately 1 out of every 5 will develop metastatic disease of the liver, and approximately 1 out of every 12 will experience pulmonary metastatic disease." It is important to note that the term "local recurrence" refers to recurrent cancer confined to the abdomen, without distant metastases, and includes, but is not limited to, anastomotic recurrence. According to most of the reports in the literature, the majority of testing during follow-up after colorectal cancer resection will be negative, and most tests will show a false positive at least 10 times more often than being a true positive. However, the exception to the large number of false-positive results is the follow-up procedures performed by colonoscopy, where most positive follow-up tests will be true positives. The use of endoscopic ultrasound increases the yield of finding recurrent cancer. The ratio of false positive to true positive will be approximately 0.6 with endoscopy, whereas the addition of endoscopic ultrasound for the detection of local recurrence increases the ratio to 4.0.

Since one of the aims of follow-up is to provide an early diagnosis at a time when the recurrent tumor is amenable to a repeat operable intervention, Kievit [25] calculated the proportion of recurrences detected that were successfully reoperated upon. The results were that in only 2.4% of patients with local recurrence can a

long-term cure (5-year survival) be achieved by regular follow-up examinations. However, the data for patients with metastasis to the liver provides much better survival results than do the data for patients with local recurrence, with up to 8.5% of all patients with liver metastasis being alive 5 years after a second operative resection. The conclusion by Kievit, who analysed a total of 267 articles concerning colon cancer resection and follow-up, was "... support that is as good or even better (than provided by the surgeon) can be provided by a patient's general practitioner or by specialized nursing personnel (therefore) there is no need for routine follow-up to be performed." However, other investigators [2] demonstrate that intensive follow-up does improve the possibility of detecting recurrent cancer at a stage when a potentially curative reoperation can be performed.

Colonoscopic examinations are not the most valuable follow-up procedures. Renahan *et al.* state that "although many clinicians favor colonoscopic surveillance (intramural detection), this is not justified." They, and others noted that intraluminal recurrences and metachronous cancers were distinctly uncommon, irrespective of the intensity of follow-up. A recent Cochrane review [29] stated that "the results of (our) review support the general principle of clinical follow-up for patients with colorectal cancer after curative treatment. The exact details of the optimal follow-up regimen still need clarification. In a report of second carcinomas developing in patients who have had a primary resection for a previous carcinoma, 3.4% were found to have synchronous carcinomas. The vast majority of these were distal to the splenic flexure, but only 42% were detected preoperatively. Ten patients had 'early' metachronous cancers found less than 3 years after the initial surgery. Four of these patients had negative findings on the initial barium enema examination but a full colonoscopic examination of the colon was not performed at the initial presentation in six patients. The conclusion was that all patients who have a primary colorectal carcinoma should have a full examination of the colon, either by pre- or postoperative colonoscopy" [43].

Kjeldsen *et al.* [7] followed 597 patients who had radical surgery for colorectal carcinoma. Patients were randomized into frequent follow-up, or virtually no follow-up. In the latter group, examinations were performed at 5 and 10 years after surgery. The results were that recurrence was equally frequent between the two groups, but the diagnosis was made 9 months earlier in the group who had intensive surveillance, and a greater proportion of the patients in that group had surgery with curative intent than those with a less intensive follow-up. However, there was no improvement in overall survival or in cancer-related survival. The authors concluded that patients who were subjected to intensive

follow-up had an earlier diagnosis of recurrent tumor, but the survival results suggest that any major improvement by intensive follow-up is unlikely.

Stigliano *et al.* [44] followed 322 patients. All patients had colonoscopy yearly for the first 5 years and then every 2 years. Anastomotic recurrences were observed in 22 of 253 patients who underwent resection for rectal or sigmoid adenocarcinoma. Sixteen of 22 were submitted to a second curative resection with a median survival of 35 months. Metachronous adenomas were found in 24 patients with metachronous cancers. Their conclusion was: in patients resected for rectal or sigmoid carcinoma, a sigmoidoscopy should be performed every 6 months for the first 2 years for the early detection of anastomotic recurrences. In all cases, a colonoscopy should be performed every 5 years after surgery to detect metachronous lesions. Before surgery, a "clean colon" should always be established to detect possible synchronous lesions. Harris *et al.* [45] reported on 1031 patients who had a curative resection for colonic adenocarcinoma. Local recurrences were seen in 32 patients (3.1%). The mean time to local recurrence was 13 months.

Rectal cancer

Cancer of the rectum has had the reputation for high rates of recurrent tumor. Rates of local recurrence have varied from 15 to 45% [46]. These high rates for recurrent tumor in the area of the original tumor have been studied, and may be related to the type of blunt dissection of the rectal fascia usually employed for the remove of these tumors. Blunt dissection often does not remove all of the local tissue, which may contain malignant cells. Most recurrent tumors will be at or posterior to the anastomosis [47]. Recent surgical advances combined with preoperative radiotherapy have resulted in marked improvement of the 5-year surgical rate in patients with rectal cancer [48–50]. The type of surgery currently used, with better results, is total mesorectal excision during which the entire mesorectum is enveloped and resected by precise sharp dissection [46] using the advanced surgical technique and preoperative radiation therapy; the local recurrence rate was 2.4%. In this study, radiotherapy had no effect on tumors located more than 10 cm above the anal verge.

In spite of the lower rate of recurrence of rectal cancer with the recent combined approach, the incidence of distant recurrence was not different from a group who did not receive radiation therapy.

With the new approaches to therapy, the incidence of recurrent rectal cancer is similar to that of colon cancer. Since cancer in the colon or rectum has a low incidence of intraluminal recurrence, there is little therapeutic advantage to repeated colonoscopy and/or flexible

sigmoidoscopy (with or without endoscopic ultrasonography) in the follow-up of these patients, except for those intended to seek and remove metachronous neoplasms.

Stenosis

Following surgical anastomosis of the colon, stenosis may occur at the staple/suture line, and can be treated with endoscopic dilation. It has been reported, in 39 consecutive patients with postoperative benign colorectal stenoses, that all patients responded, and no recurrence of symptoms was demonstrated during a follow-up with a mean time of 2 years [51]. Benign anastomotic strictures may occur in up to 22% of patients after colorectal resections.

In patients having low anterior resections, endoscopic Savary dilators were used in patients who presented with stricture symptoms after a mean period of 7.7 months after low anterior resection [52]. In three of the 18 patients, stenosis was caused by local recurrence. After dilation, in 10 of the remaining 15 patients, symptoms disappeared, in five patients there was only partial improvement, and three of these required another type of treatment (two were treated endoscopically and one surgically). Four patients received radiotherapy and developed a stricture at the anastomosis; two of these had successful dilations. No complications were observed.

In patients who had a left hemicolectomy or an anterior resection, with strictures less than 2 mm in diameter, dilation was performed using 30–40 mm diameter pneumatic dilators ordinarily used for achalasia dilation [53]. Seventeen of the 18 patients underwent a total of 45 dilating sessions, one patient was excluded because of a cancer recurrence at the suture line. Two complications were observed: a tiny bowel perforation in one and transient mucosal bleeding in another. Good long-term clinical results were achieved in 16 patients (94%). One report in the literature [54] described an occlusive web at a colo-anal anastomosis after proctosigmoidectomy. Transrectal ultrasound guidance was used to pass a needle across the web, permitting placement of a guidewire across the occlusion and subsequent successful balloon dilation. Eight patients were described who had a colo-colon anastomosis with stricture [55]. Following dilation, four of the five symptomatic patients were relieved of their symptoms, and the strictures remained patent. Four other patients required redilation at 2 months. One patient had a colonoscopic perforation during repeat attempts at dilation of a stricture. Pietropalo *et al.* reported [56] that balloon dilation was more effective than bougienage for treating postoperative colonic strictures. The overall failure rate was 2.5% with no morbidity or mortality in 42 patients with stenosis.

Appearance of anastomosis

Ulcers may occur at an anastomotic site [57]. In the investigation of patients with iron deficiency anemia and evidence of gastrointestinal blood loss, colonoscopy was performed, and in six patients with colonic anastomoses, ulcers were seen at the anastomosis. The time delay between surgery and detection of anastomotic ulcer ranges from 1 to 28 years. Three patients in this series had previously undergone surgical resection for anastomotic ulcers, with the revision being of no benefit, with recurrent ulcers and continued bleeding. Weinstock and Shatz [58] during the evaluation of 321 patients having had resections for colonic neoplasms reported that inflammatory polyps at the anastomosis were the most commonly observed abnormality. Staples or sutures were visible in 11% (Figs 40.5, 40.6) and strictures were seen in 7%. Recurrent carcinoma at the anastomosis



Fig. 40.5 Staple near a blind end at a colon resection site. The anastomosis is distal to this area.



Fig. 40.6 Staple at anastomosis. Beyond the anastomosis are two lumens; the upper is the blind end, the lower is the proximal end.

was found in 6 of 116 patients, occurring between 0.5 and 2 years after surgery. Recurrent carcinoma usually appeared as ulcerated submucosal lesions, bulky luminal masses, or polypoid lesions. In two patients however, mucosal erythema, edema and friability of the anastomosis were the only endoscopic evidences of underlying carcinoma. Another report of the appearance of anastomoses stated that 117 consecutive colonoscopies were performed for evaluation [59]. The most common anastomotic feature was the presence of large blood vessels around the anastomosis, occurring in 80% of patients. A fine white line at the anastomotic edge was seen in 55% of patients. Radial white scars, indicative of suture tracks, were seen in about 40% of patients, with exposed sutures in 12% and exposed staples in 24% of patients.

Evaluation of a colostomy

Patients may have a colostomy for protection of a distal anastomosis. This colostomy is typically a loop of bowel with two limbs, proximal and distal. If colonoscopy is to be performed prior to closure of the colostomy (usually for evaluation of the colon for synchronous lesions), both limbs must be intubated. The preparation is similar to that for an intact colon, but irrigation into the distal limb may be required or enemas per rectum can be administered to cleanse that portion. Intubation of both limbs can be accomplished with the patient supine, but the left lateral position may afford the best visualization of the rectum.

If the colostomy is an end colostomy, it is necessary to know whether the rectum and anus have been resected or whether there is a segment of rectum that has been closed and left *in situ* (Hartmann pouch).

End colostomies can be prepped and intubated as above, but inspection of the rectal segment can usually be accomplished without the requirement for enemas since that blind pouch is not in continuity with the fecal stream.

Bypass colitis

In the event that a segment of colon has been bypassed from the fecal stream, mucosal abnormalities may develop and resemble idiopathic inflammatory bowel disease [60]. The surface may be friable, telangiectatic, and granular. The area may bleed spontaneously, and biopsies will reveal chronic inflammatory changes.

Summary

In patients operated upon for cure of colorectal cancer, one-third to one-half will have recurrent cancer, but intraluminal recurrences are relatively uncommon, being seen in 3–14% of cases. All patients must have a full

colonoscopic evaluation of the colon in the perioperative period to permit a complete examination of the bowel. This examination will allow detection of synchronous colon cancer and adenomas. If that examination is negative, subsequent colonoscopy should be offered at 3 years and if normal, every 5 years [61]. Most recurrences occur within 2 years of the initial surgery. More advanced stages of the primary tumor are associated with a higher recurrence rate. Because most local recurrences are extraluminal, it has been considered that colonoscopy alone is of limited usefulness in the detection of recurrences. A US Multisociety Task Force on colorectal cancer [61] stated that "although colonoscopy can detect recurrent colon cancer, anastomotic recurrences occur in only about 2% of colon cancers and are generally accompanied by intra-abdominal disease that cannot be resected for cure." Because of the low, but not zero, incidence of recurrent cancer at the anastomosis, Rex [46] has suggested "surveillance at 1 year after the clearing colonoscopy, followed by colonoscopy at 3–5 years intervals, appears reasonable and safe for most patients." Rectal cancer, treated with current neoadjuvant chemoradiation and total mesorectal excision, has a similar prognosis, and falls into the same surveillance schema as colon cancer.

Most postoperative strictures are not due to recurrent cancer, and can be dilated successfully via standard colonoscopic techniques with balloon or bougies (if the stenosis is in the rectum).

The endoscopic appearance of the anastomosis has been reported in only a few descriptive articles, but the most commonly found abnormalities are large blood vessels at the anastomosis or inflammatory polyps.

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Chapter 41

Magnifying Colonoscopy, Early Colorectal Cancer, and Flat Adenomas

Hiroshi Kashida and Shin-ei Kudo

Introduction

Chromoendoscopy or dye endoscopy is a technique that employs dyes that are sprayed onto the mucosal surface during the endoscopic examination for confirmation and detailed observation of gastrointestinal lesions. Although used in the upper gastrointestinal tract, dye spraying is particularly valuable in colonoscopy. The procedure involves spraying small amounts of dye onto the intestinal wall when abnormal findings are identified. Chromoendoscopy is useful for confirming small colorectal lesions for determining their lateral extent, and for clarifying their gross configuration; especially the presence or absence of a depression within them.

Materials and methods for chromocolonoscopy [1]

Two methods are popular at present, one involves using the dye to enhance visualization of the surface topography, and the other uses different colored chemical compounds that stain the surface cells.

Contrast method

The dye accumulates in concave areas and clarifies unevenness of the colon wall. Usually 0.2% indigo carmine solution is employed although several compounds are available. Sprayed dye is retained in depressed portions, which makes unevenness of the lesion conspicuous. Even lesions with an apparently flat surface to gross visual inspection are often minimally depressed and/or elevated when the irregularity is augmented by dye which fills crevices and runs off the higher elevation.

Staining method

This method relies on the capability of colonic surface cells to absorb fluid. A common dye is 0.05% crystal violet solution which stains the absorbent epithelium of the large bowel. The orifices of the crypts themselves are not stained. This technique is critical in evaluating the pit pattern with magnifying scopes. Frequently both dyes, indigo carmine and crystal violet, are used consecutively

to achieve differential effects which are amplified by using magnification endoscopy. The first dye should be washed away before the other dye is sprayed.

Procedure

When a lesion or an abnormal area is encountered, feces or mucus over that portion should be washed away before the dye is applied. Water is a sufficient flushing agent, and no additives are necessary. Contrast dye such as indigo carmine can be injected through the forceps channel with a syringe. A staining dye such as crystal violet is usually injected through a catheter. The catheter permits precise application just over the lesion. A large volume of contrast dye should be avoided because it will result in excessive darkening of the image. Any excess must be removed by suction or washed with water before observation. It takes a minute for crystal violet to stain the mucosa after spraying.

Magnifying endoscopy

Dye spraying can be employed during routine examination with an ordinary colonoscope, but it is especially useful when combined with magnifying colonoscopy. Magnifying colonoscopes or zoom colonoscopes became commercially available in Japan about 10 years ago, and are now being used throughout the world. Zoom colonoscopes have all the basic functions of conventional colonoscopes, therefore they can be used during routine examinations with a standard view. The magnified view can be obtained instantaneously by rotating the magnification knob of the scope or stepping on the foot controller.

The combination of chromoscopy and magnifying colonoscopy is useful for the differential diagnosis of a colorectal lesion, and for predicting the depth of a cancer, because it enables observation of the microanatomy of the lesion.

Gross appearance and chromoendoscopy

Classification of the gross appearance of colorectal adenomas and early carcinomas has been proposed by the Japanese Research Society for Cancer of the Colon

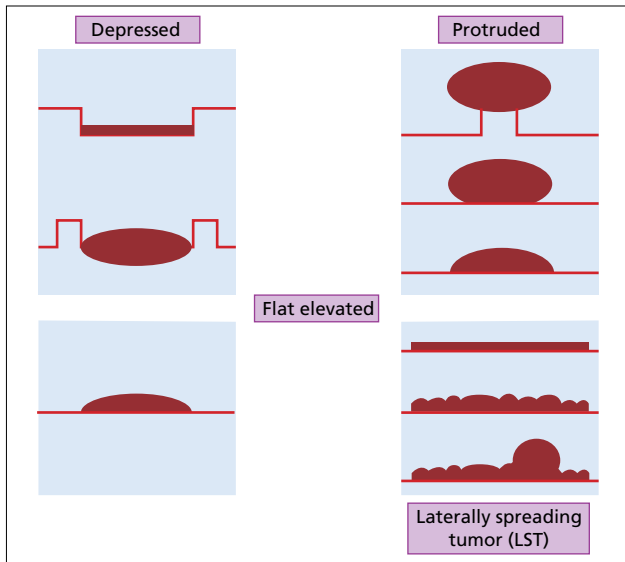


Fig. 41.1 Classification of gross appearance of early colorectal carcinoma and adenoma.

and Rectum, but it is fairly complicated. We use a more simplified classification which divides all lesions into three categories: protruded, flat elevated, and depressed (Fig. 41.1). Recognition of depression is very important, because depressed lesions often harbor invasive cancer despite a small diameter (even when less than 10 mm in size) (Table 41.1). Some lesions having a depression are actually elevated above the surface as a result of submucosal invasion and proliferation of the tumor cells. Such lesions must not be mistaken for ordinary elevated neoplasms, as they are quite different in biologic behavior. Chromoendoscopy is particularly essential for diagnosing these lesions, as it is possible to overlook the depressed area in the midst of a diffusely elevated polyp.

Surface structures of the colon

The surface microstructure of colorectal epithelium was first analyzed using dissecting microscopes on resected specimens in the 1970s. The normal surface mucosal morphology was described by Bank *et al.* [2], and subsequent investigators have detailed the structural altera-

tions in colorectal epithelial neoplasms. In the early 1980s Nishizawa *et al.* [3] reported on the characteristic surface structural difference between normal colonic mucosa, adenoma, and adenocarcinoma. Studies on the surface microstructure had been started on stomach diseases earlier, but these were not pursued at that time because the stomach mucosa is often too damaged by the erosive effect of gastric acid and/or the inflammatory changes induced by *Helicobacter pylori* infection, to obtain a clear magnified image. On the other hand, a normal colon is usually free of superficial inflammatory change, thus rendering the large bowel mucosa suitable for magnifying observation.

The development of magnifying fiber colonoscopes enabled visualization of the microstructure of the mucosa and various colorectal lesions *in vivo*, instead of *in vitro* [4]. The advent of commercially available magnifying videocoloscopes with high-power resolution in the 1990s accelerated the study of the microanatomy of colonic lesions [5]. The combination of chromoscopy and magnifying colonoscopy is useful for detecting small localized lesions, for their differential diagnosis, and for determining not only the lateral extent but also their depth [6]. Some investigators have also reported on analysis of the diffuse mucosal changes in inflammatory bowel diseases using magnifying colonoscopes.

Pit pattern classification

In the parlance of chromoscopy, the openings of the colonic crypts are referred to as “pits,” and the specific arrangement of the openings of the glands in normal mucosa and in various kinds of lesions is called the “pit pattern.” Although there have been a variety of different classifications, the most frequently used at present is our description [7], which divides the pit patterns into six groups: types I, II, III_L, III_S, IV, and V. These specific pit patterns can be used to predict the histologic structure of a lesion. The pits of normal mucosa (Kudo’s type I) are round and regular in both size and arrangement. The pits of hyperplastic polyps (type II) are larger than normal pits, and instead of round, are star or onion-like, but are regularly arranged. Types I and II pit patterns are characteristic of nonneoplastic lesions.

Table 41.1 Rate of invasive cancer in colorectal neoplasms.

Appearance of colorectal neoplasm	Diameter of lesion (mm)				Total			
	< 10	11–20	> 21					
Depressed	64/343	18.7%	51/73	69.9%	12/14	85.7%	127/430	29.5%
Flat elevated	3/6820	0.04%	19/614	3.1%	48/199	24.1%	70/7633	0.9%
Protruded	41/8754	0.5%	115/1183	9.7%	50/165	30.3%	206/10102	2.0%
Total	118/15917	0.7%	185/1870	9.9%	110/378	29.1%	403/18165	2.2%

Lesions which show compactly arranged pits that are smaller than normal (type III_s; “s” stands for “short” or “small”) are characteristically depressed. Adenomas with small, compact crypts are not frequently found, but are considered to be precursors of de novo advanced cancers. The small pits reflect the crowding of cells in these precursor lesions.

In polypoid adenomas, the pits often appear elongated (type III_L; “L” stands for “long” or “large”) and sometimes branched (type IV). Types III_s, III_L and IV are adenomatous pit patterns.

Type V pit pattern is seen in cancers, and subdivided into two groups. In deeply invasive or advanced cancers the surface of the lesion is rough and often ulcerated; therefore it is almost devoid of pits and looks unstructured. Such a pit pattern is named V_N (“N” stands for “nonstructural”). Opposed to the findings in advanced cancers is the more structured pit pattern in severely dysplastic adenomas and minimally invasive carcinomas where the pits are in a somewhat irregular array, but not in a completely chaotic arrangement. Such an irregular pattern has been named type VI (“I” stands for “irregular”).

Many studies using magnifying colonoscopes show that the observed pit pattern corresponds well to those seen with dissecting microscopes.

Surface pit pattern and the structure of colonic glands

There have been several attempts to evaluate and further understand the three-dimensional structure of localized colonic lesions. The authors compared the pit pattern at colonoscopy or stereomicroscopy with histologic sections taken in the horizontal axis (parallel to the mucosal surface) [7]. Precise calibration with microscopy [5] permits measurement of the width of individual pits of type I, II, III_L, III_s, and IV. These widths were: 70 ± 20 μm,

90 ± 20 μm, 220 ± 90 μm, 30 ± 10 μm, and 930 ± 320 μm, respectively.

Similar results were reported recently by Tamura *et al.* [8], who studied the colonic glands using scanning electron microscopy (SEM). The first studies concerning the analysis of pit patterns using SEM were reported by Shields *et al.* [9], Rubio *et al.* [10], and Sano *et al.* [11]. This method, using much higher magnifications than those achieved during endoscopy, is costly and time-consuming. Nevertheless, SEM studies are of considerable academic importance for the understanding of the three-dimensional structure of colonic polyps and cancers.

Rubio and his colleague [1,12] are attempting to plot out a planimetric tridimensional histologic pattern incorporating the surface profile from biopsy specimens, using scanned images of serial tissue sections manipulated with computer software.

Gross appearance of colorectal neoplasms and their pit pattern (Table 41.2)

Considerable interest has developed in endoscopic evaluation of the surface pit pattern in both normal and pathologic conditions. There are definite correlations between the gross appearance and the pit pattern of a colorectal lesion. Depressed lesions present with either types III_s or V pit pattern; the latter implies that the lesion is cancerous. Almost all flat and protruded neoplasms have pit patterns that correspond to types III_L or IV pits.

Pit pattern and histology (Table 41.3)

The pit pattern closely correlates with the histology of the lesion. Lesions which present only with type II pit pattern are considered nonneoplastic, and are seldom removed. Once this pattern is identified, the overall

Appearance of colorectal neoplasm	Pit pattern type					Total
	III _L	IV	III _s	V		
				I	N	
Depressed	62	1	234	16	117	430
			54.4%	3.7%	27.2%	100%
			└──────────┬──────────┘ (85.3%)			
Flat elevated	3944	299	58	117	56	4474
	88.2%	6.7%				100%
	└──────────┬──────────┘ (94.8%)					
Protruded	5926	1872	8	228	66	8100
	73.2%	23.1%				100%
	└──────────┬──────────┘ (96.3%)					
Total	9953	2172	300	361	239	13 004

Table 41.2 Gross appearance of colorectal neoplasm and pit pattern.

Table 41.3 Pit pattern of colorectal neoplasms and histology.

Pit pattern type	Adenoma		Submucosal cancer (T1)	Total
	Low-grade	High-grade		
III _s	202 88.6%	17	9 3.9%	228
III _L	7832 95.7%	354	0 0%	8186
IV	1473 76.6%	376	73 3.8%	1922
I	127	145 62.5%	67	339
V				
N	14	58	166 69.7%	238
Total	9648	950	315	10 913

accuracy of pit pattern analysis is 95.5% for differentiating between neoplastic and nonneoplastic colorectal polyps [1].

In neoplastic lesions, pit pattern analysis is useful for distinguishing between adenomas, early signs of cancer, and invasive cancers. The majority of polyps which have only type III_s, III_L, or IV pits are low-grade adenomas. The tumors of type VI encompass a variety of lesions from benign adenoma to invasive carcinoma. These lesions with type VI pit pattern are removed endoscopically, and additional treatment consisting of surgical colectomy and lymph node dissection is considered after histologic analysis of the resected specimen. Seventy per cent of the lesions with type VN pit pattern are invasive cancers, which means that these lesions are not resected endoscopically but treated surgically from the time of first diagnosis.

It cannot be denied that there are some limitations to the pit pattern diagnosis, as pit patterns reflect the changes on the surface of lesions without the capability of knowing what lies deep to the visible portion of the lesion. However, investigators agree that changes in the deeper layers are also reflected on the surface to some extent; therefore pit patterns can be used as surrogate markers reflecting abnormal cellular proliferation at the basal layers of the colonic crypts. Pit pattern analysis is beginning to be widely understood and is becoming widely embraced throughout the world [13–15].

So-called flat adenoma and depressed lesion

There is some confusion about depressed and flat lesions among western colonoscopists. It is possible that part of the difficulty in acceptance of this concept is that “flat” adenomas are not absolutely flat, but are often slightly elevated. The terminology “flat adenoma” was coined by Muto *et al.* [16] in 1985. It referred to a type of neoplastic lesion that was slightly elevated and plateau-like, with

a reddish surface and sometimes a central depression. The definition of “flat” requires that the thickness of the adenomatous component is not more than twice that of the adjacent nonneoplastic mucosa. In addition to the flat-surfaced lesion, a depressed variety of flat adenoma was described, which started the confusion regarding depressed lesions and flat elevated adenomas. Some benign adenomas appear to have a depression and resemble depressed-type early cancers [17]; however, the depression in a “depressed lesion” is rather extensive and clearly demarcated. By contrast, the “depression” in flat elevated benign adenomas is actually a shallow concavity or an ill-defined pseudodepression. Flat elevated adenomas with a pseudodepression should be differentiated from truly depressed lesions, because the former are almost invariably benign. A critical part of the understanding of this distinction is that depressed lesions are not to be considered to be flat adenomas, but should be regarded as a different entity. Confusion over this concept has been compounded because many authors discuss flat adenomas and depressed lesions together. Their nature should be discussed separately. Comprehensive terms such as “nonpolypoid” or “superficial” may also be misleading and the use of these descriptions should be chosen carefully.

Laterally spreading tumors (LST) are flat elevated adenomas which spread extensively along the colonic wall and which by definition are very short in height [5] (Figs 41.2, 41.3). These lesions are sometimes malignant, but not as advanced as one would expect when compared with their large diameter.

Characteristics of flat elevated adenomas and depressed lesions

When Muto *et al.* [16] reported on 33 “flat adenomas” they pointed out that more than 40% of such lesions contained focal carcinomas or severely dysplastic tubules.

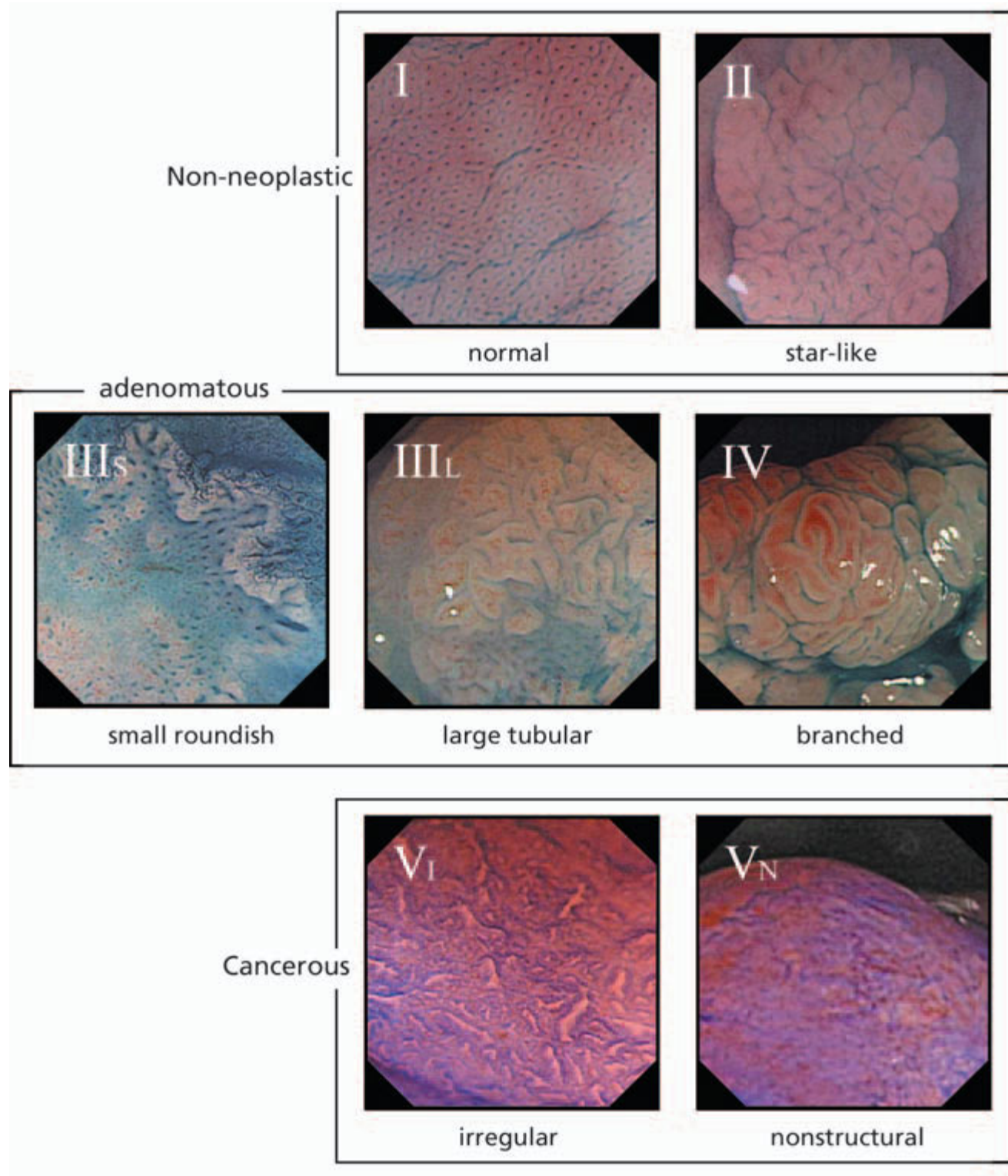


Fig. 41.2 Pit pattern classification.

In the series of Wolber and Owen [18], the proportion with high-grade dysplasia in 29 flat adenomas was virtually identical to that in the study of Muto *et al.* Because of our deep interest and with the use of chromoendoscopy

and magnification colonoscopy, there is no doubt that we have encountered far more cases of flat elevated adenomas than other investigators (Table 41.1). Invasive carcinoma is present in 0.04% of flat elevated adenomas less than 10 mm in diameter and 3.1% for those 11–20 mm. The rate of invasive cancer is slightly lower than,

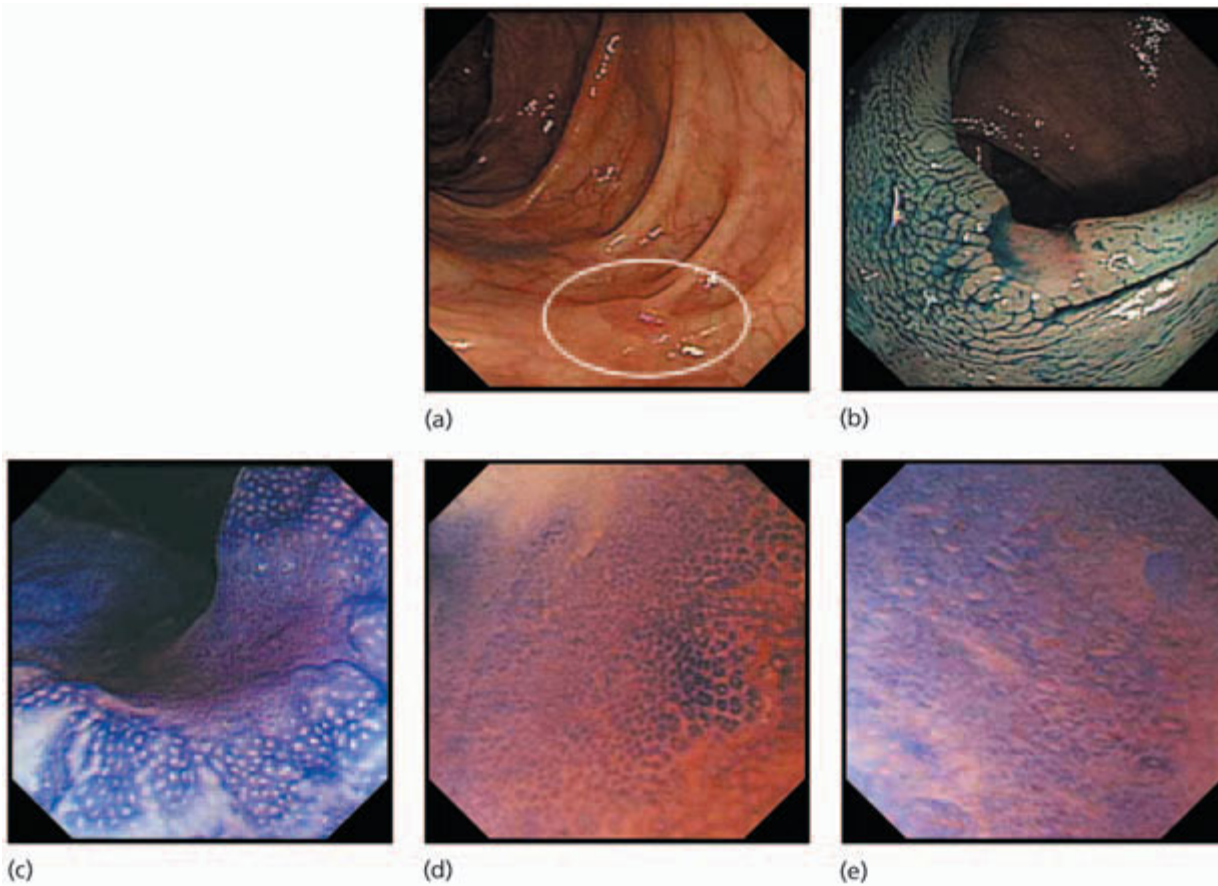


Fig. 41.3 A case of a depressed lesion in the transverse colon, 9 mm in diameter. (a) Ordinary colonoscopic view (circle surrounds the lesion). (b) Chromoendoscopy with indigo carmine. (c) Chromoendoscopy with crystal violet and slight

magnification. (d) Highly magnified view shows small compactly arranged type III pits. (e) Pit pattern was slightly irregular in part (type VI). The lesion was endoscopically removed and was shown to have minimally invasive cancer.

but not remarkably different from, that in protruded polyps (Table 41.1) (Figs 41.4–41.6). Therefore, our findings are that flat lesions are usually benign or only focally malignant and grow very slowly, and do not become invasive cancer until they are rather large. By contrast, the rate of invasive carcinoma in depressed lesions is 18.7% when the lesion does not exceed 10 mm and 69.9% in those of 11–20 mm. Cancer in depressed lesions grows rather rapidly, advancing at an early stage [19,20]. Muto *et al.* [16] were right in pointing out that lesions “. . . with a central depression” were more malignant than others, but their original description did not emphasize the differentiation between truly depressed lesions and flat elevated adenomas with a pseudodepression.

Diagnosis of flat elevated adenomas and depressed lesions

Whether depressed or not, there have been relatively few cases of nonpolypoid early colon cancers reported

by western researchers [21–25]. We think the cause is that candidate lesions are overlooked as a result of misunderstanding of the concept or because proper diagnostic methods are not used [26,27]. High-magnification colonoscopy and chromoscopy clearly improve the detection of nonpolypoid neoplastic lesions [28,29].

Despite the term “flat,” there are few adenomas that are perfectly flat, and the majority of small adenomas are slightly elevated [17]. Detecting a tiny area with a slight color change is important; some lesions are slightly reddish, others may appear pale or discolored [30]. Bleeding spots, interruption of the capillary network pattern, or slight deformation of the colonic wall may suggest the existence of a neoplastic lesion [5].

Some flat elevated adenomas appear to have a depression at a first sight, but it may not be a true depression [17]. When a topical spray of dye is applied over a depressed lesion, a true depression appears rather extensive and has a roundish shape, while the “depression” of the flat adenomas is ill defined and has only a thorny or groove-like appearance [31].

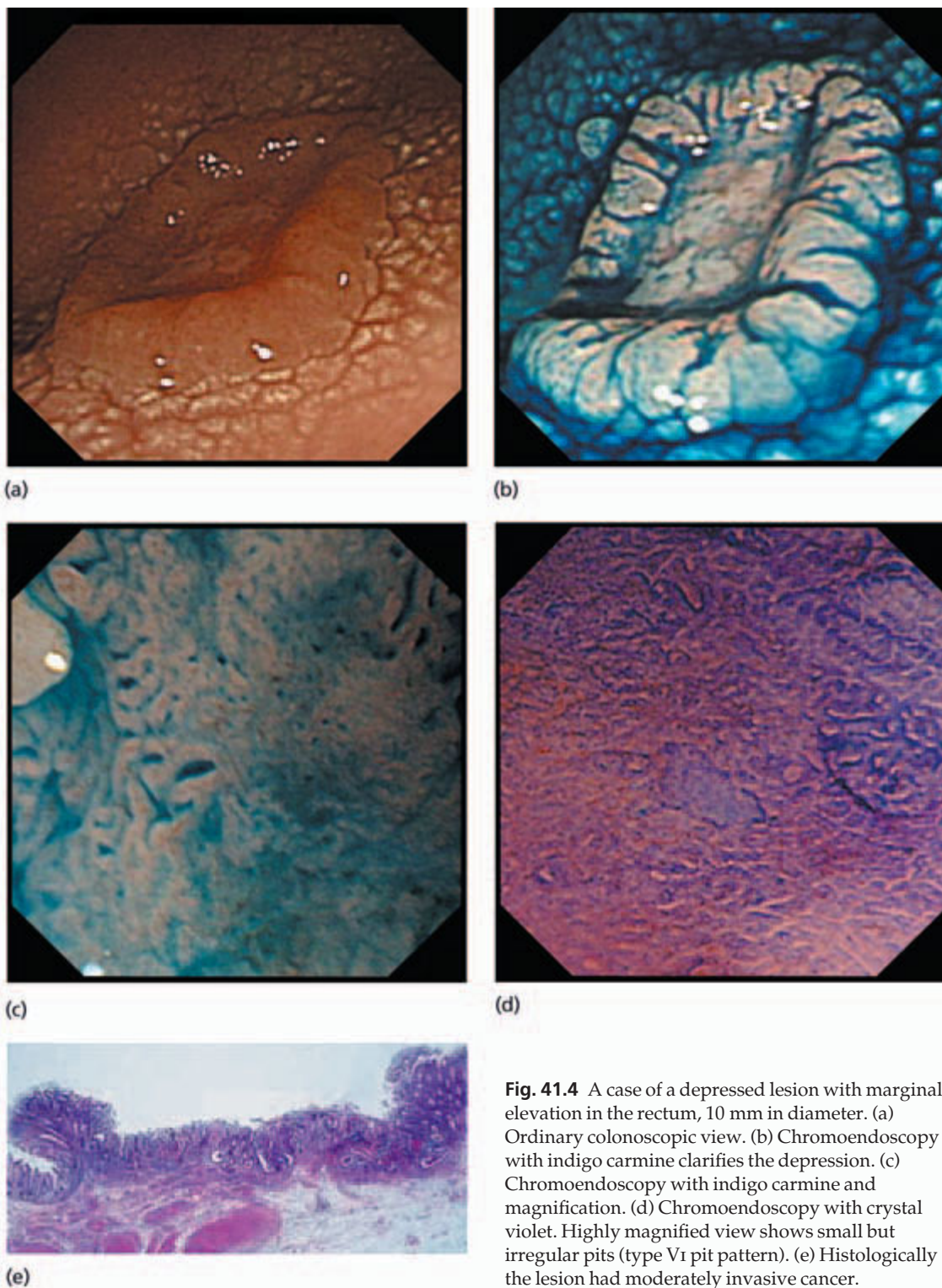


Fig. 41.4 A case of a depressed lesion with marginal elevation in the rectum, 10 mm in diameter. (a) Ordinary colonoscopic view. (b) Chromoendoscopy with indigo carmine clarifies the depression. (c) Chromoendoscopy with indigo carmine and magnification. (d) Chromoendoscopy with crystal violet. Highly magnified view shows small but irregular pits (type VI pit pattern). (e) Histologically the lesion had moderately invasive cancer.

The depressed type of colorectal cancer can be either absolutely depressed or it can be accompanied by a slightly elevated margin (Figs 41.2–41.4). The periphery is usually covered with normal mucosa and is elevated because of compression by the carcinoma or because

of submucosal proliferation of tumor cells. It is worth noting that the elevated margin does not usually consist of adenomatous tissue. The transition from carcinoma to the adjacent normal colonic mucosa is usually abrupt without lateral spread of adenoma. There can occasionally

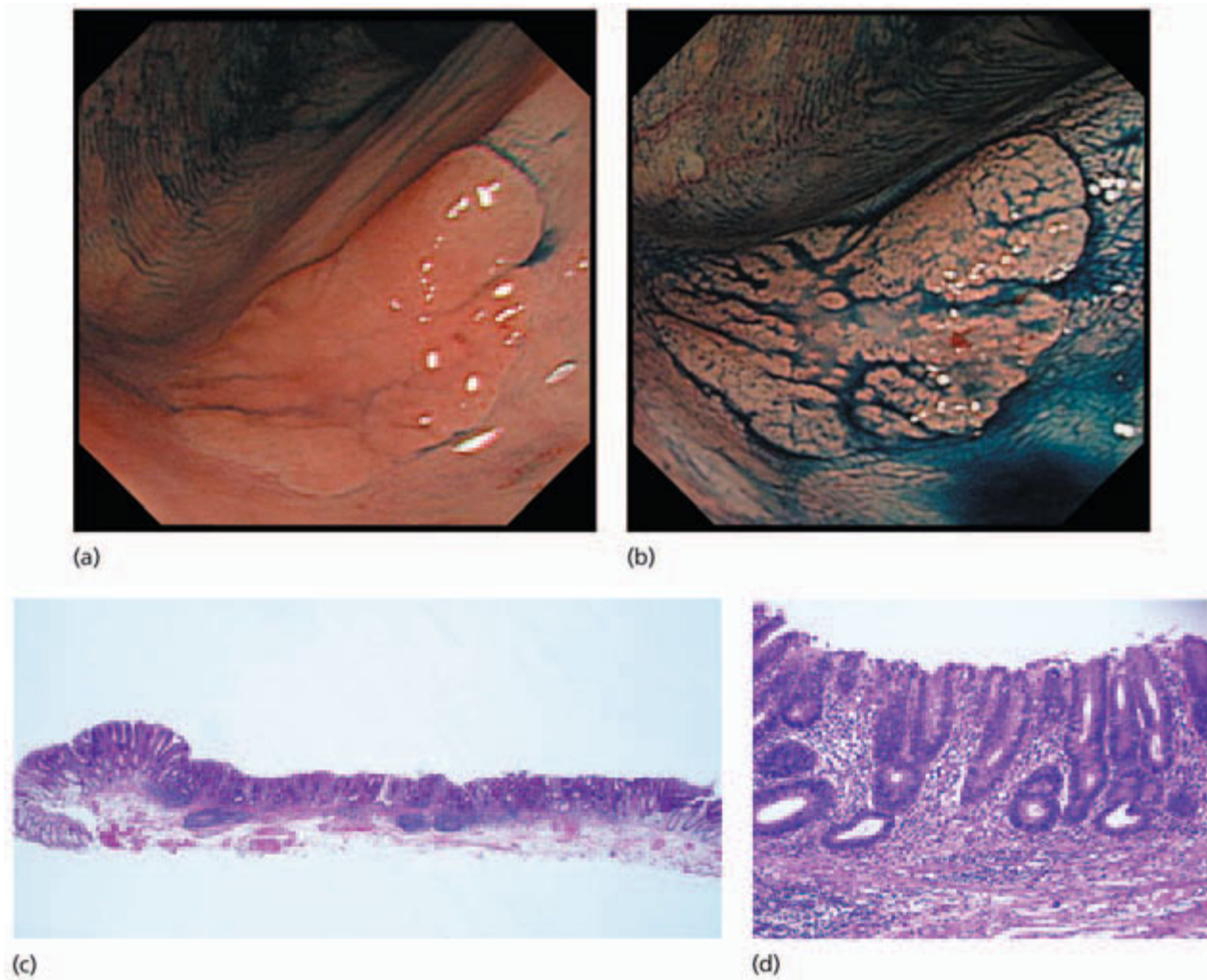


Fig. 41.5 A case of a flat elevated lesion in the sigmoid colon, 10 mm in diameter. (a) Ordinary colonoscopic view (with small amount of dye precisely placed). (b) Chromoendoscopy with indigo carmine delineates

the boundary of the lesion. The pit pattern is type III_L. (c) The lesion was endoscopically removed and was shown to be low-grade adenoma. (d) High-power microscopic view.

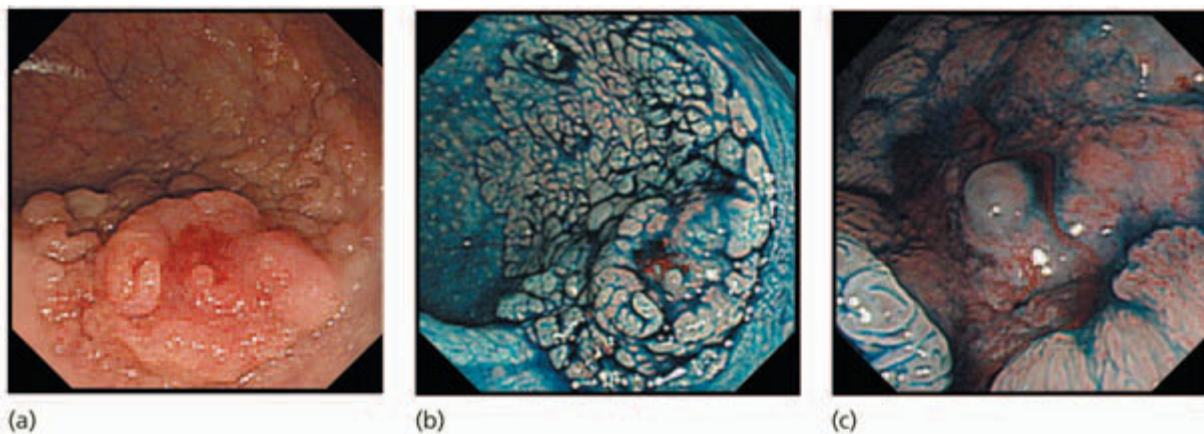


Fig. 41.6 A case of a flat elevated depressed lesion in the rectum, 47 mm in diameter. (a) It is difficult to assess the lateral extent of the lesion by ordinary colonoscopic view. (b) Chromoendoscopy with indigo carmine delineates the boundary of the lesion. (c) Highly magnified view shows that

the tumor consists mainly of type IV pits, but partially of nonstructural pit pattern (type V_N) in the coarse nodular portion of the lesion. The lesion was treated surgically and had invasive carcinoma deep into the submucosa.

be a few glands adjacent to the cancer that show adenoma-like changes, but these could be reactive to the tumor and not related to carcinogenesis.

Magnifying colonoscopy and chromoscopy enable the examiner to see the microstructure of the mucosal surface and any lesions. There are definite correlations between the gross appearance and the pit pattern of a colorectal lesion. Depressed lesions present with type III_s or type V pit pattern. Almost all of flat elevated adenomas consist of type III_L or IV pits. The pit pattern analysis by magnifying colonoscopy and chromoendoscopy facilitates the differentiation between flat elevated adenoma and depressed lesions.

Summary

Chromoendoscopy and magnification colonoscopy are useful for an accurate diagnosis of colorectal neoplastic lesions, especially depressed and flat elevated types. They also help predict the histology, and therefore are useful in determining the treatment options; endoscopic or surgical.

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Chapter 42

Flat and Depressed Colorectal Neoplasia in the Western Hemisphere

G.S. Raju and Pankaj J. Pasricha

Introduction

Knowledge about colon cancer prevention has evolved in the last century. As discussed elsewhere in this book, there is a substantial body of literature that supports the concept that colorectal cancers arise slowly as a result of incremental genetic alterations (adenoma–carcinoma sequence). Cancer should therefore typically develop from grossly visible polyps, with the size of the latter correlating with their malignant potential. This paradigm forms the basis of current clinical recommendations in the USA for colon cancer screening and prevention. On a practical note, it has also allowed most American gastroenterologists to feel comfortable ignoring small (less than 0.5–1 cm) lesions. However, even though the majority of clinically significant cancers may develop in the classic manner, a growing body of evidence suggests the existence of an alternative, albeit less common, pathway originating from so-called nonpolypoid (flat and depressed) lesions.

As far back as 1974, Morson [1] estimated that although two-thirds of colorectal cancers arise from polypoid lesions, the origin of the remainder remained unexplained. Although nonpolypoid dysplasia has typically been noted in the setting of other colorectal diseases such as inflammatory bowel disease or familial adenomatous polyposis [2–7], it may also occur sporadically in the average-risk population. These lesions are difficult to detect, a problem compounded by the general lack of familiarity with this lesion among most North

American gastroenterologists. This chapter reviews the literature on this subject and attempts to address some of the clinical controversies and questions surrounding it.

Definitions

Spectrum of nonpolypoid lesions and their morphogenesis

Tetsuichiro Muto of Japan is credited with the first recognition of the small flat adenoma as a distinct entity in 1985 [8]. Indeed much of what is known today about these lesions comes from Japan, where their existence and significance has since become well established and free of the controversy surrounding these lesions in the West. The Japanese Research Society for Cancer of Colon and Rectum has classified colorectal neoplasms as either protruded (polypoid) or superficial (nonpolypoid) lesions, with the latter further categorized as flat, flat elevated, depressed, or some combination thereof (Table 42.1, Fig. 42.1) [9]. Occasionally, an additional term, “laterally spreading tumor,” has also been used to describe what can probably be considered a large flat adenoma [10].

According to one hypothesis, both polypoid and nonpolypoid tumors arise from a small dysplastic lesion that grows exophytically (to form a protuberant lesion), endophytically (to form a depressed lesion), or laterally (small and large flat lesions) [10] (Fig. 42.2).

Table 42.1 Classification of colorectal carcinoma (Japanese Research Society for Cancer of Colon and Rectum).

	Japanese classification	Macroscopic appearance
<i>Protruding lesions</i>	Ip Ips Is	Pedunculated polyps Subpedunculated polyps Sessile polyp
<i>Superficial lesions</i>		
Flat elevated lesions	Ila Ila + Ilc	Flat elevation of mucosa Flat elevation with central depression
Flat lesions	Ilb	Flat mucosal change
<i>Depressed lesions</i>	Ilc Ilc + Ila	Mucosal depression Mucosal depression with raised edge

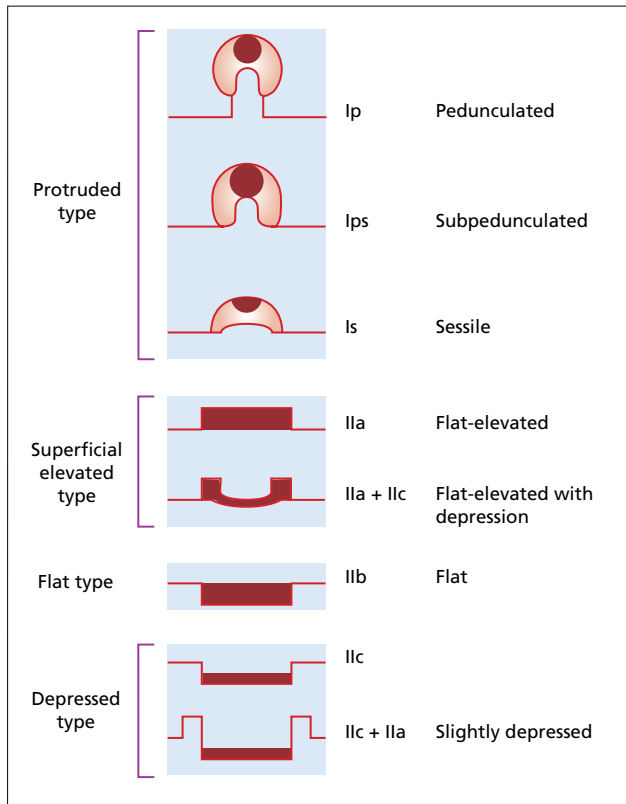


Fig. 42.1 Japanese classification of early colorectal cancer based on endoscopic, radiographic, macroscopic, and histologic observations. (From Matsui *et al.* [9].)

useful working definition is that of an endoscopically visible flat and/or depressed mucosal lesion with a height that is less than half the diameter of the lesion [11]. Typically, most such lesions are less than 2 mm high [12]. Small flat adenomas are thus minimally elevated lesions less than 10 mm in diameter; lesions with larger diameters but still relatively flat may be called laterally spreading tumors, although the term “large flat adenoma” may be preferred. Flat adenomas are typically more erythematous than the surrounding mucosa (hyperplastic polyps can also appear “flat” but typically are of the same color as the surrounding normal mucosa); however, small lesions are easy to misdiagnose or miss altogether and may require special techniques for detection (see later).

Depressed lesions are flat lesions with a definite central depression (not to be confused with simple grooves or pseudodepressions); their size may vary. They may be very difficult to find and a strong index of suspicion needs to be maintained for small areas of color change (relatively pale or erythematous compared with the surrounding mucosa). A useful technique for accentuating these lesions during routine endoscopy is repetitive air inflation and deflation, when the surrounding mucosa moves more quickly than the lesion and elevates around the depression. Representative images of these lesions are shown in Figs 42.3 and 42.4. Specialized techniques to detect these lesions endoscopically are discussed later in this chapter.

Endoscopic criteria

Flat and depressed tumors can be defined histologically as well as endoscopically. Although strict criteria for endoscopic recognition have not been agreed upon, a

Pathologic criteria

Histologically, flat adenomas are characterized by slightly elevated dysplastic mucosal plaques, never greater than twice the thickness of adjacent nondysplastic mucosa

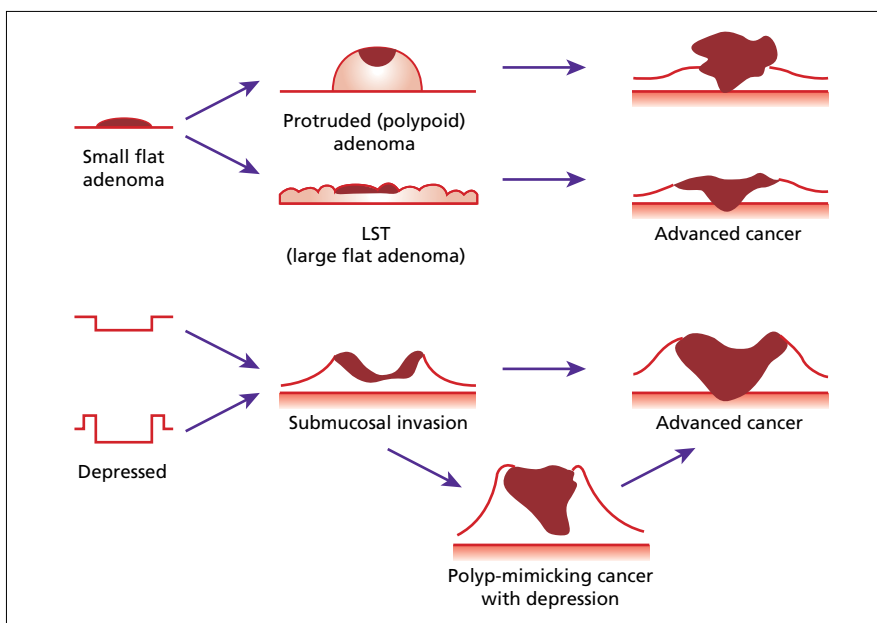


Fig. 42.2 Developmental process of nonpolypoid colorectal neoplasms. (From Kudo *et al.* [10].)

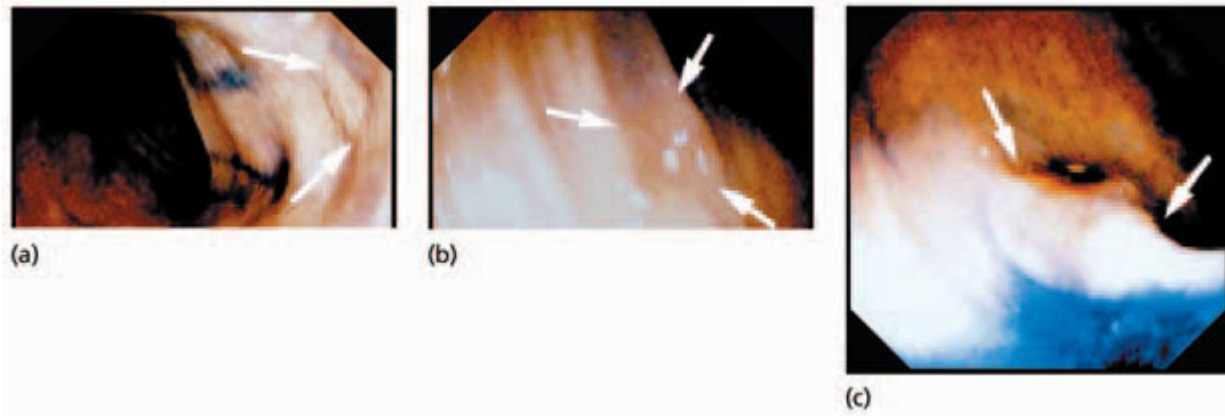


Fig. 42.3 Macroscopic subtypes of flat and depressed tumor: (a) flat elevated type, composed of flat elevation without depression of the surface; (b) slightly depressed type, composed mainly of depressed surface; (c) flat elevated with depression type, composed of an area of depressed surface surrounded by an area of elevation. (From Saitoh *et al.* [20].)

(with the height being measured from the muscularis mucosa to the top of the lesion) [13], and by the lack of exophytic polypoid configuration. The Japanese also follow a pathologic classification of colorectal neoplasms that is somewhat similar to their gross appearance (Fig. 42.4). The degree of correlation between endoscopic and pathologic criteria has not been well studied, and most studies rely on one or the other method to classify these lesions.

Epidemiology of flat and depressed lesions in the West

Originally considered a Japanese “anomaly,” flat and depressed lesions are being increasingly recognized in the Occidental population in diverse regions of the world, including Australia [14], Europe, and North America (Table 42.2). Some of these larger studies are described in detail below.

Sweden

Jaramillo and colleagues [17] studied 232 patients in Stockholm between 1992 and 1993 after excluding inflammatory bowel disease and hereditary colorectal polyposis syndromes. Using high-resolution video endoscopy and indigocarmine chromoendoscopy, these investigators found 109 colorectal flat neoplastic lesions in 55 of 232 patients (about 24%). These lesions were generally seen in patients over 60 years of age (78%) but not in patients under 40 years of age and were twice as common in men than women. Most (71%) were 0.5 cm or less, 21% were 0.6–1.0 cm, and 8% were more than 1.0 cm. Low-grade dysplasia was seen in 86% and high-

grade dysplasia in 12% of flat lesions. Adenocarcinoma was diagnosed in 3% of flat lesions. Flat lesions with a central depression showed high-grade dysplasia more often than those without central depression (43% vs. 7%).

Germany

Kiesslich and colleagues [21] studied 100 consecutive patients during routine colonoscopy using vital staining with indigocarmine solution (0.4%, 1–10 mL) on all visible lesions as well as in the rectum if macroscopic examination was unremarkable. A total of 52 patients had 105 visible lesions (89 polypoid, 14 flat, 2 depressed). The mean size of the lesions was 1.4 cm. Among the 48 patients with mucosa of normal appearance, 27 showed 178 lesions after staining (176 flat, 2 depressed) with a mean size of 3 mm. On histologic investigation, 210 lesions showed hyperplastic or inflammatory changes, 67 were adenomas, and six were cancers.

UK

The incidence of flat adenomas in an asymptomatic population (3000 subjects, aged 55–64 years) participating in a large randomized controlled trial of flexible sigmoidoscopy screening was investigated in Leicester General Hospital [19]. Three subjects had a total of four flat lesions, i.e. 1 per 1000 people screened. Three contained severely dysplastic lesions, and one was a focus of adenocarcinoma. Three of the four lesions were less than 5 mm in size and the fourth was 15 mm in diameter.

In a prospective study of 210 consecutive patients attending for routine colonoscopy in Leeds, an experienced Japanese endoscopist [18] used a standard Olympus 200 L colonoscope and the 200Z magnifying colonoscope with indigocarmine chromoendoscopy; 68 adenomas were found, of which 40 (59%) were polypoid, 26 (38%) were flat, and two (3%) appeared depressed. The majority of adenomas contained mild to moderate dysplasia. Four were severely dysplastic, three were in a

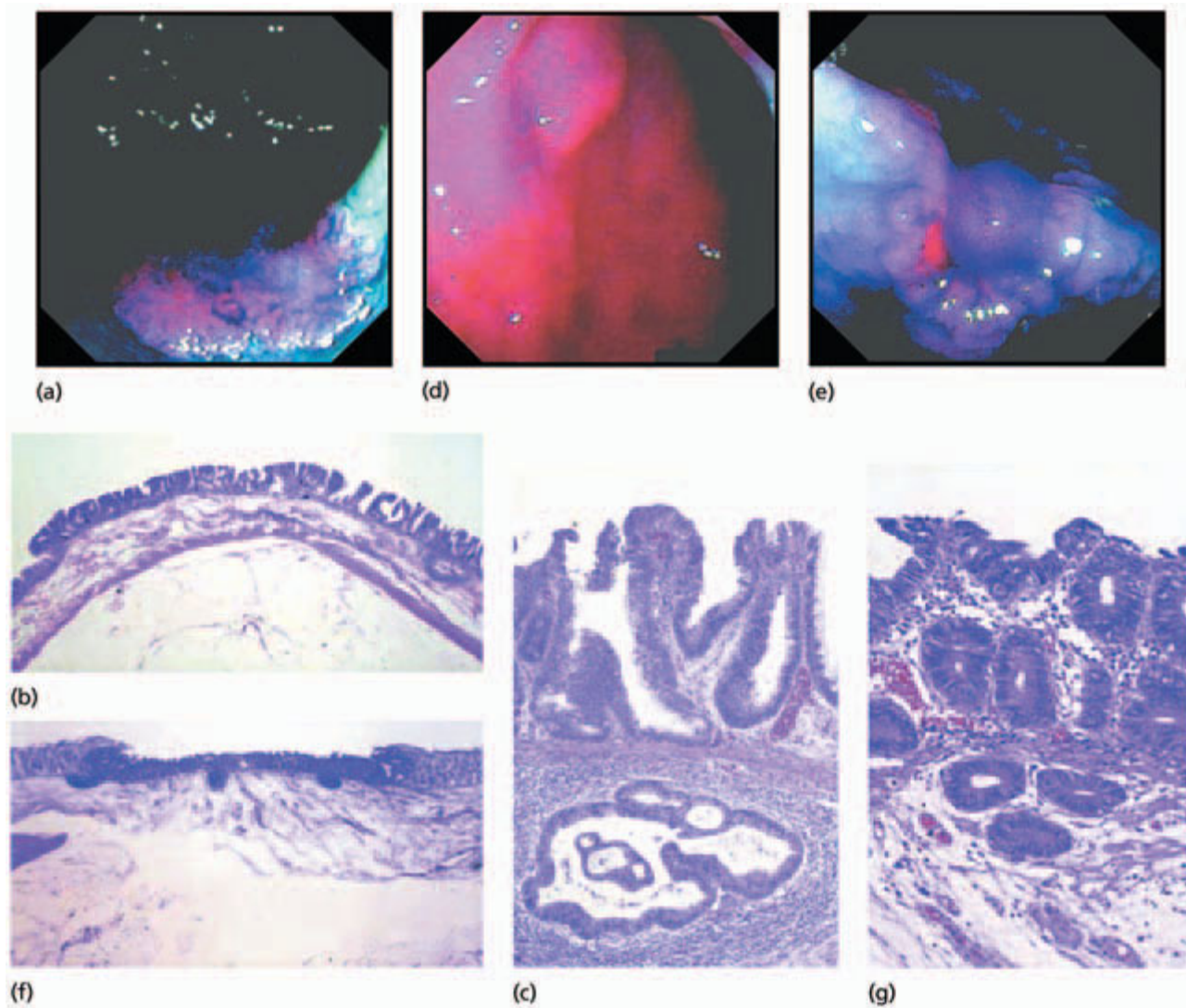


Fig. 42.4 (a) Endoscopic view of a flat-elevated lesion (26×22 mm in diameter) in the transverse colon after spraying with indigocarmine solution. The height of the tumor was extremely low in relation to the size of the entire lesion. This lesion did not show marked depression. (b) Histologic features showing a flat-elevated and smooth surface (H&E, original magnification $\times 12.5$). (c) Well-differentiated adenocarcinoma associated with tubulovillous adenoma. Minute submucosal invasion surrounded by lymphoid stroma was observed

(H&E, original magnification $\times 330$). (d) Endoscopic view of a reddish depressed lesion (8×6 mm in diameter) in the descending colon adjacent to a flat-elevated lesion. After spraying with indigocarmine solution, the depression of this lesion was found to be clearly demarcated (e). (f) Histologic features showing endophytic growth (H&E, original magnification $\times 40$). (g) Well-differentiated tubular adenocarcinoma showing minimal submucosal invasion (H&E, original magnification $\times 250$). (From Sakashita *et al.* [35].)

protruding lesion, and one in a 6-mm depressed lesion. Two of the three Dukes' A cancers were either flat or depressed lesions.

In another prospective study by the Leeds group of investigators [12] of 1000 consecutive patients attending for routine colonoscopy between June 1995 and March 1999, a single European colonoscopist also used a standard Olympus 200 L colonoscope and the 200Z magnifying colonoscope with indigocarmine chromoendoscopy; 321 adenomas were found, of which 202 (63%)

were polypoid, 117 (36%) were flat, and two (0.6%) were depressed. Most adenomas contained areas of mild to moderate dysplasia; 31 (10%) were severely dysplastic. The likelihood of Dukes' A cancer or severe dysplasia increased from 4% (3/70) in small flat lesions to 6% (9/154) in small polyps, 16% (8/50) in larger polyps, 29% (14/49) in large flat lesions, and 75% (3/4) in depressed lesions. Slightly over half (54%) of the lesions containing severe dysplasia or Dukes' A cancer were flat or depressed.

Table 42.2 Incidence of flat and depressed lesions in the Western Hemisphere.

Reference/country	Study population	Method of examination	Flat and depressed lesions
Hunt & Cherian [14] Australia	Case reports of flat carcinoma of the colon	Videocolonoscopy	3 cases
Wolber & Owen [15] Canada	Surgical pathology specimens between 1988 and 1989 (18 months); excluded UC and FAP	Histopathology of resected specimens	8.6%
Lanspa <i>et al.</i> [16] USA	Routine colonoscopy for various indications ($n = 148$)	Videocolonoscopy	12%
Jaramillo <i>et al.</i> [17] Sweden	Routine colonoscopy for various indications ($n = 232$)	Magnification endoscopy and chromoendoscopy	23%
Fujii <i>et al.</i> [18] UK	Routine colonoscopy for various indications ($n = 210$ consecutive patients)	Magnification endoscopy and chromoendoscopy	13%
Hart <i>et al.</i> [19] UK	Colon cancer screening in asymptomatic population (aged 55–64 years) ($n = 3000$)	Flexible sigmoidoscopy	0.13%
Rembacken <i>et al.</i> [13] UK	Routine colonoscopy for various indications ($n = 1000$)	Magnification endoscopy and chromoendoscopy	12%
Saitoh <i>et al.</i> [20] USA	Routine colonoscopy for various indications ($n = 211$)	Chromoendoscopy	22.7%
Kiesslich <i>et al.</i> [21] Germany	Routine colonoscopy (inflammatory bowel disease excluded)	Magnification endoscopy and chromoendoscopy	56%

North America

In a review of surgical pathology data of 340 adenomas examined between 1988 and 1989 at the Vancouver General Hospital, Canada, 29 (8.5%) adenomas were classified as flat adenomas. Flat adenomas were found in 18 (8.6%) of the 210 patients. Multiple adenomas were found in 12 of the 18 patients (40 adenomas total) and multiple flat adenomas were identified in nine patients. Two patients had concurrent flat ulcerated colonic carcinomas without identifiable polypoid precursor adenoma. At colonoscopy, all the adenomas were sessile, flat, plaque-like or an abnormal fold, and less than 1 cm in diameter. All 29 flat lesions were tubular adenomas. However, there was a 10-fold greater frequency of containing high-grade dysplasia than an analogous polypoid adenoma with an equivalent spherical diameter [15].

In an often-cited “negative” study of 148 patients referred for colonoscopy to Creighton University Medical Center, Nebraska from September 1989 to September 1990 (excluded patients with hereditary colon cancer family syndrome), 157 polyps were found in 57 patients. Of these, 35 patients had adenomas; 12 had only flat adenomas while six had both flat and other adenomas. The flat adenomas had the same prevalence and associated risk factors as other adenomas, except for younger age of onset [16].

A prospective study of the prevalence of flat and depressed colorectal adenomas was performed on American patients in Galveston, Texas, by a Japanese investigator using dye-assisted colonoscopy between June 1, 1998 and February 28, 1999 [20]. Patients with inflammatory bowel disease and polyposis syndrome were excluded. A total of 298 polypoid lesions were detected. After excluding 110 lesions that were hyperplastic polyps, the remaining 188 lesions excised (from 102 patients) comprised 66 lesions of the flat and depressed type and 122 with a polypoid appearance. Flat and depressed lesions were seen in 48 of the 211 patients (22.7%). Flat and depressed lesions were difficult to detect with conventional colonoscopy and required dye spray; 62% of the flat and depressed lesions were found only after the use of indigocarmine dye. Histologically, 82% of the flat and depressed lesions were adenomatous in nature compared with 67% of polypoid lesions ($P = 0.03$) and the incidence of adenomas tended to be higher in IIc (slightly depressed) and IIa + IIc (flat elevated with depression) than in IIa (flat elevated) types of lesions. Flat and depressed lesions contained invasive cancer more often than did polypoid lesions (4.5% vs. 0%; $P = 0.04$). All these three patients were whites and the average size of these advanced flat and depressed lesions was smaller than that of the polypoid lesions (10.75 ± 2.7 mm vs. 20 ± 2.9 mm; $P < 0.05$). The Dukes stage of the flat and advanced cancers was

more advanced despite the small size of these tumors, with subserosal extension in one case and lymph node metastasis in another. Flat and depressed adenomas showed significantly stronger fragile histidine triad (FHIT) expression and lower p53 reactivity than similarly sized polypoid adenomas, whereas proliferative and apoptotic indices were similar in both groups.

Biologic and clinical significance of flat lesions

This is an area of considerable ongoing controversy but one that is potentially of great clinical importance. Several of the studies discussed above seem to reinforce the view that Japanese gastroenterologists have held for some time now, namely that nonpolypoid colorectal lesions behave differently from their more common polypoid counterparts, with the adenoma–carcinoma progression being accelerated and, in some instances, bypassed altogether, giving rise to the concept of a *de novo* cancer. This issue is now examined in some detail.

Flat lesions or small polyps?

Despite what has been described above, it has been argued that flat and depressed tumors do not represent a distinct category of colorectal lesions and should be simply regarded as very small polypoid adenomas [22–24]. Evidence cited for this belief includes a study in patients with familial adenomatous polyposis which showed that adenomas typically grow horizontally to a diameter of 0.5 cm before beginning vertical growth [25]. Thus, according to one school, all colorectal neoplasia begins as a flat lesion. This of course would be a purely semantic issue were it not for the sinister implication of a greater likelihood of finding advanced pathology in flat and depressed lesions.

However, some experts in the USA have vociferously denied this, based on several plausible arguments. First, it has been claimed that the high-grade dysplasia reported to be associated with these lesions is simply a reflection of differences in diagnostic criteria used by American and Japanese pathologists [26,27]. Indeed the concept of cancer itself may be quite different, with western pathologists requiring invasion of the submucosa or beyond. Japanese pathologists, on the other hand, are willing to label as cancerous those lesions showing severe cytologic atypia, even though the epithelial cells remain confined to the mucosa (a finding that would be called high-grade dysplasia within an adenoma by their western counterparts). These differences can have dramatic effects on histopathologic interpretation, as shown by Schlemper and colleagues [26]. In this study, eight expert pathologists from Japan, North America, and Europe individually reviewed slides of 20 colorectal

lesions from Japanese patients. Western pathologists diagnosed suspected or definite carcinoma in only 20% of these as compared with the 64% incidence reported by Japanese pathologists. In fact agreement between the two groups was seen in only 9 of 20 cases. Whereas some of these discrepancies were due to differences in nomenclature (such as intraepithelial cancer vs. high-grade dysplasia), what was more surprising was that some of the cancers diagnosed by the Japanese were reported simply as adenomas with low-grade dysplasia by the western pathologists. Other reports have suggested that even within Japan, the interpretation of flat and depressed lesions may vary from institution to institution, in part perhaps due to the extent of familiarity with these lesions [28]. This suggests that apart from differences in nomenclature, differences in the criteria used for histopathologic classification and their importance may also contribute to the discrepancies in the results of studies on flat lesions between the various regions of the world.

A second argument is based on the marked reduction in colorectal cancer incidence demonstrated by the National Polyp Study, in which all lesions visible by standard colonoscopy were removed [29]. During a follow-up of 8400 person-years, which was 97% complete, only five new cancers were detected. According to one of the authors of that study, “if small flat adenomas with appreciable malignant potential had been missed during colonoscopy, flat small cancers without associated benign adenomatous tissue should have been detected during this careful follow-up surveillance” [24].

The National Polyp Study results also form the basis of a third argument. Although it did not prospectively classify lesions as flat or polypoid, a recent retrospective analysis of histologically resected specimens collected during the trial suggested an incidence of flat adenomas in 27% of all adenomas removed at the index examination [30]. The incidence of high-grade dysplasia in flat adenomas was low (around 1%) and not higher (and perhaps even lower) than that in polypoid adenomas. Multivariate analysis of the follow-up data showed no evidence of a greater tendency for advanced adenomas to be found at surveillance colonoscopy.

Despite the plausibility of these arguments, evidence is accumulating that supports the hypothesis that these lesions are truly a separate clinical and biologic entity. Several recent studies from Japan (using internationally accepted nomenclature) as well as studies from the West using local pathologists and standards have confirmed that flat and depressed lesions may well have a real risk of advanced pathology (see below). Further, the results of the National Polyp Study are not necessarily reassuring. Despite a very rigorous protocol of careful examination of the entire colon with removal of all identified

polyps, five cancers were still discovered. This may simply reflect the limitation of human skills; however, more disturbing is that cancer was seen in lesions as small as 6 mm (with the others being 8, 15, 15, and 25 mm); three of these cancers were detected within 3 years of the index colonoscopy. Although the morphology of these lesions is not specifically commented upon, these findings emphasize the fact that small aggressive cancers do exist in the western world. Similarly, the retrospective histologic analysis of resected polyps cited above does not differentiate between simple flat lesions and those with a predominant depressed component, a distinction that is now being recognized as critically important (see below).

Association with advanced pathology

When small flat and depressed lesions are compared as a group with their polypoid counterparts, a striking difference in the incidence of high-grade dysplasia and cancer has been observed as was first reported by Muto. This observation is not confined to the Japanese population, as shown by Wolber and Owen from Canada [15] who found high-grade dysplasia in 41% of flat adenomas but in only 4% of polypoid lesions. Similarly, flat and depressed lesions are more often associated with invasive cancer, a finding that has also been confirmed in the USA by our group who reported an overall incidence of invasive cancer in 4.5% of these lesions [20]. We also found that the average size of all flat and depressed advanced lesions (severe atypia and cancer) was significantly smaller than polypoid advanced lesions (about 11 vs. 20 mm) and that the stage of the flat and depressed cancers was disproportionate to their size, with extension to the subserosa in one case and lymph node metastases in another. These findings are consistent with most Japanese reports [31–33].

The risk of high-grade dysplasia and cancer with flat and depressed lesions may display some regional variations. A previous report employing similar diagnostic criteria found a higher incidence of advanced pathology in flat lesions from a Japanese population compared with a Swedish one [34]. Of the 141 flat neoplasms seen in Tokyo, 24.8% had high-grade dysplasia, 7.0% intramucosal carcinoma, and 9.9% invasive carcinoma. On the other hand, of the 90 flat mucosal neoplasms seen in Stockholm, 13.3% had high-grade dysplasia, 1.1% intramucosal carcinoma, and 1.1% invasive carcinoma.

Depressed lesions are more important than simple flat lesions

In recent years it is also becoming increasingly clear that not all nonpolypoid lesions are equivalent in this regard,

with the greatest risk of advanced pathology being associated with lesions with a prominent depressed morphology rather than the “pure” flat polyp. This has been seen in Japanese [10,35] and western [13] populations (Fig. 42.5).

Depressed lesions are also increasingly being reported as more likely to be rapidly growing and invasive [36,37]. When cancer develops in such lesions, it is less likely to be associated with an adenomatous component [36] and *K-ras* mutations are distinctly uncommon or absent altogether [35]. The distinction between simple flat lesions and those with depressed features was not always made in the older literature but clearly has very important implications for screening and treatment (see later). It is therefore critical that future studies classify these lesions more carefully.

De novo colorectal cancer and the relationship between early cancer and flat and depressed lesions

According to the Japanese literature, many nonpolypoid early colorectal carcinomas (confined to the submucosa) [38] are not associated with an adenomatous component [10,35]. This has led investigators to hypothesize an alternative to the classic adenoma–carcinoma sequence for carcinogenesis, at least in a small proportion of cases [39,40]. Early colorectal cancer is clearly not confined to Japan: Stolte and Bethke [41] have reported the largest series from the western world, consisting of 155 patients seen over a 7-year period. About 60% of these lesions, defined as submucosally invasive cancers without evidence of precursor adenomatous tissue, were of the polypoid type, with the rest being of the flat and depressed type.

If early colorectal carcinomas are defined as superficially invasive cancer only, then it appears that the vast majority of early colorectal carcinomas of the flat type are not accompanied by adenoma [42,43]. This may be explained in at least two ways. First, flat adenomas are not precursors to flat carcinomas and the latter arise *de novo* [43]. Alternatively, flat cancers may quickly replace the small cluster of adenomatous cells from which they arise [44].

Again, it appears important to distinguish depressed lesions from other flat lesions as this morphologic pattern is least associated with adenomatous tissue and is most likely to invade the submucosa (Fig. 42.6).

Differences in genetic and biologic markers between flat and polypoid lesions

The classic adenoma–carcinoma sequence in polypoid colorectal lesions involves a series of genetic “hits” whose nature and sequence have been reasonably well

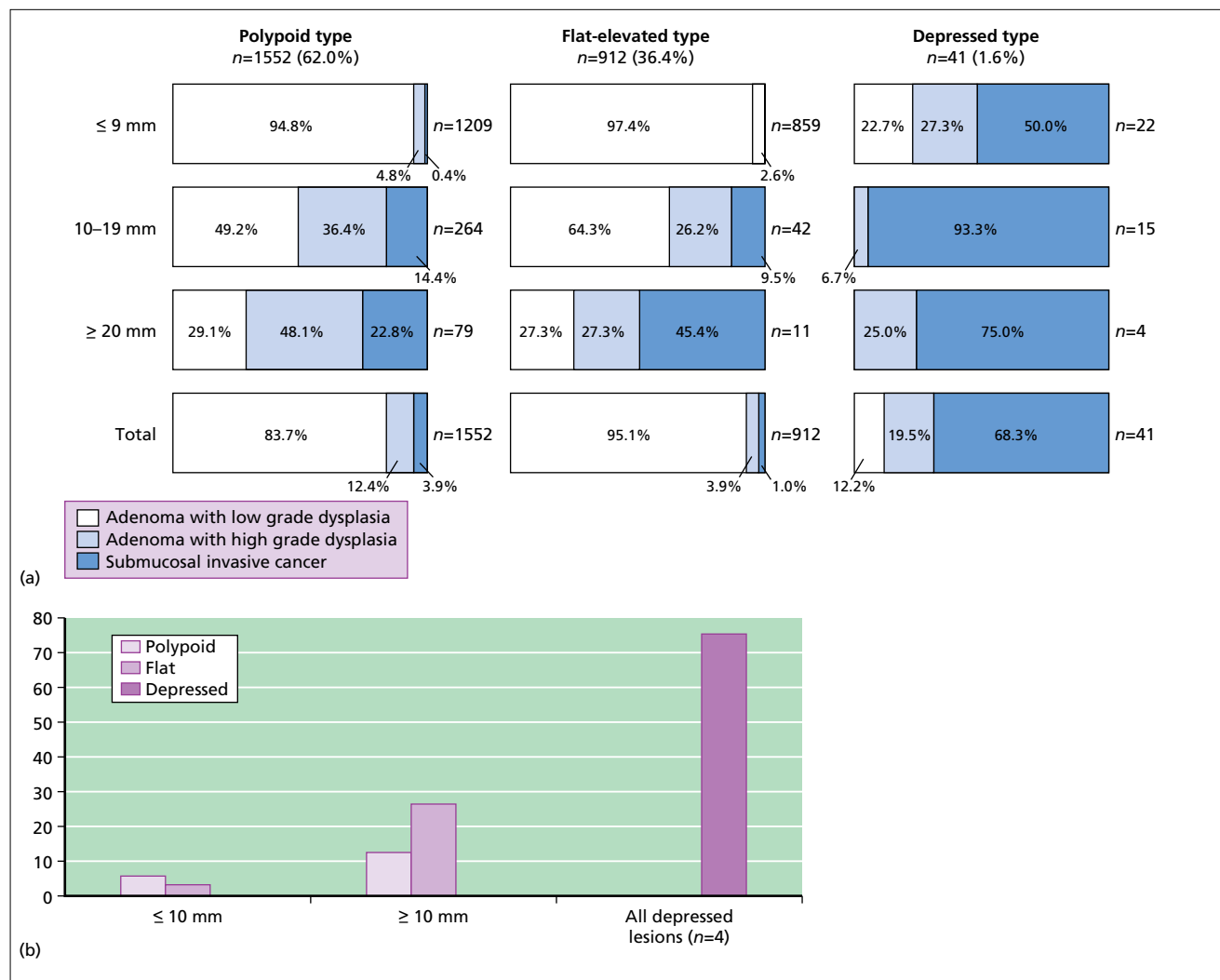


Fig. 42.5 (a) Relationship between histologic finding and tumor size according to morphology in Japanese patients. (From Sakashita *et al.* [35].) (b) Likelihood of Dukes' A cancer or severe dysplasia according to morphology in British patients. (Adapted from Rembacken *et al.* [13].)

defined. If nonpolypoid lesions deviate significantly from this paradigm, a powerful case can be made for a distinctive identity. Although these studies are only just beginning to emerge, several important differences have indeed been found (Table 42.3).

Colorectal carcinogenesis and flat and depressed lesions

The significance of these findings and how they relate to the putative differences in biologic and clinical behavior remains to be resolved. However, based on the findings discussed above, a hypothesis supporting a distinct pathway to carcinogenesis has begun to take shape. The

classic multistep genetic model for colorectal carcinogenesis proposed by Vogelstein and colleagues [60] proposes mutations in the *APC* gene (and associated loss of heterozygosity of chromosome 5q) as a very early, if not initial, step in this sequence, being found in the majority of tumors, even those of very small size. This is followed by changes in the *ras* gene, allowing progress to larger more dysplastic tumors. Later, p53 mutations may be important in the transformation to cancer. In contrast, it is now clear that *K-ras* mutations are distinctly uncommon and indeed may be absent altogether in flat and depressed lesions, particularly in those with a predominant depressed feature (see above discussion). *APC* mutations have also been examined [53] in at least one large study of 47 adenomas with high-grade dysplasia (intramucosal cancer by the Japanese approach), about half of which were polypoidal and the others flat and depressed lesions. Overall, *APC* mutations were nearly twice as common (44% vs. 25%) in the former. Further, when the flat and depressed groups were analyzed, this

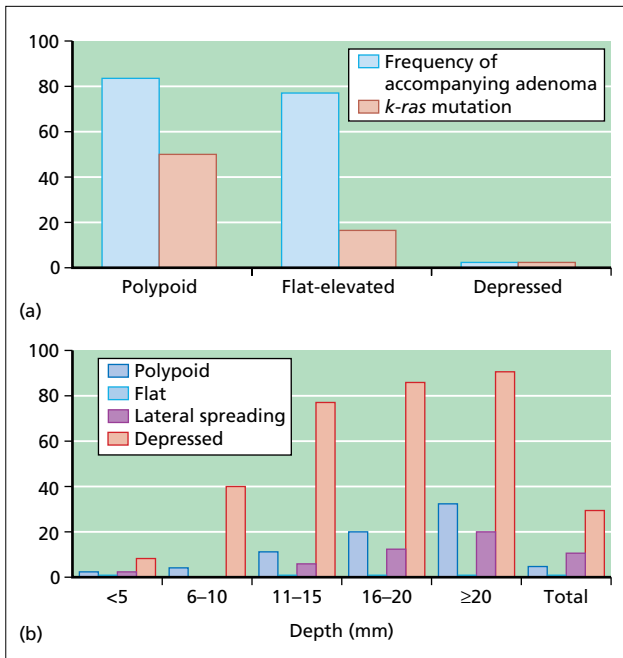


Fig. 42.6 Distinguishing features of depressed lesions. (a) Distinguishing features of depressed lesions. (From Sakashita *et al.* [35].) (b) Rate of sub mucosal invasion according to morphology. (From Kudo *et al.* [32].)

difference appeared to be contributed entirely by the depressed lesions, only 13% of which showed an APC mutation compared with 45% of the flat lesions. In contrast, several studies have shown that p53 mutations are

similar in polypoid and nonpolypoid tumors [54,56,57] or lower in the latter [20,55].

These findings have led Watanabe and Muto [39] to speculate a genetic model for colorectal tumorigenesis that varies according to the ultimate morphology of the tumor (Fig. 42.7). According to this, simple flat lesions closely follow the genetic pathway of their polypoid counterparts, with the exception perhaps of a low frequency of *ras* mutations. Depressed lesions, on the other hand, may follow a distinct route that involves as yet uncharacterized genetic mutations, leading to accelerated carcinogenesis or in some cases *de novo* cancer. In this setting, the absence of *ras* mutation may be the limiting factor in terms of tumor size: without such mutations, flat lesions do not grow larger but nonetheless may progress to malignancy. It is also conceivable that the lesser degree of collagenosis and angiogenesis [59] induced by flat lesions may contribute to the restriction on their growth; alternatively, this may simply reflect different growth requirements of these neoplastic cells. Finally, based on both rodent [61] and human [62] data, flat lesions are more likely to be associated with subjacent lymphoid nodules than their polypoid counterparts. This curious finding has led some to speculate that M cells (epithelial cells that cover colonic lymphatic tissue) may represent the precursors of the dysplastic cells found in flat lesions.

Clearly, these studies are in their infancy and much needs to be learned about the molecular and biologic basis of nonpolypoid adenoma development and carcinogenesis.

Table 42.3 Biological characteristics of flat and depressed lesions.

Biologic or genetic markers	Difference between flat lesions and polypoid lesions	Reference
G ₁ cell-cycle phase regulatory genes	Cyclin D2 and CDK4 reduced in flat lesions; PRB (retinoblastoma protein) increased in flat lesions	45
Bcl-2 expression and apoptosis	Decreased in depressed lesions	46
K-ras expression	Absent or decreased in flat and depressed lesions	37, 47-49
APC mutations	Less frequent in flat and depressed lesions Similar (small number of cases; no direct comparison with polypoid lesions)	53 48,54
Transforming growth factor- α type II receptor expression, replication error incidence	No changes (compared with published literature on polypoid lesions)	48
Fragile histidine triad expression p53 expression	Increased in flat lesions Decreased in flat lesions No change	20 20,55 46, 47, 54, 56-58
Collagen expression and microangiogenesis	Reduced in flat lesions	59
CD95 (Fas ligand)	No difference	20
Ki-67 expression	No difference Reduced in depressed lesions	20,46 37

* Western populations.

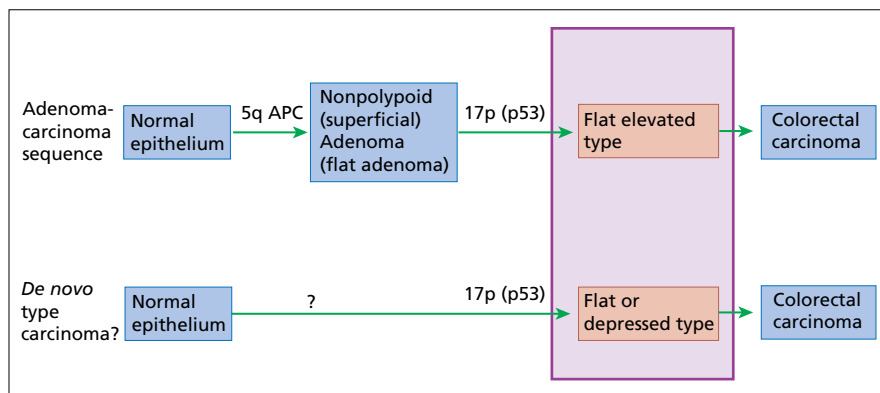


Fig. 42.7 Genetic model for nonpolypoid (superficial) early colorectal carcinoma. (From Watanabe & Muto [39].)

Challenge of endoscopic detection of flat and depressed lesions

It is clear from the above discussion that the final role of flat and depressed lesions in the overall morbidity and mortality from colorectal cancer, particularly in the West, has not yet been established. While there may be genuine differences in the behavior of these lesions in different ethnic populations, it is equally obvious that these lesions can no longer be dismissed casually in people of European descent. An unfortunate and perhaps unintended consequence of the validation of the adenoma–carcinoma sequence in the majority of cases has been the readiness of gastroenterologists to ignore small lesions encountered during colonoscopy. Ironically, the remarkable reduction in incidence of colorectal cancer demonstrated by the National Polyp Study may largely have been due to the rigor with which any identifiable polyp was pursued and removed (in other words, distinguishing between morphologic types of small lesions is a purely academic exercise if all of them are resected). Since then, however, we have moved in the opposite direction, because of a formidable combination of expediency and complacency. The Galveston study compared the findings in the study group (using dye spray and the assistance of a skilled Japanese gastroenterologist) to a control group of patients undergoing colonoscopy by an experienced American endoscopist alone [20]. These results provided a “current practice” perspective that may be generalizable to the wider gastroenterology community in the USA. Overall, nearly twice as many polyps and nearly four times as many small (<5 mm) adenomas were found in the study group. Therefore, many small polyps are either routinely missed or ignored under current methods of colonoscopy.

Although there is no current evidence to suggest that detection and removal of all flat and depressed lesions during the initial colonoscopy will provide greater prophylaxis against the development of colorectal cancer

over subsequent years, the opposite has not been proven either. Recent studies showing an unexpectedly high rate of second colorectal cancer during surveillance colonoscopies (with some cancers being detected despite several colonoscopic examinations within the preceding few years) have raised the alarming possibility that some cancers do indeed follow an aggressive and accelerated pathway and their precursor lesions may not be readily detectable [63]. Clearly, larger studies with long periods of follow-up will be required to address this issue and provide a definitive argument for changing the current endoscopic approach to small polyps. In the meantime, it is clear that gastroenterologists owe it to their patients to remain vigilant, with a high index of suspicion for any peculiarities of the colonic mucosa.

In this regard, the Japanese have long ago routinely adopted chromoendoscopy as an aid to detection of these tumors and have also recently developed optical zoom endoscopy. The utility of these techniques has also developed in the western population [13,20,21]. The details of both these techniques are covered in other chapters in this book. However, it is important to emphasize that these procedures not only involve additional time but also require training and orientation for their proper use. In particular, surface characteristics of tumors, based on the pit pattern, need to be learned as they provide the basis for accurate prediction of the true histologic nature of such tumors (Figs 42.8 & 42.9). Kiesselich and colleagues [21] have also shown that such an approach can be useful in the western population. They used the pit pattern system (with indigocarmine) to classify lesions with a sensitivity of 92% and a specificity of 93%. Lesions with pit patterns III–V showed higher rates of dysplasia.

In the future, other forms of “bioendoscopy” [64], including optical coherence tomography, will undoubtedly be used to help unravel the enigma of the flat and depressed lesion. Once these lesions are found, endoscopic mucosal resection techniques can be used successfully to remove these lesions; further therapeutic

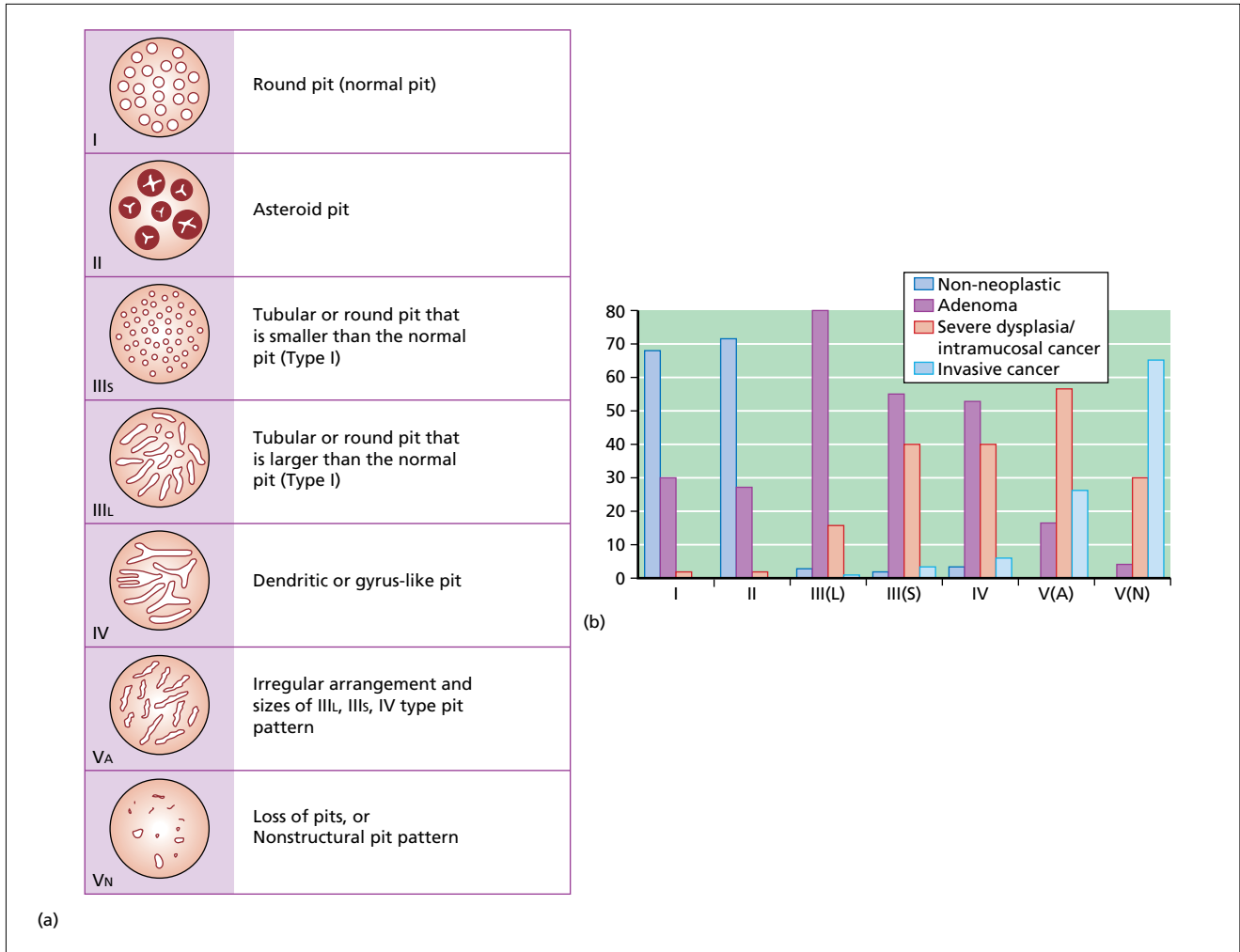


Fig. 42.8 (a) Schematic illustration of pit patterns that may be of predictive value in small polyps. (From Nagata *et al.* [65].) (b) Correlation between pit patterns and histologic findings. (Data from Kudo *et al.* [32].)

decisions will depend upon the results of the histologic interpretation of the depth of invasion, if any.

Summary and clinical approach

It should be clear that as yet no consensus exists on what to do with flat and depressed lesions. We have made the argument that these lesions have the potential to be clinically quite significant and therefore gastroenterologists should remain alert to their existence. It is of utmost importance that “colonoscopic” investigators in the USA abandon the position of denial and move on to plan definitive studies that can either disprove or prove this hypothesis. At the same time, further translational studies will be invaluable in providing insight into alternative pathways of colorectal carcinogenesis.

While the results of these studies are awaited, we believe a strong case can be made for an aggressive policy of detection for at least one subtype of nonpolypoid lesions, that with a prominent component of depression. This is based on the substantial evidence that depressed lesions have clear differences in terms of their invasive potential, coupled with differences in the frequency of *ras* mutations and accompanying adenomatous components. In order to detect these flat and depressed lesions, gastroenterologists in the West have to acquire the tools of their Japanese counterparts, such as chromoendoscopy and magnification endoscopy, so they can be in a position to truly assure their patients that all lesions with malignant potential will be diligently sought and removed. At the same time, it is quite possible that most simple flat lesions less than 5 mm in size and without a depressive component may not be any more threatening than their polypoid counterparts. Final validation of these approaches needs further studies and until then they can be at best regarded as speculative.

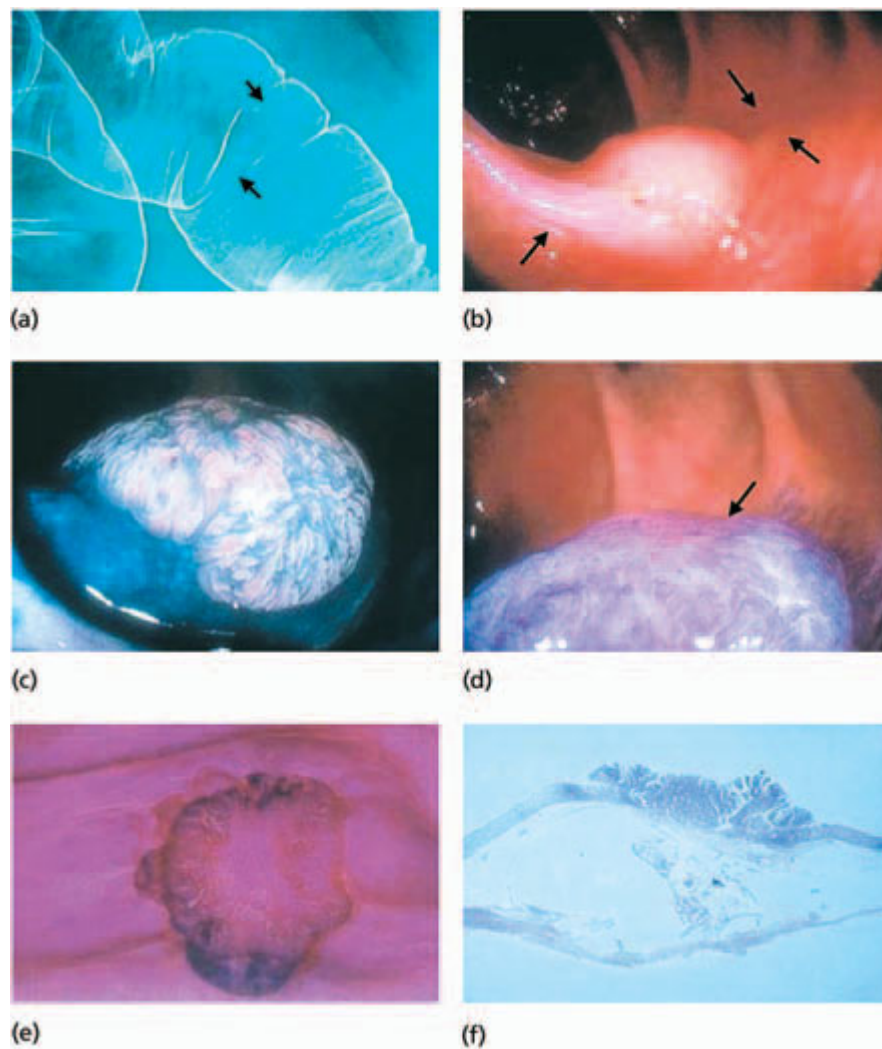


Fig. 42.9 (a) Barium contrast radiograph (case 2) showing polypoid lesion with fold convergence (arrows) in transverse colon. (b) Colonoscopic view of polypoid lesion with fold convergence (arrows). (c) Magnifying view after spraying indigocarmine dye showing clear delineation of lateral margin and type VA pit pattern. (d) Magnifying view with crystal violet staining showing type VN pit pattern in depressed area (arrow) and type VA pit pattern at lateral margin. (e) Stereomicroscopic view showing type VN pit pattern in central depressed area and normal round pits along margin (H&E, original magnification $\times 4$). (f) Photomicrograph of cross-section of resected specimen showing subserosal tumor invasion of mucinous adenocarcinoma (H&E, original magnification $\times 4$). (From Nagata *et al.* [65].)

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Chapter 43

Chromoendoscopy

David E. Fleischer

Introduction

Yogi Berra, the newsworthy Hall of Fame baseball player and philosopher, has been quoted as saying “you can observe a lot by watching.” As gastrointestinal endoscopy has emerged as a critical subspecialty in the evaluation and treatment of digestive diseases, its most influential leaders have looked for ways to expand the basic endoscopic task of “observing.” Scientific achievements in computer technology, miniaturization, aeronautics, robotics, biochemistry, and other disciplines have been adapted to endoscopy. This has led to remarkable advances in diagnostic and therapeutic opportunities at endoscopy. The dreams of Schindler, Hirschowitz, and others have been realized and extended beyond even their most extraordinary visions.

Chromoendoscopy (CE) is a technique in which tissue stains or dyes are applied to the gastrointestinal mucosa. The purpose of using CE is (i) to detect abnormalities that are not seen in its absence; (ii) to characterize those abnormalities; and (iii) to delineate the margins of those abnormalities. CE may or may not be combined with magnification endoscopy (ME).

For years, investigators have been enamored with the possibility that CE (and ME) might amplify the benefits of routine gastrointestinal endoscopy in specific settings and for specific indications. CE has the appeal of being simple, inexpensive, and safe. It has been used with some frequency in Japan, China, and other areas of Asia. CE has not been widely used in the USA and Europe. The number and types of dyes that have been used for CE in the gastrointestinal tract have been limited and have not changed much for the past 20 years. ME has been available for more than a quarter of a century, and its development is closely linked to advances in other areas of optics. The potential for enhanced magnification techniques to revolutionize the field of endoscopy is great and there is a theoretical possibility that with “optical biopsy” there will be an evolution of the endoscope into a microscope.

Magnification colonoscopy allows visualization of the minute structures of the colonic surface. The first magnifying colonoscope was described by Tada and colleagues in 1975 [1] with the ability to magnify $\times 10$. Several models have been developed since then. Their

optical systems differ from the conventional endoscope, with a fixed focusing system. There are two types of magnifying colonoscopes. One type has an adjustable focusing system that provides both a conventional image and a magnification factor of $\times 10$ to $\times 35$. The other type has two separate optical systems (e.g. Olympus CF-UHM, Tokyo, Japan) manipulated by a control on the head of the scope: one system is conventional, the other is an ultrahigh magnification of $\times 170$ [2].

High-resolution video endoscopy is distinct from CE and ME but can be used with either. With this technology, the image seen is not magnified but rather the resolution is increased. With conventional endoscopy the number of pixels displayed is approximately 100 000–200 000, but with high resolution the number of pixels may be 400 000 or 800 000. Both CE and ME are techniques that can be applied throughout the digestive tract. Many of the principles addressed here are relevant to the entire gastrointestinal tract. Colonic chromoendoscopy involves the application of tissue stains and dyes to the mucosal surface at the time of colonoscopy or sigmoidoscopy. Magnification colonoscopy and a discussion of flat adenomas is covered in Chapter 41.

Classification of tissue stains

Tissue stains have been used to detect abnormal lesions, to characterize or categorize the type of pathology identified, and to delineate their borders. The characterization would be particularly important if resection or ablation were contemplated. Well-defined borders could be useful for guiding therapy and determining whether all of the abnormal tissue was treated.

Tissue stains have been classified into three categories: absorptive stains, reactive stains, and contrast stains (Table 43.1).

Absorptive stains

These stains identify specific epithelial cell types or cellular constituents by preferential entry into cells. Examples of this type of stain are Lugol’s solution and methylene blue. Lugol’s iodine solution has been used primarily in the upper digestive tract, where its uptake by the normal glycogen-containing squamous cells of

Table 43.1 Types of tissue stains.

Category	Stain	Mechanism	Examples
Absorptive (vital)	Lugol's solution	Stains epithelial cells or cellular elements by preferential entry into cell	Stains glycogen in normal cells of esophagus
	Methylene blue	Stains actively absorbing cells (intestine, colon)	Enters normal absorptive tissue
	Cresyl violet	Absorbed by glands of Lieberkühn	Stains margins of pits on colonic mucosal surface
Reactive	Congo red	Identifies cellular products	Changes color from red to dark blue or black in acidic environment (pH < 3). With methylene blue, "bleaches" neoplastic cells
Contrast	Indigocarmine	Highlights tissue topography	For distinction of diminutive polyps For detection of flat colonic mucosal lesions

the esophagus helps to define healthy tissue; dysplastic or neoplastic cells, which do not contain glycogen, do not stain [3]. Methylene blue is taken up by absorptive cells such as intestinal and colonic cells. Methylene blue enters the cytoplasm of absorptive tissues, and the absence of staining usually indicates neoplastic changes. Methylene blue is considered nontoxic when sprayed on the surface of the intestinal mucosa [4,5]. Patients may notice blue–green discoloration of urine and stools after use of this agent. Staining is evident within 2–3 min and begins to fade after 15–20 min but persists up to 24 h. Ishii and colleagues [6] in Japan used methylene blue in a 0.05% solution to highlight suspicious flat colonic lesions. A mucolytic agent was not used.

Another absorptive stain described in the literature for detection of colon lesions is crystal violet [7,8], which stains the margins of the pits on the mucosal surface, allowing very clear distinction of the pit pattern. This is in contrast to indigo dye, which collects inside the pit orifices and poorly demarcates the pits. However, complete mucus removal by washing with water is required for accurate staining and diagnosis. Kudo and colleagues [8] describe five types of pit patterns that correlate with histologic diagnosis and stereomicroscopy (Fig. 43.1). Simple round or stellate pits correspond very well to nonneoplastic lesions (normal, inflammatory, or hyperplastic polyps). The disadvantage is that a magnifying colonoscope (e.g. Olympus CF200Z) of $\times 100$ power is required to identify these patterns. Cresyl violet is generally not available for *in vivo* staining in the USA.

Crystal violet is preferentially taken up by the Lieberkühn gland openings (crypts), which appear as dots or pits (Fig. 43.2). The size and distribution of these crypts vary, depending on the histology of the lesion. Crystal violet should only be used when diagnostic precision will lead to management changes. For example, it may be difficult to differentiate small round pits as found in adenomas from the disrupted crypt patterns in early invasive cancers. Lesions with a severely disrupted crypt pattern are likely to invade deep into the submu-

cosa, making surgical resection the optimal treatment. The overlying material must be removed by washing the mucosal surface with water, with or without proteinase. A few drops of crystal violet in 0.05% solution are then applied using a nontraumatic catheter (PW.1 V or PW.5 V; Olympus America, Inc., Melville, NY) (Fig. 43.3). After a couple of minutes the lesion can be scrutinized with a magnifying colonoscope. Lesions situated behind a fold can be easily visualized by using the catheter to push the mucosa.

Reactive stains

Reactive stains identify cellular products, such as the change in color of a pH indicator. An example of a reactive stain is Congo red. This stain changes color from red to dark blue/black in the presence of acid with a pH < 3. Ishii and colleagues [9] have used a combination of Congo red and methylene blue to highlight colonic neoplastic lesions. Colonic neoplasms bleach the Congo red and methylene blue sprayed on their surface in sharp contrast to the red-colored mucosa of unaffected areas. These authors studied 51 patients with colorectal tumors and sprayed 0.05% methylene blue over suspicious lesions followed by 0.6% Congo red solution, and observed the mucosa for 2–3 min. Adenomas (63%) and adenocarcinomas (77%) tended to bleach the dye combination, which may be of use for detecting early or flat adenomas. Also of significance was that, of 40 nonneoplastic polyps seen, none bleached the dye combination.

Contrast stains

Contrast stains are not absorbed by epithelial tissue and highlight tissue topography by pooling in epithelial crevices and depressions. The primary contrast stain used in the colon is indigocarmine dye (ICD), which is derived from indigo, a blue plant dye, and carmine, a red coloring agent formed from cochineal by the addition of alum [10,11]. Like methylene blue, this dye is considered

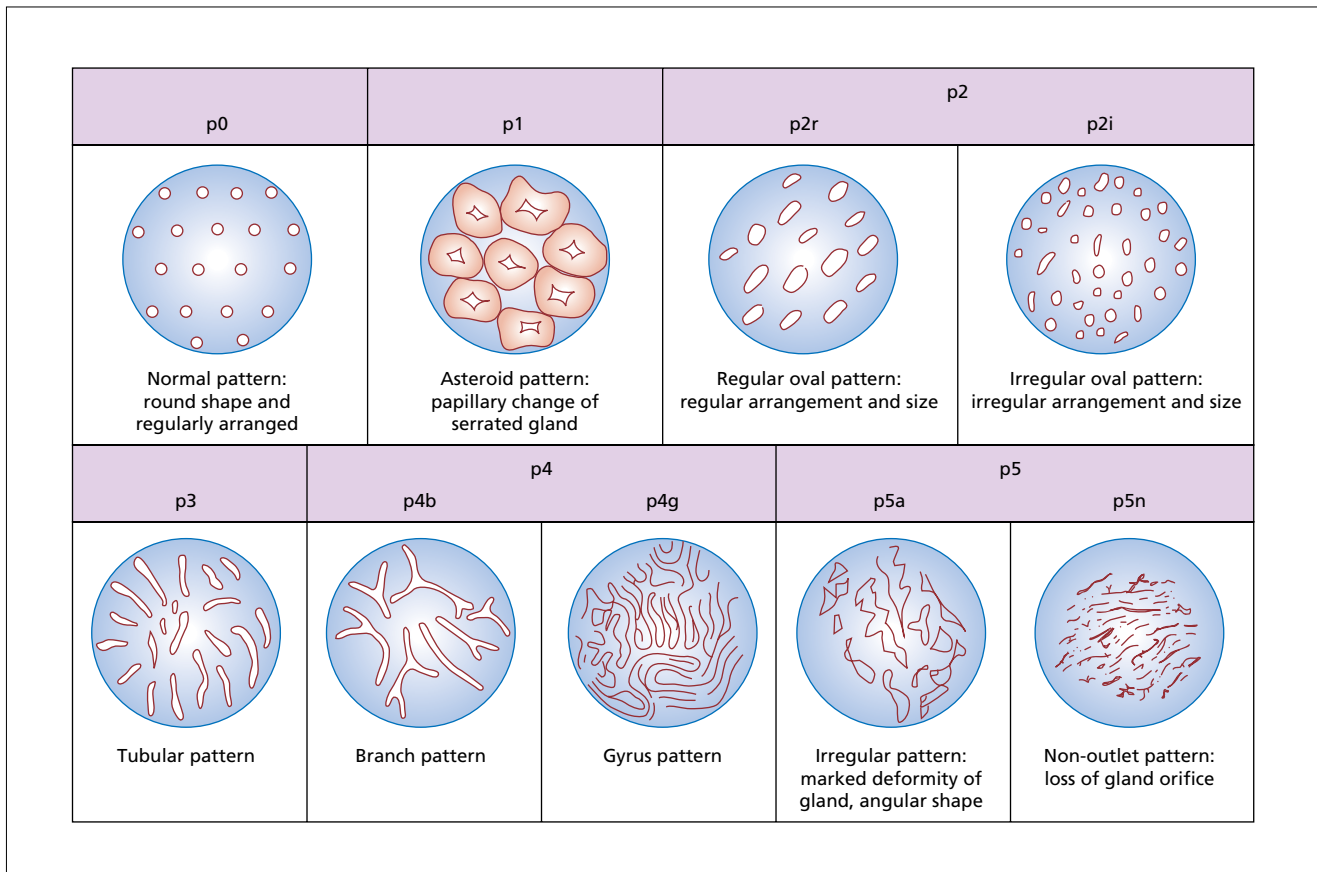


Fig. 43.1 There is a progression of pit shape and organization from normal with round shape and regular arrangement to irregular pattern and marked deformity with cancer. Courtesy of Dr S. Kudo, Showa University.

nontoxic, although systemic adverse effects have been noted on intravenous administration [12]. When sprayed topically on colonic lesions, the concentration of ICD used has been 0.1–0.8% (full strength) [13]. The estimated maximal safe daily intake of ICD is 2.5 mg/kg body weight.

To stain the colonic wall, ICD is most commonly applied via a spray catheter at the time of endoscopy. However it can be delivered orally. Mitooka and colleagues [14] used 100 mg of indigocarmine powder in an acid-dissolving capsule 30 min prior to gut lavage with 2 L of a polyethylene glycol solution. They studied 105 patients over 8 months using the oral stain and found at least one polyp in each of 70 patients (66.7%) and at least one neoplastic polyp in 58 (55.2%). The authors comment that the polyp rates were higher than seen in previous studies on Japanese patients, suggesting that

Fig. 43.2 Crystal violet is an example of an absorptive stain. It is taken up by the glands of Lieberkühn. Courtesy of Dr S. Kudo, Showa University.

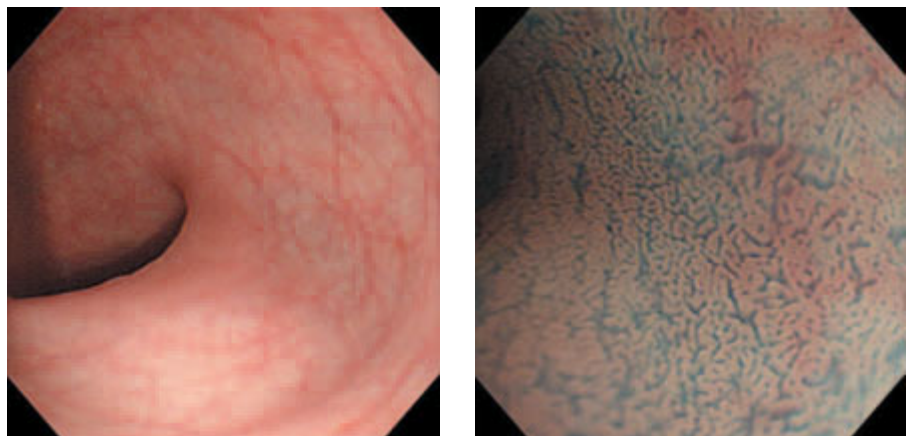




Fig. 43.3 Spray catheter: commonly passed through biopsy channel and then sprayed by hand-held syringe or pump. (Courtesy of Olympus America, Inc., Melville, NY.)

this method might improve detection of small colonic lesions that could be overlooked with conventional colonoscopy. The average percentage of good to excellent ICD contrast with this method varied from 82% in the cecum to 53% in the rectum. This route of administration was first described in 1992 and has not become popular. It is more common to deliver ICD either through a spray catheter or flushed through the biopsy channel. Generally, 3–5 mL are used with 15 mL of air, or 20 mL of dye with no air. Before the dye is applied, any overlying material and mucus should be washed off with a strong flush of water. It is important not to spray the water directly onto the lesions because bleeding has the same effect as mucus in masking the crypt pattern.

Applications in the colon

There have been two main areas in which CE with and without ME have been used in the colon. The main use has been for the detection, characterization, and delineation of polyps and neoplasms. For both diminutive and flat polyps otherwise not seen with routine endoscopy, CE has led to an increased diagnostic yield. Using high-resolution endoscopes and/or ME with CE, investigators have been able to identify topographic

characteristics that have a high degree of correlation with the histology of polyps. Using ME and stereomicroscopy, endoscopists have studied tumorous lesions of the colon and classified these lesions according to the configuration of their “pit patterns” [8]. Using ME, aberrant crypt foci of the colon can be found and are felt to be precursors of adenomas and cancer [15]. The risk is highest when aberrant crypt foci are large and have dysplastic features. The topic of ME and flat adenomas is covered in Chapter 41. In some instances CE is used to delineate the margins of the neoplastic tissue so that endoscopic resection can be more accurate. Another use of CE has been to assess colonic mucosa in diseases such as ulcerative colitis. The use of CE for evaluating colonic diseases is a topic of interest to endoscopists around the world [16].

Diminutive polyps

The classification, definition, histology, and biology of colon polyps are addressed in Chapters 31–33. One question that has fascinated colonoscopists is whether one can predict the histology of polyps on endoscopic examination. At this time, we cannot make this differentiation with conventional colonoscopy, especially with diminutive polyps. Some work has been done using CE with ME or high-resolution endoscopy to distinguish adenomatous from nonadenomatous polyps. The ability to do this accurately would be a significant step in reducing the cost of colon cancer screening by eliminating the need for biopsies and a follow-up colonoscopy if only hyperplastic polyps were seen on screening sigmoidoscopy, since it is believed that hyperplastic polyps are not a risk factor for colon carcinoma.

In 1994, George and colleagues [17] from the Cleveland Clinic used 0.2% ICD spray to evaluate 89 diminutive polyps in 41 patients undergoing screening colonoscopies. Four polyps were adenomatous (5%) and 60 (67%) were hyperplastic; 25 were classified as “other,” of which 21 (24%) were normal and four (5%) were either lymphoid aggregates or inflammatory bowel disease. The endoscopists were only able to predict correctly 47% of the polyp histology after ICD spraying (68% of the hyperplastic polyps). However, a standard colonoscope was used, which seems to indicate that ICD alone is not sufficient to determine the pit pattern of diminutive polyps.

In 1995, Axelrad and colleagues [18] from Georgetown University used 0.2% ICD spray with a Fujinon 400 series colonoscope (high resolution, $\times 1.5$ magnification) to predict the histology of multiple polyps in 36 patients (12 retrospective, 24 prospective) during a colonoscopy. Hyperplastic polyps had a characteristic pitted pattern (Fig. 43.4a) and adenomatous polyps had a sulcus pattern (Fig. 43.4b). In the prospective part of the trial,

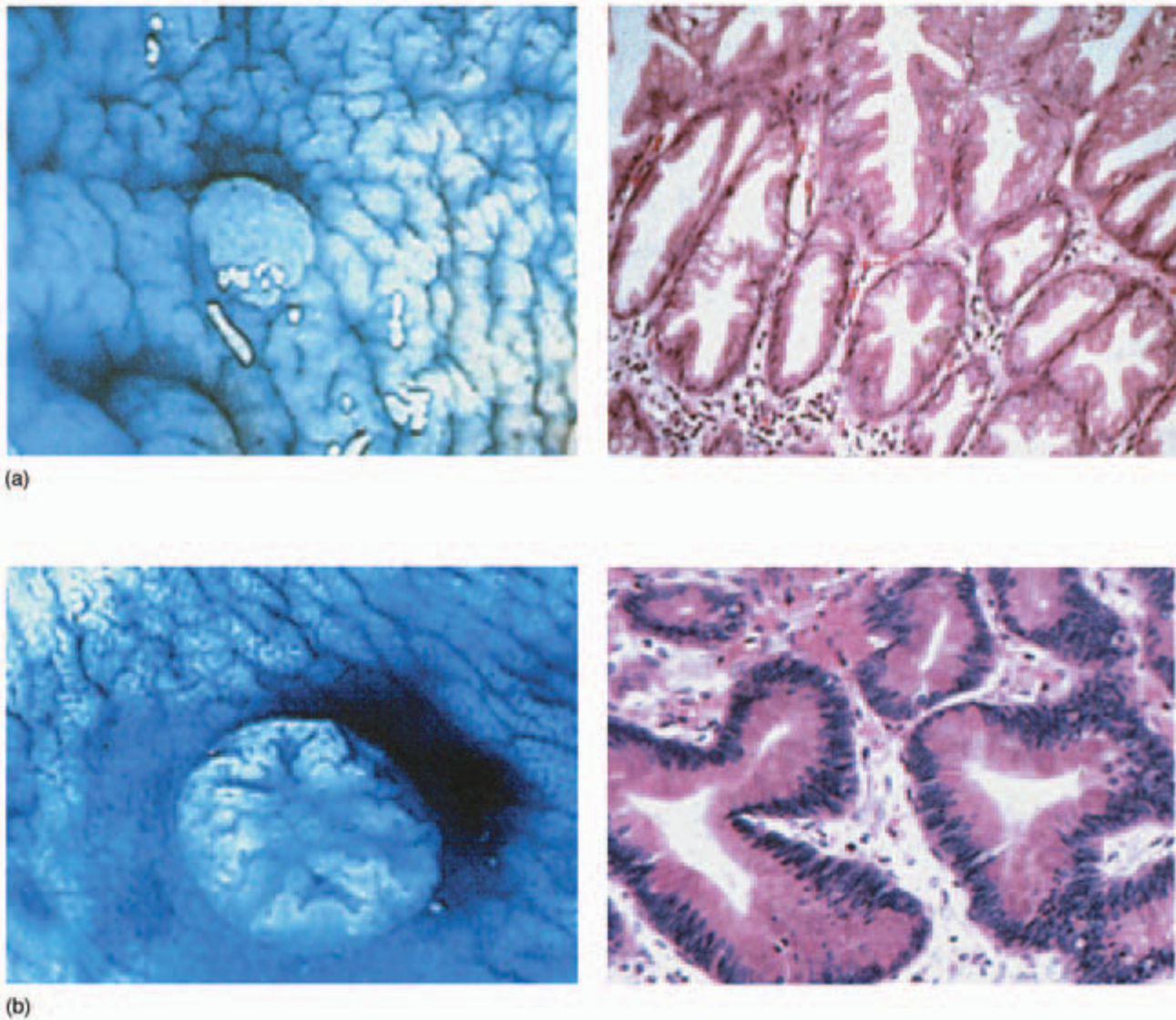


Fig. 43.4 Chromoendoscopy for diminutive polyps: (a) typical pitted pattern seen with hyperplastic polyps; (b) adenomatous polyps show sulcus pattern. (Fujinon colonoscope 400 series, Fujinon, Wayne, NJ.)

the diagnostic accuracy for adenomatous polyps was 93% (13 of 14) and for hyperplastic polyps was 97% (31 of 32). There were nine polyps in the “other” category and if these were considered as nonneoplastic, then this method had a 93% sensitivity and 95% specificity for detecting adenomas. There did not appear to be any difference in the accuracy of this trial comparing the magnified high-resolution prediction with a non-magnified high-resolution prediction. All but one of the 55 polyps seen in the prospective phase were less than 10 mm in size. A limitation of the procedure was that the cecum was not reached in 12% of the patients using the specialized 15-mm colonoscope.

In 1996 Fry and colleagues [13] at Georgetown University repeated a similar trial with 0.4% ICD spray (rather than 0.2%) and used high-resolution colonoscopy without magnification. The diagnostic accuracy for adenomatous polyps was 96% (25 of 26) and for hyperplastic polyps was 88% (22 of 25). The sensitivity for adenomatous polyps was 96% and the specificity 81%.

A multicenter study using conventional high-resolution colonoscopes and flexible sigmoidoscopes (Fujinon, Inc., Wayne, NJ) involved gastroenterologists at academic medical centers [19] and primary care physicians. Neither group had prior exposure to CE techniques. Using CE with ICD, both groups evaluated 520 polyps in 299 patients. The resected polyps comprised 193 adenomas (37%), 225 hyperplastic polyps (43%), and 102 others (20%). In this multicenter study, the overall sensitivity and specificity were each 82% but the negative predictive value was 88% (92% in the center

Characteristic	All centers
Number of patients	299
Number of polyps dyed	520
Mean size (mm)	4.7
Number \leq 5 mm	407
Number distal to splenic flexure (within reach of sigmoidoscope)	444 (85%)
Number of diminutive polyps (\leq 5 mm) distal to splenic flexure	353 (68%)
Number of adenomas distal to splenic flexure	151/193 (78%)
Number of hyperplastic polyps distal to splenic flexure	192/225 (85%)
Number of "others" distal to splenic flexure	84/102 (82%)

Table 43.2 Characteristics and distribution of all polyps. (From Eisen *et al.* [19].)

with the greatest experience). The negative predictive value is the most important parameter with regard to screening because it represents the technique's power of predicting that a polyp is not an adenoma. Table 43.2 shows the location, distribution, and histology of all polyps encountered by site. In total, 520 polyps with a mean diameter of 4.7 mm (range 2–10 mm; 353 distal polyps were diminutive, i.e. 5 mm or less) were evaluated. Hyperplastic polyps ($n = 225$) were most often seen in the rectum and sigmoid (192 of 225; 85%), as were adenomas ($n = 151$ of 193; 78%). The "other" category ($n = 102$) consisted of normal colonic mucosa, lymphoid aggregates, and inflammatory polyps.

A study similar to the American multicenter study was carried out in Japan by Kanamori and colleagues [20]. The overall designs of the two studies were similar, and 0.4% ICD (in contrast to 0.8% ICD in the American study) was used with an Olympus colonoscope (Tokyo, Japan). The study evaluated 1468 polyps from 1018 colonoscopies, of which 1201 were adenomas and 267 were hyperplastic polyps. The sensitivities for polyp differentiation with CE and routine colonoscopy were, respectively, 96.6% and 73.4% ($P < 0.0001$); specificities were, respectively, 96.6% and 92.1% ($P = 0.077$). The mean diameter of the polyps was 4 mm (range 1–20 mm).

CE provides additional information about diminutive polyps. Although the accuracy is not 100%, CE could be used to stratify patients with diminutive polyps. For example, those with no polyps might receive their next screening examination at a longer interval (e.g. 10 years), whereas those found to have a "hyperplastic polyp" (for which the negative predictive value could be expected to be about 90%) would receive the examination at a shorter interval (e.g. 5 years). CE allows the endoscopist to avoid taking a biopsy, with implications for saving time and money and for reducing risk, all of which will make screening more appealing to the patient, the provider, and the funders.

Neoplastic polyps and adenocarcinoma

Since most sessile and pedunculated polyps and most carcinomas are obvious without using tissue sprays, the

main application for CE in this category has been for flat adenomas and in some instances to define tumor depth in attempts to clarify the possibility of endoscopic resection (Fig. 43.5). In most of these cases, ME is employed and this is addressed in Chapter 41. There may be a role for CE in spraying the normal-appearing mucosa around an obvious neoplastic lesion in order to better define the margins of a sessile polyp if endoscopic resection is considered.

Ulcerative colitis

It is generally accepted that cancer in ulcerative colitis may develop in flat mucosa and that dysplasia does occur without detectable mucosal changes using conventional colonoscopy. Very few authors have reported the use of dye-spraying methods to enhance details of the surface of the mucosa in patients with ulcerative colitis [2,21,22]. Tada and Kawai [2] in Japan compared endoscopic findings by Roth's classification (active phase, chronic active phase, chronic quiescent phase)

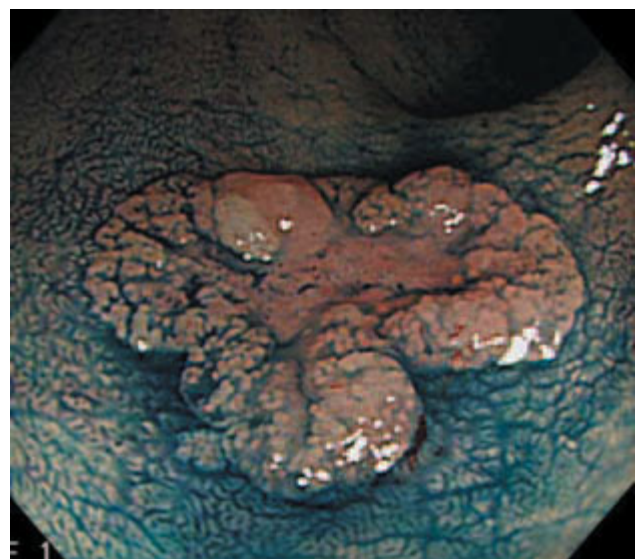
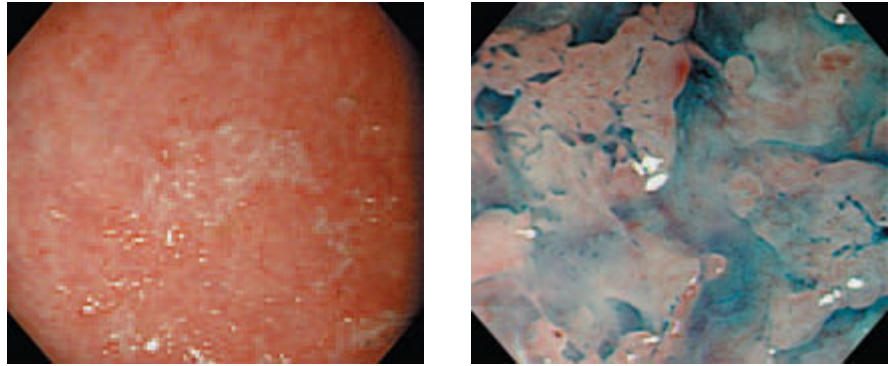


Fig. 43.5 Use of chromoendoscopy to define and delineate flat adenoma. Courtesy of Dr T. Fujii.

Fig. 43.6 Pronounced changes of ulcerative colitis with nodular mucosa and ulceration. Spray with indigo carmine shows coarse mucosa with irregular lesions. Courtesy of Dr M. Fujiya.



with histologic findings (active, almost healed, healed). They reported that the chronic quiescent phase did not correlate well with histologic findings of almost healed (44%) and healed (55%). However, the CE grade corresponded 100% with histologic classification of activity when there was erythema, erosions, and irregular or no pits. There was also 100% correlation with healed histology when CE showed normal color, no erosions, and regular pits.

Jaramillo and colleagues [21] in Sweden combined magnification with 0.5% ICD spraying to evaluate morphology and histology of flat mucosal polyps in patients with ulcerative colitis. At histology, flat polyps were found to be either flat adenomas (14%), adenomas with dysplastic cells in the base of the crypts (5%), hyperplastic polyps (34%), inflammatory mucosa (7%), or mucosa in remission (40%). Only one polyp of the adenomas (1 of 15, or 7%) had high-grade dysplasia; none of the polyps had a central depression, which was consistent with a previous study by Jaramillo and colleagues [23] on patients with nonulcerative colitis. In this study, 43% of flat polyps with a central depression had high-grade dysplasia compared with 7% of flat polyps without a central depression. This could mean that flat polyps without a central depression have a low potential for malignancy.

In addition to using colonoscopy for cancer surveillance in ulcerative colitis, it can also be used to assess disease activity (see Chapter 48). Fujiya and colleagues [24] used magnifying colonoscopes (Olympus, Tokyo, Japan) and 0.1% ICD to assess disease activity in ulcerative colitis. They developed a classification system to assess disease activity (Fig. 43.6). The colonoscopic findings were compared with histology and the usefulness of the classification system to predict relapse was prospectively analyzed in 18 patients. There was a better correlation with histopathology for magnifying colonoscopy than for conventional colonoscopy. In the 18 patients studied prospectively, 7 of 9 with minute defects of the epithelium relapsed within 6 months while the correlative nonrelapsing rate was significantly lower in patients with minute defects.

Summary

CE is a simple and inexpensive technique that is separate from, and can be used independently of, ME and high-resolution endoscopy. In the upper digestive tract, CE alone with Lugol's iodine has been extremely valuable for screening for dysplasia and early esophageal cancer in patients at high risk for squamous cell carcinoma of the esophagus [3]. Both high-resolution endoscopy and ME present opportunities for enhancing the use of CE. Additional opportunities exist for using color enhancement techniques such as infrared wavelengths and narrowband imaging. It has been disappointing that advances in CE have not moved in parallel with developments in ME, high-resolution endoscopy, and other technologies. There is an opportunity for the advances in biology and chemistry of tissue staining to play a greater role in endoscopic/microscopic analysis.

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Chapter 44

Optical Techniques for the Endoscopic Detection of Early Dysplastic Colonic Lesions

Ralph S. DaCosta, Brian C. Wilson and Norman E. Marcon

Introduction

Colon cancer is associated with high morbidity and mortality rates, as well as tremendous emotional and economic costs in western countries. It is well accepted that most malignant colonic lesions arise in preexisting adenomatous polyps. Japanese authors, such as Kudo and colleagues [1], have theorized that some cancers arise *de novo* and present as small, flat, depressed lesions with high-grade dysplasia and indeed, even in lesions 1 cm or less, with invasion into the submucosa. Commonly, when patients present with clinical symptoms, large and symptomatic tumors have typically reached an advanced stage, resulting in poor prognosis and significantly reduced chance for cure.

Since prognosis and ultimate survival are related to lesion size and stage (i.e. mural invasiveness and positive node status), the ideal scenario would be to detect lesions in the earliest premalignant form, before they have reached the point of escape from cure. The presumption is that outcomes such as survival and quality of life would be significantly enhanced by administering treatment while the lesion is still localized to the mucosa.

Despite the reduction in the incidence of colon cancer in screened populations as a result of conventional endoscopic methods using white-light endoscopy (WLE) plus polypectomy [2,3], their clinical effectiveness remains suboptimal. Why is this? Readily visible lesions that are adenomatous and therefore removed have been shown to reduce the incidence. The question arises whether small subtle lesions (i.e. flat adenomas, flat-depressed adenomas) are missed because of inadequate preparation and/or lack of visual recognition by endoscopists who are not searching for these lesions carefully (see Chapter 30). Additionally, unless visibly obvious alterations in tissue topography (i.e. nodules, raised plaques, or changes in surface texture and color) are present, premalignant lesions may go undetected during routine endoscopic surveillance. Using back-to-back colonoscopies, Hixon and colleagues [4] and Rex and colleagues [5] reported that even an experienced endoscopist could miss 15–24% of neoplastic polyps (< 1 cm), and up to 6%

of larger polyps were overlooked at the time of colonoscopy. Bensen and colleagues [6] confirmed this significant colonoscopic miss rate for neoplastic and hyperplastic polyps. Possible explanations for the miss rate of lesions greater than 1 cm are multifactorial, including bowel preparation and anatomic situations, such as extensive diverticular disease, sharp angulated flexures, and prominent colonic folds (ribbing). Development of adjunctive endoscopic technology may reduce the inherent miss rate of lesions less than 1 cm associated with conventional WLE, and thereby reduce the long-term rates of occult colon cancer in this group of patients.

Normal tissues undergo changes in phenotype and genotype as they progress through various distinct pathologic stages of dysplasia toward invasive cancer [7]. Typically in the West, endoscopic surveillance is targeted at groups with premalignant disorders and associated higher risk(s) for cancer, including those with Barrett's esophagus, long-standing chronic ulcerative colitis (UC), and familial adenomatous polyposis. These various high-risk groups are often subjected to poorly defined surveillance algorithms. The detection of small dysplastic lesions is largely dependent on the experience of the endoscopist and the identification of subtle changes in mucosal topography. In the absence of these changes, the endoscopist relies upon protocols for multiple random biopsies to detect dysplasia, as in surveillance of chronic UC. In addition, the extent and precise assessment of depth of invasion of the dysplastic lesion in the tissue is often not effectively determined with WLE [8].

An area of recent controversy has been the low reported incidence in the Western Hemisphere of flat adenomas and small depressed carcinomas of the colon. (see Chapter 42). Japanese authors have described these lesions for several years [1,9–11]. Some western endoscopists suggest that this is a Japanese phenomenon. However, recent studies by Japanese endoscopists examining European and North American patients reported an incidence comparable to Japanese patients [12]. Why is this so? It would seem that important factors are careful and thorough examination by an experienced endoscopist using chromoendoscopy in an adequately

prepared bowel. The adjuvant use of dye spraying and magnification endoscopy can improve detection and differentiation, but tend to be time-consuming, labor-intensive, and not commonly used outside Japan [13].

Nevertheless, detection of flat adenomas under white-light imaging alone can be difficult. Distinguishing between hyperplastic and adenomatous polyps is often not possible. The ability to detect and identify dysplasia within fields of transformed mucosa remains another major clinical problem. For example, identifying flat dysplasia and which polyps are dysplastic in the background of long-standing chronic inactive UC is problematic. Also, *in vivo* differential diagnosis between benign hyperplastic polyps and adenomatous polyps of the same size and shape continues to be challenging. For instance, if the endoscopist is highly confident that the polyp is adenomatous and less than 5 mm, it must be removed. On the other hand, lesions shown to be hyperplastic can be left behind, therefore saving time and processing costs. Such clinical issues provide strong motivation to develop and evaluate alternative but complementary endoscopic systems with higher sensitivities and specificities for detection of dysplasia and early malignant lesions in the colon.

The search for such alternative diagnostic techniques has led to the evaluation of several optically based methods with the potential to revolutionize modern endoscopy. This chapter provides a basic overview of the most well-developed optical technologies that offer a promising means of improving the endoscopic detection of early malignancy in the colon. They include fluorescence spectroscopy and imaging, Raman spectroscopy, light-scattering spectroscopy, optical coherence tomography, confocal fluorescence microimaging, and immunophotodetection.

Basic tissue optics

Tissues are a complex mixture of biomolecules. The interaction of light in tissue can be described by two fundamental properties by which photons and these biomolecules interact: *scattering* and *absorption* (Fig. 44.1). When light of a particular wavelength illuminates the tissue surface, some of the light is reflected from the surface. The remainder enters the tissue and can be either scattered by tissue microstructures or absorbed by tissue molecules. These light photons are scattered diffusely throughout the tissue. Those scattered close to the tissue surface can be reemitted from the surface, without a change in wavelength (diffuse reflectance). A small number of excitation photons are scattered several times and escape from the tissue surface, while a smaller number of these photons escape the surface after only a single scattering event. Conventional WLE images are composed of light which is both specularly and diffusely reflected by tissues. Most photons are scattered deep into the tissue and are eventually absorbed by tissue components. Photons can be absorbed by both chromophores and fluorophores. The former comprise molecules that do not emit photons once an excitation photon is absorbed, while the latter will emit a photon of longer wavelength, producing fluorescence (see next section).

The depth of penetration of incident light is dependent on wavelength, since the wavelength-dependent tissue absorption and scattering determine the extent by which light will be attenuated. The probability of a photon being absorbed per unit distance through tissue for a given wavelength can be described as the absorption coefficient, μ_a . This value is determined by the concentration and absorption cross-section of the various chromophores in the tissue. In tissue, the dominant

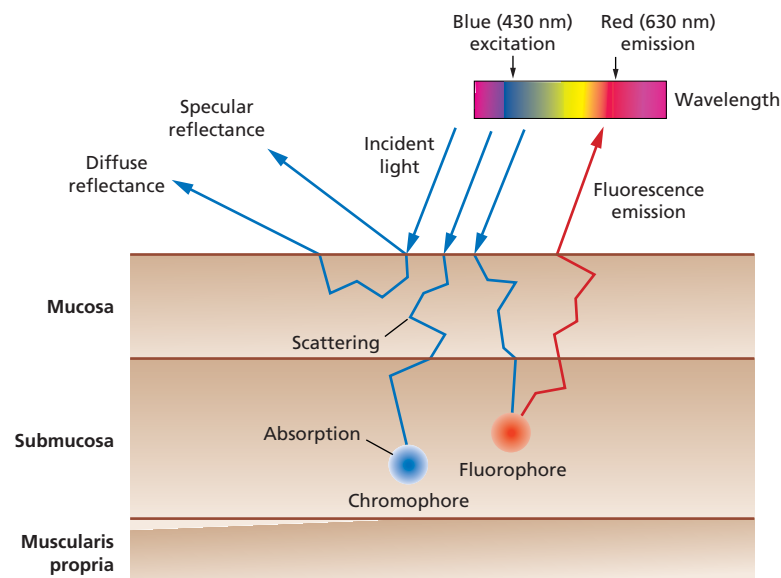


Fig. 44.1 The interaction of light with tissue.

absorber is hemoglobin, which exhibits characteristic absorption peaks at 420, 540, and 580 nm.

Tissue scattering is dependent on the wavelength of the incident light and on the size and relative index of refraction of the scattering particles. Scattering for a particular wavelength can be characterized by the scattering coefficient, μ_s , which describes the probability of a scattering event per unit path length traveled by the photon in the tissue. Longer wavelengths are scattered less than shorter wavelengths, and so longer wavelengths penetrate deeper into tissue. In biologic tissues, scattering dominates absorption.

Tissue autofluorescence

Illumination of tissue with ultraviolet (UV) or short-wavelength visible light from a laser source or filtered lamp results in the emission of fluorescence light of a longer wavelength by endogenous tissue molecules (fluorophores). This *autofluorescence* arises mainly from:

- components of connective tissues (i.e. collagen, elastin);
- cellular metabolism-related coenzymes such as reduced nicotinamide adenine dinucleotide (NADH), flavin adenine dinucleotide (FAD), and flavin mononucleotide (FMN);
- aromatic amino acids (i.e. tryptophan, tyrosine, phenylalanine);
- byproducts of heme biosynthesis (i.e. porphyrins);
- lipopigments (i.e. lipofuscin, ceroids).

Different excitation wavelengths activate different groups of fluorophores, each of which emits at a range of different wavelengths (Table 44.1). Tissues also contain molecules (chromophores) that absorb light without reemission of fluorescence. The absorption is strongly wavelength dependent and may significantly modify the *in vivo* fluorescence spectrum observed at the tissue surface. The main chromophore in gastrointestinal tissues in the visible wavelength range is hemoglobin.

While each fluorophore has a distinct fluorescence spectrum, tissues have a mixture of several fluorophores that occur in different concentrations and at different depths. Thus, the mucosa, submucosa, and muscularis propria have distinct fluorophore compositions, so that the fluorescence measured at the luminal surface comprises contributions from the fluorophores in the various layers. Since the excitation and fluorescence emission bands are often broad, relatively featureless, and overlap with one another, identifying individual fluorophores in a given tissue spectrum is difficult. Changes in the intrinsic fluorescence of the tissue layers with disease are due to alterations in their biochemical composition (metabolic state, microenvironment). In addition, changes in layer thickness or blood content contribute to the differences seen between normal and diseased tissues. Thus, the use of autofluorescence to detect early cancers or premalignant colonic lesions is dependent on changes in one or more of the following factors:

- 1 tissue architecture (mucosal thickening or loss of layered structures);
- 2 light absorption and scattering properties of each layer, particularly hemoglobin in the capillary networks;
- 3 distribution and concentration of fluorophores in the different layers;
- 4 biochemical microenvironment of the tissue, which may alter the fluorescence yield or spectral shape;
- 5 metabolic status of the tissue, e.g. changes in NADH fluorescence have been used to differentiate normal from dysplastic tissues [14].

Therefore, tissue autofluorescence is sensitive to alterations in tissue morphology and biochemistry resulting from malignant transformation, although the details are complex. The degree to which disease changes *in vivo* fluorescence measurements is significantly wavelength dependent, since the excitation and emission wavelengths used determine the dominant fluorophores involved. For example, tissue proteins, composed of amino acids, are autofluorescent only when excited by UV wave-

Table 44.1 Typical endogenous tissue fluorophores and wavelengths of their excitation and emission maxima.

Tissue fluorophore	Biologic source	Wavelength of maximum fluorescence excitation (nm)	Wavelength of maximum fluorescence emission (nm)
Collagen	Connective tissues	330	390
Elastin	Connective tissues	350	420
Tryptophan	Amino acids	280	350
NADH	Metabolic cofactor	340	450
FAD	Metabolic cofactor	450	515
Porphyrins	Byproduct of heme biosynthesis; bacterial fauna	405	635
Ceroid, lipofuscin	Lipopigment granules; age related; lipid oxidation products	340–395	430–460, 540–640

FAD, flavin adenine dinucleotide; NADH, reduced nicotinamide adenine dinucleotide.

lengths, while all other fluorophores (mentioned above) are excited by visible wavelengths. In general, as the wavelength increases, so too does the penetration depth of the excitation light. Thus there may be one or more optimal excitation or emission wavelength bands, depending on the anatomic site or application. Unfortunately, for each type of tissue the optimal excitation and emission wavelengths are not known a priori and must be determined from *ex vivo* tissue samples. This has the advantage of providing detailed fluorescence spectroscopy and microscopy, although the accuracy of the results must be considered carefully since the measured spectra may be altered by loss of blood or metabolic changes [15]. The measurement of excitation and emission matrices of known and suspected biologic fluorophores *in solu* may also help identify the optimal excitation and emission wavelength bands for tissue autofluorescence spectroscopy (see Fig. 44.4) [16].

Clinical evaluation of fluorescence endoscopy

The field of fluorescence diagnostics in gastrointestinal endoscopy is about 10 years old, and *in vivo* fluorescence imaging has only begun to appear within the last 5 years. Wagnieres and colleagues [17] recently presented a critical status report on the detection and characterization of premalignant or malignant lesions using *in vivo* fluorescence spectroscopy and imaging. Andersson-Engels and colleagues [18] recently described the current use of *in vivo* fluorescence imaging, while Bigio and Mourant [19] discussed point fluorescence measurements. DuVall and colleagues [20] reviewed tissue autofluorescence in the gastrointestinal tract and showed the first preliminary endoscopic images using an *in vivo* prototype fluorescence imaging system. DaCosta and colleagues [21] reviewed both clinical and mechanistic features of autofluorescence imaging and spectroscopy in the gastrointestinal tract. Stepp and colleagues [22] have reviewed the basic principles, techniques, and clinical experience of fluorescence endoscopy in gastrointestinal diseases, while Bohorfoush [23] presented various spectroscopic techniques being investigated in the gastrointestinal tract. Richards-Kortum and Sevick-Muraca [24] have described, from a more quantitative perspective, several optical spectroscopies, including fluorescence.

Two primary endoscopic methods (point spectroscopy and imaging) have been developed to investigate tissue fluorescence *in vivo*. Fluorescence point spectroscopy involves the use of an optical fiber probe, typically 0.5–1 mm in diameter, passed down the accessory channel of the endoscope and placed in gentle contact with the mucosa (Fig. 44.2). The majority of such probes are multifibered; typically, a central delivery fiber illuminates the tissue while a surrounding circular array of

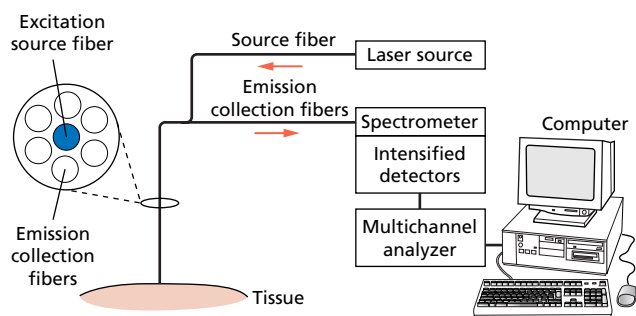


Fig. 44.2 Schematic block diagram of a typical *in vivo* fluorescence point spectroscopy system.

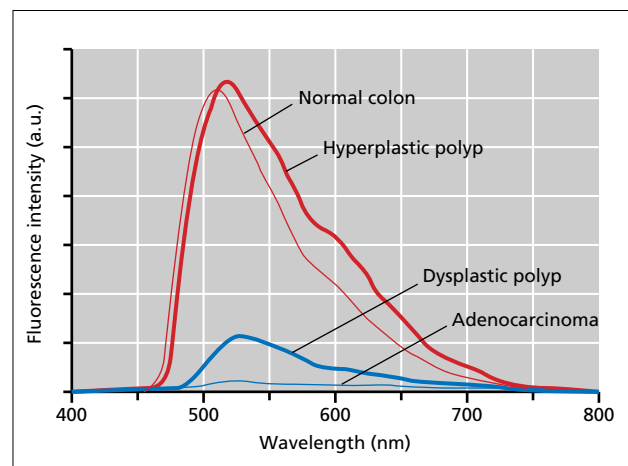
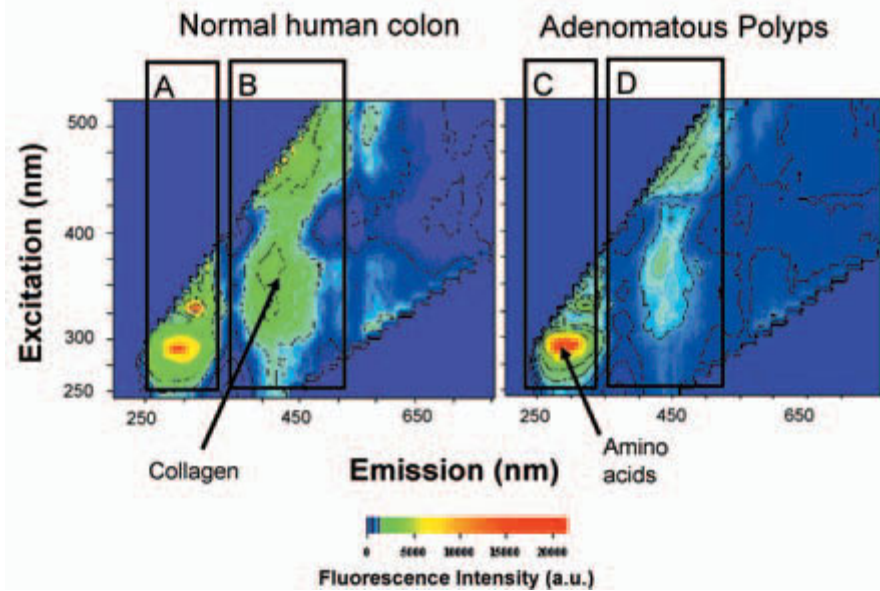


Fig. 44.3 Example of *in vivo* fluorescence spectra of normal colon, hyperplastic and dysplastic polyps, and colon adenocarcinoma. Note significant differences in fluorescence intensity and spectral line shapes between normal and abnormal tissue types.

sensor fibers collects the emitted fluorescence. Optical filters block the detection of scattered excitation light. The fluorescence light is separated into component colors by a spectrograph and displayed as a fluorescence intensity vs. wavelength line curve (Fig. 44.3). Various mathematical procedures can be applied to these spectra to extract diagnostic information, such as taking the ratio of two or more fluorescence emission wavelength bands [4,25–28]. However, the ability of some diagnostic algorithms to distinguish dysplasia from normal tissue can be significantly altered by background inflammation, such as in Barrett's esophagus and chronic long-standing UC. Therefore, different algorithms may have to be evaluated for different segments of the gastrointestinal tract. During endoscopy, fluorescence point measurements must be guided by white-light viewing of the luminal surface. However, the actual spectral measurement must be performed with the white light temporarily turned off to minimize background saturation.

Fig. 44.4 Examples of average autofluorescence excitation and emission matrices (EEM): three-dimensional plots of *ex vivo* tissues from normal human colon and adenomatous polyp collected using a surface-contact fiberoptic probe. Fluorescence intensity is represented by a color scale bar. Both tissue EEMs were measured using an optical fiber probe with a central illumination fiber and several radially displaced collection fibers, placed in contact with the tissue surface. Comparison of regions A and C shows significant increase in ultraviolet-excited endogenous fluorophores (i.e. amino acids), appearing as a red color in the adenomatous polyp (attributed to increased cellular proliferation rate). Comparison of regions B and D shows increased visible-light-induced fluorescence, appearing as a green color from connective tissues (i.e. collagen, elastin) in the normal tissue.



Fluorescence point spectroscopy was the first approach used for tissue autofluorescence diagnosis in the gastrointestinal tract. The majority of the initial studies involved tissue analysis *ex vivo*, particularly in the colon. In 1990, Kapadia and colleagues [29] applying multivariate linear regression analysis of the fluorescence emission band demonstrated accuracies of 100, 94, and 100% for identifying normal, hyperplastic, and adenomatous tissues, respectively. Richards-Kortum and colleagues [30] measured excitation and emission matrices in *ex vivo* colonic polyps, using a range of excitation and emission wavelengths (Fig. 44.4). The optimal excitation wavelengths for discrimination of normal colon from adenomatous polyps were around 330, 370, and 430 nm. Subsequently, these authors showed that adenomas could be accurately identified against normal colon using 370-nm excitation light and emission wavelengths of 404, 480, and 680 nm. Schomacker and colleagues [31] confirmed that fluorescence spectroscopy could be used to differentiate between nonneoplastic and neoplastic colon tissues with a sensitivity of 80% and specificity of 92%.

The first *in vivo* study, reported by Cothren and colleagues [32], allowed differentiation of adenomas and nonadenomatous colon tissue in 97% of cases. The first blinded study of *in vivo* fluorescence spectroscopy of the colon reported by this group identified the correct tissue type in 88% of cases, with a sensitivity of 90% and specificity of 95% [33].

To date, several algorithms have been developed in order to exploit spectral differences in autofluorescence

intensities and line shapes between normal and pre-malignant lesions [31,33–35]. Determining the contribution of specific fluorophores and the degree of light absorption due to hemoglobin has also been attempted [24,29,31,34,36,37]. However, these studies were performed mostly using UV excitation, with limited success reported for visible excitation wavelengths.

Most of the *in vivo* point spectroscopy studies to date have involved steady-state fluorescence measurements. An alternative approach based on time-resolved autofluorescence spectroscopy was demonstrated recently when Mycek and colleagues [38] reported the *in vivo* results of 17 patients with 24 polyps (13 adenomatous, 11 nonadenomatous). Time-resolved fluorescence spectra represent the decay of fluorescence intensity at a given emission wavelength as a function of time after a brief pulse of excitation light (~ 10 ns). The decay time of colonic adenomas was shorter than that of nonadenomas, yielding an 85% differential sensitivity, 91% specificity, 92% positive predictive value, and 83% negative predictive value. Further evaluations are required to confirm the clinical effectiveness of this technique in other anatomic sites.

To date, all point spectroscopy-based studies in the colon have involved readily visible polypoid lesions; no occult lesions have been described. Although there was a high degree of accuracy in differentiating nondysplastic from obvious dysplastic lesions, this technology is not likely to be efficient or useful in the screening of mucosal abnormalities in large-capacity organs such as the colon and stomach since the probe must contact the tissue

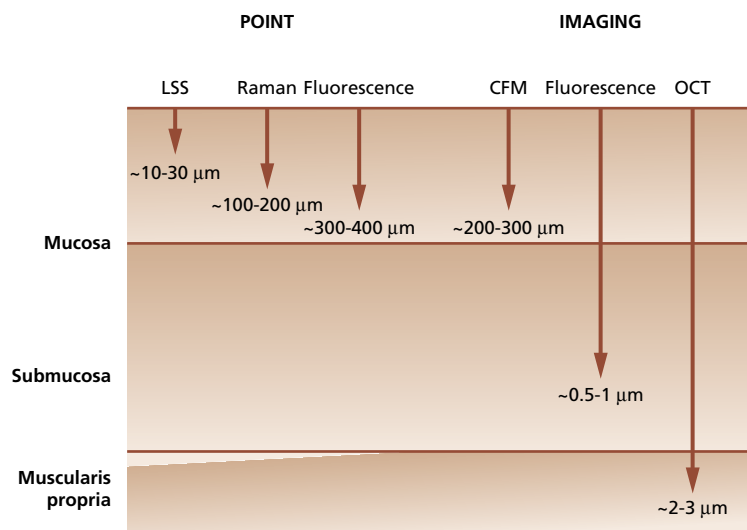


Fig. 44.5 Schematic diagram illustrating relative depths of tissue interrogation for the various optical techniques used in point spectroscopy and imaging modes.

being examined. Despite the potential benefits and relative technical simplicity of fluorescence point spectroscopy, a major drawback is the sampling of only a small volume of tissue ($\sim 1\text{--}3\text{ mm}^3$) immediately beneath the probe tip (Fig. 44.5). The technique is therefore dependent on placing the probe in the right spot (as for biopsy). Targeted sampling is only possible with lesions that are visible [39]. This inherently limits the sensitivity and specificity. In addition, unlike imaging, the information lacks the contextual information often needed to distinguish abnormal from surrounding normal tissues. Instruments that can produce fluorescence images of high resolution and in real time have recently become available [20,27,40], enabling *in vivo* light-induced fluorescence endoscopy (LIFE) imaging to evaluate large areas of the mucosal surface in parallel with WLE examinations.

WLE produces images of diffuse reflectance where the different wavelength components of a broad-band (white) light source are multiply scattered and absorbed in tissue. In WLE the applied and reflected light photons have the same wavelength, as opposed to fluorescence where the emitted fluorescence photons are longer in wavelength compared with the (near) monochromatic excitation light. Since the scattering and, particularly, absorption are wavelength dependent, the different wavelengths effectively interrogate the tissue to different depths (red being the most and blue the least penetrating). The resultant image provides the endoscopist with visual clues to the tissue surface topography and underlying patterns of vasculature.

Light-induced fluorescence endoscopy

LIFE images are formed using only selected emission wavelength bands. There are various ways in which

this can be achieved [17]. For example, the emission bands can be selected using special optical filters, and then be detected by separate cameras to form the final displayed fluorescence image. Thus real-time, false-color fluorescence images of the tissue can be viewed, with switching between this and WLE. Such a system for LIFE imaging has been demonstrated successfully for the bronchus [41,42] as a screening tool for dysplasia and carcinoma in high-risk patients, leading to a commercial system (LIFE-Lung, Xillix Technologies Corp., Canada). This instrument uses blue-light excitation, with separate red and green fluorescence imaging channels. Detection rates of moderate- to high-grade bronchial dysplasia increased by 171% using LIFE in combination with WLE, in comparison with white-light bronchoscopy alone, with only a 22% decrease in specificity.

Currently, prototype imaging systems derived from the original Xillix LIFE-Lung device are being evaluated for gastrointestinal endoscopy, and initial clinical feasibility studies have been reported by ourselves and other collaborating groups [27,28,40,43]. The most recent prototype, Xillix LIFE-GI Imaging System, uses a detachable camera module, which connects to the optical head of a conventional fiberoptic endoscope. The module contains two individual light-sensitive cameras, one for green (490–530 nm) and one for red (590–700 nm) fluorescence. The digital images are combined to produce a real-time, false-color image, where normal tissue generally appears green and abnormal tissue appears red (Fig. 44.6). The ratio of red to green fluorescence is first standardized over normal mucosa. The current system can be rapidly switched ($\sim 4\text{ s}$) between WLE and LIFE, permitting survey of wide areas of the mucosa. Sensitivity and specificity values are determined by correlating the positive (“red” fluorescence) and negative (“green” fluorescence)

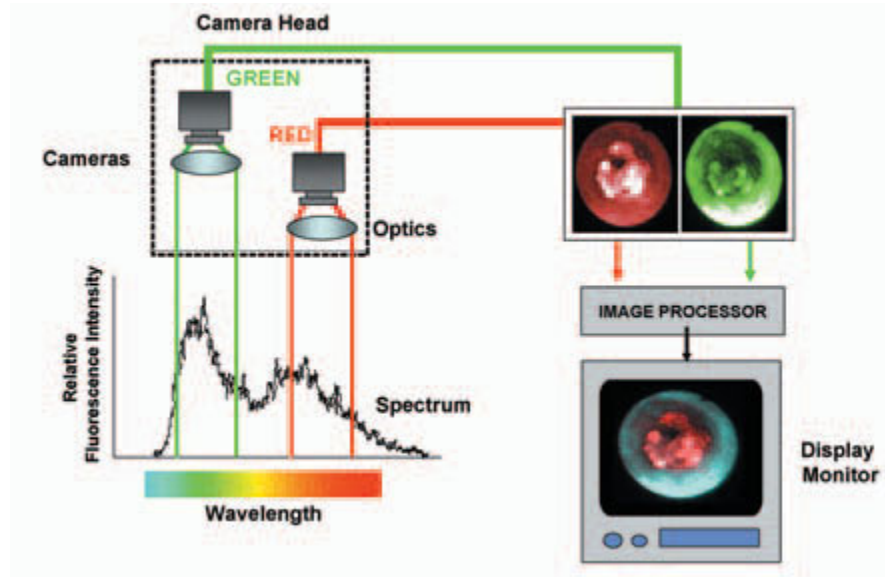


Fig. 44.6 Schematic block diagram of a typical *in vivo* fluorescence endoscopic imaging system.

images with histologic diagnosis of corresponding biopsy samples.

In a preliminary study, we demonstrated detection of atypia or higher-grade lesions in the colon with a sensitivity and specificity of 87 and 79% respectively. In the noninflamed colon, we have not had any false negatives [20]. False-positive lesions have been seen with acute colitis (Fig. 44.7a), both infective and idiopathic. Other investigators have also observed this in both animal and human studies [44]. Large pedunculated polyps of the colon are usually easily detected on WLE. However, distinguishing between growths of the same gross size and shape (e.g. an adenomatous polyp and a submucosal lipoma) may be difficult. Figure 44.7(b) shows an example of a submucosal lipoma which on fluorescence was (true) negative; this can be compared to Fig. 44.7(c), which shows a large pedunculated polyp that was (true) positive under fluorescence and was adenomatous. Diminutive polyps are extremely common and because the endoscopist cannot usually determine whether these are hyperplastic or adenomatous, they are removed or fulgurated. The LIFE imaging system can potentially differentiate between hyperplastic polyps, which have no known malignant potential, and adenomatous polyps, which should be removed. Figure 44.7(d) shows a true negative LIFE image of a hyperplastic polyp, while Fig. 44.7(e) shows a similar-appearing diminutive lesion with positive fluorescence and shown histologically to be an adenoma. While these lesions were detected as nodules by WLE, the real challenge would be to detect dysplastic lesions not recognized by obvious topographic irregularity.

In a recent *in vivo* study of 26 patients, we substantiated the usefulness of the Xillix LIFE-GI Imaging System in differentiating hyperplastic from adenomatous polyps

with a negative predictive value of 97%. For screening, there is considerable interest in the detection of flat diminutive adenomas with dye spraying, using either conventional WLE or magnification endoscopy. A recent paper from Saitoh and colleagues [45] reported that using dye spraying with conventional endoscopy increased the yield of flat adenomas by 66% compared with WLE. Comparatively, we detected about 60% of the flat dysplastic lesions which were occult to WLE, without the use of dye spraying. This is an area that requires careful study with multicenter trials [46]. However, the design of future comparative trials will be difficult because the use of dye spraying interferes with the simultaneous detection of fluorescence. Figure 44.7(f) demonstrates the fluorescence detection of a WLE-occult area of high-grade dysplasia in a 34-year-old woman with a strong family history of colon, breast, and ovarian cancer. This lesion was not seen on WLE. Detection of lesions of this type would be the ultimate goal of any effective screening program and would have a significant impact on survival.

One target group for cancer screening is patients with long-standing UC and Crohn's disease. An example of a dysplasia-associated lesion or mass (DALM) is shown in Fig. 44.7(g); the lesion can be seen as a brick-red color against a blue-green normal background.

Villous adenomas are often sessile and can cover several square centimeters of colonic mucosa. Their removal usually involves the submucosal injection of saline prior to polypectomy. Complete removal is sometimes problematic and recurrence is sometimes difficult to identify with WLE in the area of the scar. However, fluorescence endoscopy facilitates this nicely. Figure 44.7(h) shows an example of a recurrence (red area) in a postpolypectomy scar.

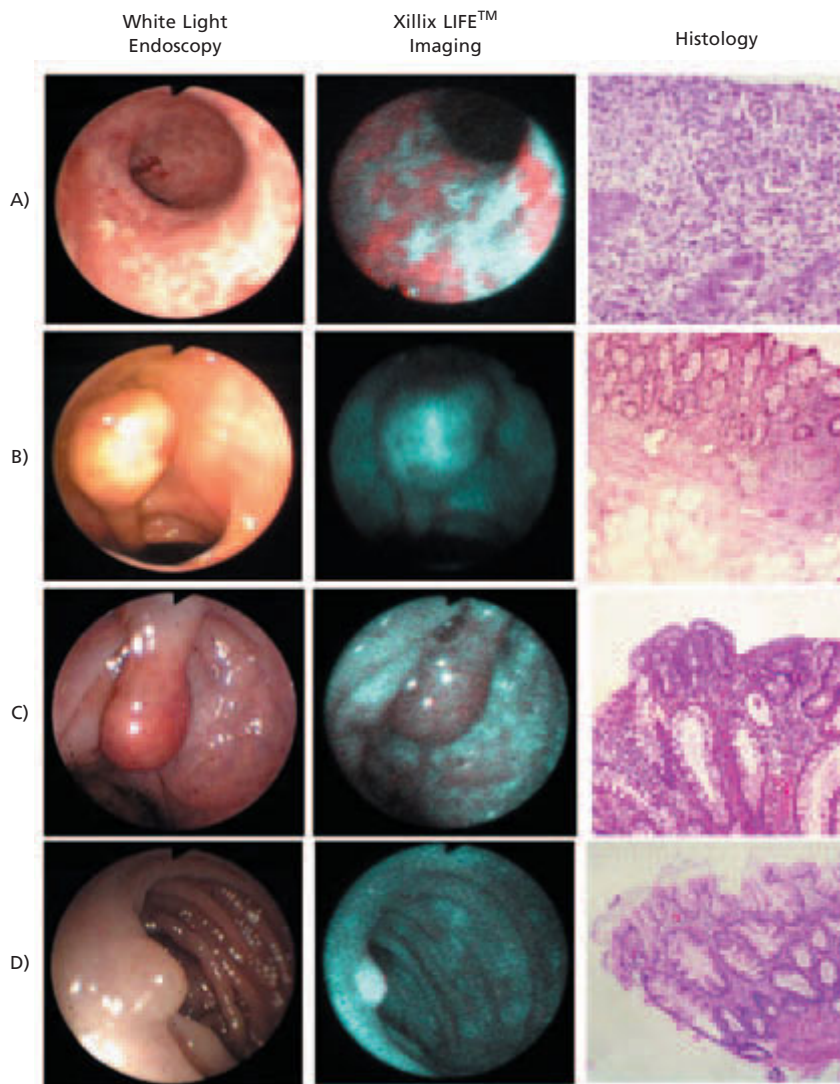


Fig. 44.7 Examples of white-light endoscopy (WLE), *in vivo* LIFE imaging, and corresponding histology of a variety of colonic lesions: (a) ulcerative colitis; (b) submucosal lipoma; (c) pedunculated adenomatous polyp; (d) hyperplastic polyp;

Factors involved in fluorescence imaging systems

Despite progress in the clinical evaluation of prototype fluorescence imaging systems, understanding of the microscopic, biochemical, and molecular origins of tissue autofluorescence and its variation with anatomic site and disease stage remains incomplete. Such understanding contributes to optimum design of clinical instruments and development of more accurate algorithms for image analysis and display.

The excitation wavelength determines which endogenous fluorophores are excited in the tissue, while the content and distribution of these fluorophores and also of absorbing chromophores vary with anatomic site, depth in tissue, and disease stage. The illumination and fluorescence detection geometry are also relevant, e.g. with wide-beam illumination, used for imaging, the detected fluorescence light has greater contribution from

tissues at greater depth than with point spectroscopy. Figure 44.8 shows the difference between the measured *in vivo* spectra of gastrointestinal tissues with narrow (point geometry) and wide-beam imaging (illumination). The dips in the spectra in the case of the latter are due to differential light absorption by blood in the submucosal capillary network. This effect is lacking in the shallow depth "sampling" of contact point spectroscopy.

Neoplasia and fluorescence imaging

In terms of the optimal excitation wavelength(s), a number of different values have been used for *in vivo* point spectroscopy: 325 nm [29], 370 nm [32,33], 410 nm [47,48], and 437 nm [20]. The data indicate some advantages of using UV wavelengths for separating normal and abnormal colon tissues according to their intrinsic fluorescence spectra, although there is concern for possible

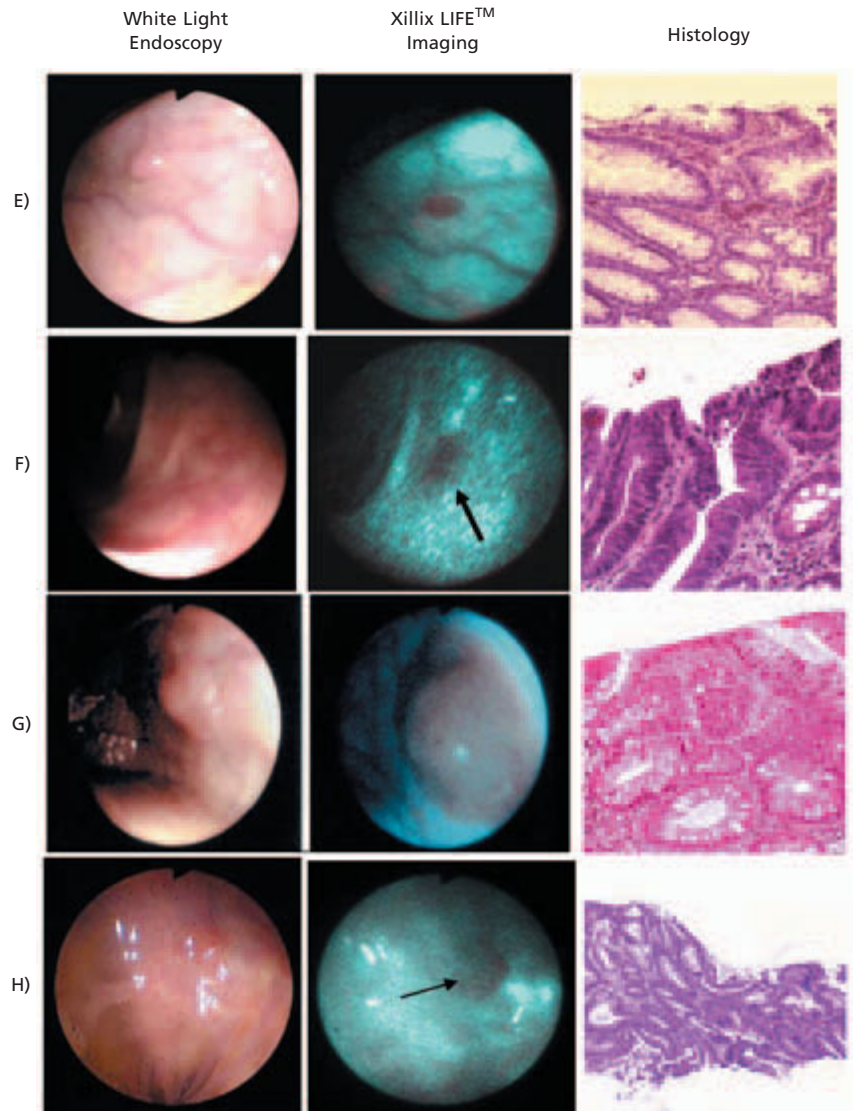


Fig. 44.7 (cont'd) (e) adenomatous polyp; (f) high-grade dysplasia occult to WLE in patient with strong familial cancer history; (g) dysplastic-associated lesion or mass; (h) postpolypectomy recurrence (dysplasia).

mutagenic effects associated with UV light. The tissue optical absorption properties are also strongly wavelength dependent, so that differences in tissue composition and architecture (i.e. squamous vs. Barrett's mucosa, normal colonic mucosa vs. adenomatous mucosa) mean that the effectiveness of any one excitation wavelength may vary with anatomic site.

To date, there have been a number of *ex vivo* studies, particularly in the colon, attempting to characterize and explain the effects of neoplastic changes on clinical measurements [15,25,29,31,34,36,37,49–51]. Most studies have been with UV excitation. Currently, it is believed that gross changes in tissue morphology and changes in mucosal blood content are significant contributors to the differences in fluorescence intensity and spectral shape seen between normal and adenomatous polyps [15,31,34,36,37,49,51]. For example, thickening of the

mucosa leads to an overall decrease in the fluorescence intensity and a loss of green fluorescence relative to red. These changes are primarily due to, respectively, reduction of the excitation light intensity reaching the submucosa and preferential absorption of the shorter wavelength components of the emitted fluorescence. However, LIFE imaging *in vivo* has also been able to differentiate between hyperplastic and adenomatous polyps of the same gross size and shape, and to detect flat adenomas that have no marked mucosal thickening and are topographically similar to surrounding mucosa. This suggests that there are important tissue changes other than, or in addition to, changes in gross morphology. These have been shown to include alterations in the local blood volume, tissue metabolic activity, and relative fluorophore concentrations [15,36,49,50]. Detailed studies of the composition, organization, and content of

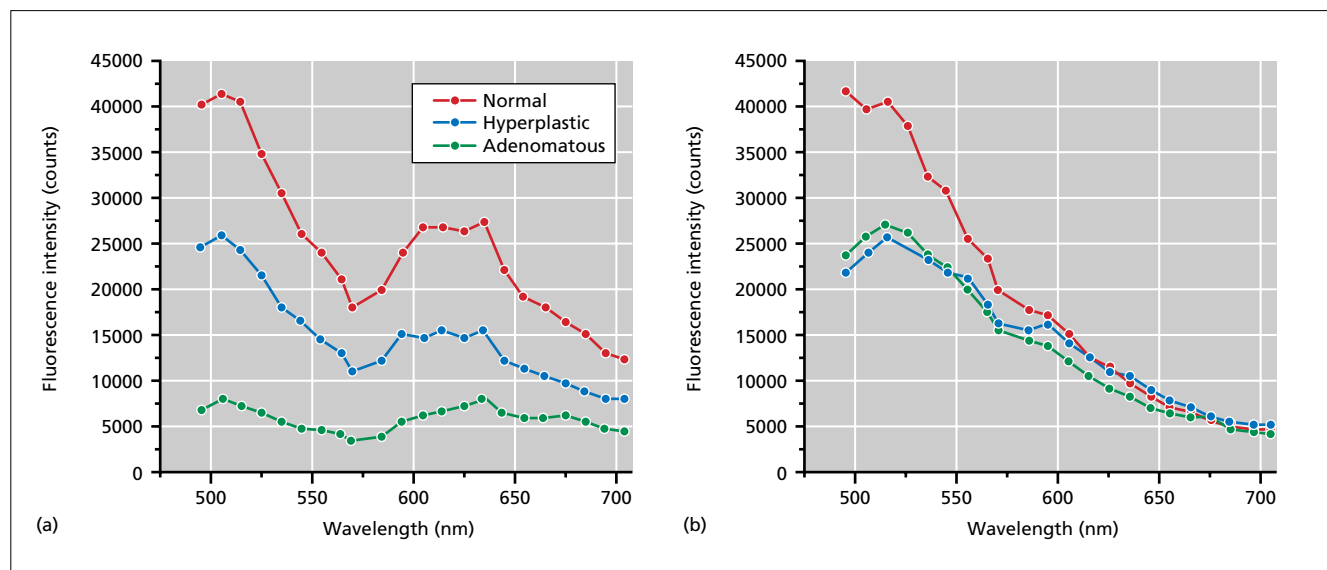


Fig. 44.8 Effect of blood absorption on measured *in vivo* autofluorescence spectra (with 442 nm excitation). Spectra corresponding to normal colon, hyperplastic and dysplastic tissues, and adenocarcinoma were measured in (a) point geometry (central delivery and surrounding collection fibers in contact with the tissue surface) and (b) imaging geometry

colonic tissue fluorophores and chromophores at different stages of malignant transformation have been performed [52].

Most mechanistic studies to date have concentrated on distinguishing normal from adenomatous polyps in the colon, yet the important question of differentiating between hyperplastic and dysplastic lesions has only recently been addressed [52]. In addition, until recently, mechanistic studies have been limited to characterizing the *macroscopic* autofluorescence features of *ex vivo* (frozen and unstained) tissue sections from biopsy or resection. Additionally, high-resolution confocal fluorescence microscopy with special immunohistologic staining and transmission electron microscopy were used in combination to characterize the cellular origins of whole living colonic crypts, and isolated living colonic epithelial cells derived from primary cell cultures of normal, premalignant, and malignant gastrointestinal tissues [53].

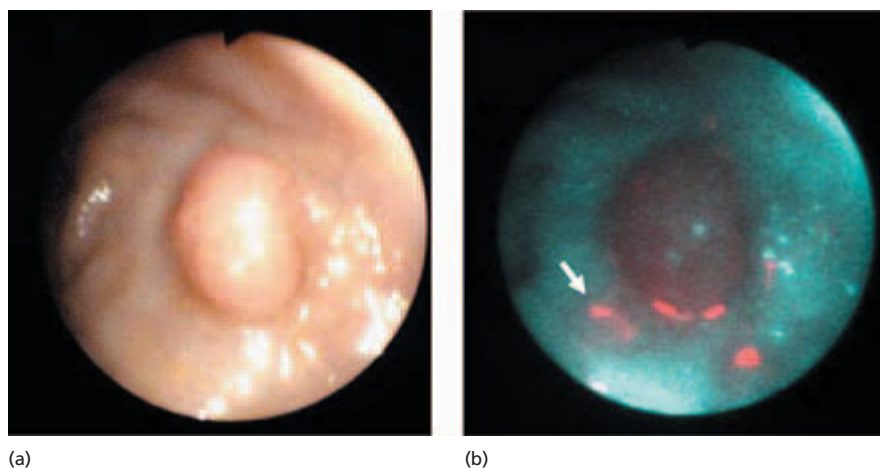
Problems with fluorescence imaging systems

Currently, there is an intense effort to investigate the *in vivo* characterization of normal and dysplastic gastrointestinal tissues using fluorescence imaging and point spectroscopy devices adjunctively to WLE. Which system(s) will prove to be the most clinically suitable remains to be determined, as each is associated with certain

(with wide-field illumination of the tissue surface and spectral measurement made at the central point). Note significant differences in spectral fluorescence intensity and line shapes between point and imaging geometries.

advantages and disadvantages. In general, for a given excitation wavelength, point spectroscopy allows the collection of a fluorescence spectrum, with a wide emission bandwidth, which may be repeated for other excitation wavelengths. A major disadvantage of WLE-guided fluorescence point spectroscopy as a diagnostic tool in the gastrointestinal tract is the necessity to perform many "point" measurements over a large tissue area. This is not only time-consuming but also has the potential of missing lesions occult to WLE. Fluorescence imaging techniques usually allow large areas of tissue to be examined "instantaneously" but with limited spectral information. The effectiveness of either technique is dependent on whether a localized measurement is interpretable alone, or whether surrounding tissue is required for contextual comparison to detect and localize a lesion [17]. Point spectroscopy has aided the design of fluorescence imaging devices and helped identify the optimal excitation and emission wavelengths. Imaging systems have been able to detect unknown lesions over large tissue surfaces, perform lesion localization and margin identification quickly, and monitor therapy. Additionally, the use of fluorescence imaging has been used in conjunction with nonfluorescent pharmacologic agents to improve lesion visualization. For example, Namihisa and colleagues [54] investigated the use of norepinephrine (20 mL of 0.02%) sprayed onto the gastric lesions of seven patients with gastric cancer, who were imaged

Fig. 44.9 Example of (a) *in vivo* white-light endoscopy and (b) LIFE (autofluorescence) images of an adenomatous polyp. Note the “brick-red” fluorescence of the polyp against a cyan-colored normal background, and the bright areas of endogenous porphyrin fluorescence (arrow) caused by residual feces at the edge of the polyp.



with conventional WLE and LIFE-GI imaging before and after spraying. The authors concluded that this method improved the visualization of the lesion boundary with LIFE-GI imaging because the normal mucosa became paler than the tumor after spraying norepinephrine. Whether this method is applicable to colonic imaging is a subject of current investigation.

Early experience with clinical fluorescence imaging systems showed that autofluorescence from endogenous porphyrins in fecal bacteria and bile salts interfered with image interpretation. For example, porphyrin fluorescence appeared as a bright scarlet red against a deeper brick-red color of an adenomatous polyp (Fig. 44.9). This issue has now been resolved with the modification of camera systems.

In the presence of either acute colitis or long-standing chronic inflammatory bowel disease, the presence of inflamed mucosa results in nondysplastic fluorescence (i.e. false positives) (see Fig. 44.7a). However, this is also a problem encountered in the interpretation of random biopsies read by experienced gastrointestinal pathologists attempting to diagnose dysplasia against a background of inflammation. Because of background inflammation, which can be confounding even to the pathologist, it is recommended that patients with long-standing chronic inflammatory bowel disease undergo their surveillance colonoscopy when the disease is quiescent and inactive. Under these circumstances it is possible to identify dysplastic lesions with the LIFE imaging system (see Fig. 44.7g for classic DALM, where the sessile lesion is brick red against the blue-green background).

Exogenous photosensitizer-induced fluorescence

Exogenous fluorescent drugs or prodrugs that induce fluorescence offer an alternative for fluorescence diagnosis, and to date clinical studies have largely exploited the selective localization in neoplastic tissue of photo-

sensitizers used in photodynamic therapy, many of which are also inherently fluorescent. Examples include hematoporphyrin derivative, tetra(*m*-hydroxyphenyl) chlorin, chlorine e6, phthalocyanines, benzoporphyrin derivative, Photofrin II, and tin etiopurpurin. There are several advantages to using drug-induced fluorescence:

- 1 the fluorescent signal is strong compared with autofluorescence, resulting in simpler and cheaper instrumentation;

- 2 optimum excitation and emission wavelengths are known a priori, which allows for subtraction of the “background” tissue autofluorescence.

However, diagnostic effectiveness of drug-induced fluorescence depends on the degree of selective localization of the drug within premalignant lesions and the procedures must be performed at the optimum time for drug pharmacokinetics, which may vary from patient to patient and tissue to tissue. Use of fluorescent drugs also involves extra costs and regulatory issues and, although much lower drug doses are needed for diagnosis than typically used therapeutically, another concern may be cutaneous photosensitization.

The compound 5-aminolevulinic acid (ALA) has shown promise in obtaining good fluorescence contrast between normal and neoplastic tissues. It is well established, in many *in vitro* and *in vivo* systems, that administering ALA in excess results in elevated endogenous synthesis of protoporphyrin IX (PpIX) via the heme biosynthesis pathway [55,56]. PpIX is a fluorescent photosensitizer that has a distinct red fluorescence emission between 625 and 725 nm. Since the PpIX is endogenously generated, there is often a high degree of tissue specificity, with particular localization in the mucosal layer of internal hollow organs, such as the lung [57], bladder [58], and gastrointestinal tract [59]. Although not well understood, in general PpIX appears to be generated, or accumulated preferentially, in malignant tissues. However, contradictory results have been reported

in *in vitro* studies of the differential synthesis of ALA-induced PpIX in tumor and normal epithelial cells [60]. Moreover, *in vivo* results have demonstrated significant variation in PpIX fluorescence from lesion to lesion in the same patient [56] and a strong dependence on anatomic site [61]. Imbalances in concentrations of endogenous iron, porphobilinogen deaminase, or ferrochelatase (an enzyme involved in conversion of PpIX to heme) are considered possible reasons for increased tumor cell production of PpIX [62]. ALA has shown rapid metabolic breakdown [63], with few adverse effects, and a short duration of skin photosensitivity [64]. Chemical modification of ALA (e.g. ALA esters) has shown some promise in increasing tissue penetration [65]. Additionally, administration of exogenous compounds such as deferoxamine [26], an iron chelator that inhibits conversion of PpIX to heme by ferrochelatase, may enhance PpIX accumulation, thereby allowing lower ALA doses. However, the optimal ALA dose and time delay before fluorescence detection remains at issue [66].

ALA-induced PpIX fluorescence can be detected *in vivo* using both point spectroscopy and fluorescence imaging, although imaging is the preferred method. In a study by Eker and colleagues [67] in 41 patients, the spectra from 32 adenomas, 68 normal sites, and 14 hyperplastic polyps were obtained with a fluorescence point spectroscopy system; 21 of the patients had been given a low dose of ALA before the examination. Light of 337, 405, or 436 nm wavelength was used as excitation. This group found that 337-nm excitation, 100% sensitivity, and 96% specificity were obtained between normal mucosa and adenomas, while 77% of the hyperplastic polyps were classified as nonneoplastic. Interestingly, when exciting with 405 and 436 nm, the possibility of distinguishing different types of tissue was considerably better in the patients given ALA than in the patients not given ALA. Messmann and colleagues [66], employing the D-Light system (Storz, Germany) used previously to image drug-induced fluorescence in bladder, lung, and esophagus, studied six patients with colonic disease, one with UC, and two with rectal polyps. This nonlaser light source is based on a 300-W xenon short-arc lamp that delivers high-intensity light into a fiberoptic light guide. The system is capable of delivering broad-spectrum white light as well as filtered blue light (380–440 nm) for excitation of PpIX in tissues. The endoscopist can switch between either mode using a footswitch or a camera-mounted button. Fluorescence is detected by a charge-coupled device (CCD) camera with special fluorescence filters that reduce interference from reflected blue excitation light. With this instrument, these authors also demonstrated that active inflammation was associated with a high false-positive rate related to background inflammation.

Clinical evaluation of exogenous fluorescence-inducing drugs

To date, several key reports have been published on the clinical effectiveness of prodrugs, such as ALA, to detect preneoplastic gastrointestinal lesions. The majority of these reports have been in Barrett's esophagus, where the results are controversial in its ability to detect dysplasia.

The number of reports on the *in vivo* use of subtherapeutic doses of ALA in the colon is limited. Messmann and colleagues [44] reported an experimental rat model of UC in which ALA-PpIX fluorescence was used to enhance the detection of low-grade dysplastic lesions. The best results were obtained with 75 mg/kg ALA: dysplasia (low grade and high grade) was detected with a sensitivity of 92%, although the specificity was disappointing at 35%. Focal lesions as small as five abnormal crypts were observed in *ex vivo* tissue samples, which is a significant finding since aberrant crypts are thought to be the earliest precursors to dysplastic lesions in the colon [13,68]. The major limitation of this study was that UC also showed appreciable concentrations of PpIX, resulting in high false-positive rates, although identification of low-grade dysplasia against an active background of colitis may be difficult even for the skilled pathologist using biopsied tissues [69]. Lowering the ALA dose increased the specificity, with a notable decrease in the false-positive rate, although at the price of reduced sensitivity, which may have been partly due to the use of the unaided eye for detecting the fluorescence. Messman and colleagues [66] suggested improving the technique by topical administration of ALA, optimizing the time period between drug administration and fluorescence observation, and attempting to detect high-grade dysplasia in quiescent colitis. An alternative may be to keep the ALA dose low and increase the detection sensitivity, for example using a high-sensitivity imaging system (see below) [70].

Regarding the use of exogenous photosensitizers such as ALA, the detection of dysplasia in a background of chronic UC is fraught with methodologic issues related to background inflammation, which is associated with high sensitivity and low specificity. The role of these agents in the detection of subtle areas of dysplasia that are occult to WLE in routine colonoscopic screening has not been evaluated, but will likely be hampered by issues of methodologies, expense, and potential toxicity [66].

For use in the colon, local administration of ALA has been investigated in animal models for tumor detection [71]. The aim of this study was to detect cancer in the rat colon before macroscopic visibility. Multifocal colon carcinomas were induced by carcinogen. Local photosensitization with ALA was performed by lavage.

Using green (514 nm) excitation light, red fluorescence (635 nm) was detected with the naked eye using a filter (< 515 nm) to block the reflected excitation light. A total of 99 macroscopically visible carcinomas and four macroscopically visible dysplasias were examined, and fluorescence diagnosis detected 16 additional carcinomas and 41 additional dysplasias. In addition, the combination of tissue autofluorescence and ALA fluorescence for differentiating normal colon from hyperplastic and adenomatous polyps was investigated by Eker and colleagues [67]. In this study, fluorescence spectra from 32 adenomas, 68 normal sites, and 14 hyperplastic polyps in 41 patients were collected with a point monitoring system. Low-dose ALA was administered to 21 of the patients before the examination. Excitation light wavelengths including 337, 405, or 436 nm were used. With 337 nm excitation, 100% sensitivity and 96% specificity were obtained between normal mucosa and adenomas. Of the hyperplastic polyps, 77% were classified as non-neoplastic. However, excitation with 405 and 436 nm allowed much better distinction of different tissue types in the patients given ALA than in the patients not given ALA. The first study to examine colon PpIX distributions microscopically was reported by Regula and colleagues [72], who evaluated 18 patients with colorectal, duodenal, and esophageal tumors after oral administration of 30–60 mg/kg ALA for photodynamic therapy. Biopsies of tumor and adjacent normal mucosa were taken over a 1–72 h interval. These specimens were examined by quantitative fluorescence microscopy for assessment of sensitization with PpIX and showed glandular localization of ALA-induced PpIX. Additionally, 10 patients were given a second dose of ALA a few weeks later and their tumors were treated with red (628 nm) excitation light. With 30 mg/kg ALA, the highest fluorescence values were detected in the duodenum and esophagus, and the lowest in the large bowel. Doubling the ALA dose in patients with colorectal tumors improved the PpIX sensitization ratio in tumor and normal mucosa. Also, treated patients showed superficial mucosal necrosis in the areas exposed to laser light. This study also documented two patients with mild skin photosensitivity reactions and five with mild nausea and vomiting.

Furthermore, the optimal mode of ALA administration (oral vs. systemic) and the associated pharmacokinetics were studied by Van den Boogert and colleagues [73]. This study showed that *in situ* synthesis of porphyrins rather than enterohepatic circulation contributes to PpIX accumulation, while confocal laser scanning microscopy showed selective porphyrin fluorescence in epithelial layers. Also, peak levels and total production of porphyrins were found to be equal after oral and intravenous ALA administration. The conclusions of this study were that administration of 200 mg/kg ALA resulted in accumulation of PpIX, 1–6 h after administra-

tion, in all tissues except muscle, fat, skin, and brain, and that understanding the time–concentration relationship would be helpful in selecting dosages, routes of administration, and timing of ALA photodynamic therapy.

Is there a future for the use of this technique in colonic disease? Currently, the literature does not support the view that ALA will be useful in the colon; however, new ongoing research into modified versions of ALA may change this. Chemical modification of ALA into its more lipophilic esters seems to be promising in overcoming these problems [74].

ALA–PpIX fluorescence has also been studied in a variety of other organs, such as Barrett’s esophagus [66,75], bladder [65], oral cavity [76], and brain [77]. Peng and colleagues [60] have recently reviewed the use of ALA for photodynamic therapy, while Marcus and colleagues [78] have summarized both the clinical and preclinical development of ALA as a fluorescence diagnostic agent. Further studies will continue to investigate the complementary aspects of exogenous fluorescent compounds and fluorescent imaging systems with conventional endoscopy. Their use in everyday endoscopic practice will be influenced by extra costs, regulatory approval, possible drug-related toxicities, and overall cost-effectiveness as part of a screening program.

Raman spectroscopy

The Raman effect is the inelastic scattering of light by molecules. It is named after Chandrasekar Raman who discovered it and, indeed, won the Nobel Prize for physics in 1930. Raman spectroscopy has been evaluated as a means of obtaining detailed information about the molecular composition of tissue. Unlike fluorescence and reflectance spectra, Raman spectra are “molecule-specific” and offer much narrower spectral features from signals obtained as deep as 500 μm from the tissue surface. However, since the Raman effect comprises a very small fraction (about 1 in 10^7) of the incident photons, it is more difficult to implement than fluorescence. Raman signals are much weaker than autofluorescence and they can be masked by the broad-band fluorescence background. In addition, specially designed optical fiber probes are required to minimize the fluorescence and Raman signals generated in the probe itself.

In WLE, most photons are scattered in tissue without a change in energy or wavelength (elastic scattering that is responsible for diffuse reflectance). The Raman effect is an inelastic process, where the scattered photon’s energy is changed and this Raman scattering light is shifted to a lower frequency, i.e. longer wavelength. The molecular information contained in the Raman emission spectrum can be extracted by using a spectral analyzer, yielding a fingerprint-like signature for the tissue sample. Since molecular bonds possess a unique pattern of Raman

spectral peaks, the molecular composition of a tissue sample can be determined.

Raman spectroscopy is sensitive to a wide range of specific biomolecules such as proteins, lipids, and nucleic acids. Since the onset of cancer is accompanied by changes in biochemical composition, Raman scattering offers a potentially powerful diagnostic technique. Generally, near-infrared (NIR) light (~ 700–1300 nm) has been used for *in vivo* Raman spectroscopy. NIR light penetrates deeply into tissue and NIR excitation minimizes tissue fluorescence compared with visible light.

It is also possible to use UV light to induce Raman spectra. This has the advantage of producing tissue autofluorescence that is well separated from the detected Raman spectral bands. By using optical filters, unwanted background fluorescence can be reduced. Also, in UV resonance Raman spectroscopy, certain Raman spectral bands can be appreciably amplified using excitation light corresponding to a particular absorption band. However, compared with NIR light, UV light does not penetrate deeply into tissues and is potentially mutagenic, thereby limiting its use clinically.

In a paper by Shim and Wilson [79], potential artifacts in Raman spectroscopy due to handling of *ex vivo* tissue samples collected from biopsy were determined. It was concluded that tissue samples should be immediately frozen and then, prior to Raman spectroscopy, should be acclimatized at room temperature in phosphate-buffered saline (PBS) and immersed in PBS during spectroscopic examination. This study demonstrated that Raman spectroscopy and microscopy could be performed on biopsied tissues. Using a specially designed optical probe, *ex vivo* spectra were able to differentiate dysplasia from intestinalized metaplasia in esophageal biopsies with a sensitivity of 77% and a specificity of 93%.

Clinical evaluation

Several investigators have used different configurations to acquire *in vivo* Raman spectra, but there are few reports for the gastrointestinal tract [80]. Moreover, the majority of studies to date have evaluated *in vivo* Raman spectroscopy in Barrett's esophagus, with a very limited number of reports on Raman spectroscopy of the colon. Recently, Shim and Wilson [81] designed and built an NIR fiberoptic device for *in vivo* Raman spectroscopy measurements and reported the first *in vivo* Raman spectra of human gastrointestinal tissues measured during routine clinical endoscopy, with acceptable signal-to-noise ratio and short collection times. This was achieved by using the system with an optically filtered fiberoptic probe (~ 2 mm diameter) capable of "beam-steering" that was passed through the endoscope instrument channel and placed in contact with the tissue

surface [82]. The spectra from normal and diseased tissues revealed only subtle differences. Sophisticated computational techniques, such as principal components analysis and artificial neural networks, are being investigated as an approach for analyzing the full Raman spectrum and hence extracting the full diagnostic content, in order to distinguish subtle spectral differences among these spectra. One type of neural network analysis differentiated esophageal dysplasia from metaplasia with a sensitivity of 77% and a specificity of 93%. These diagnostic algorithms are being refined to improve these results and, furthermore, to give the best discriminating power in classifying the various dysplastic grades (indefinite vs. low-grade dysplasia vs. high-grade dysplasia). Once optimized, these algorithms can be used in a prospective fashion to assess the potential of Raman spectroscopy for Barrett's tissue differentiation. Moreover, the recent demonstration of the feasibility of obtaining *in vivo* Raman spectra of the gastrointestinal tract (Fig. 44.10) is a critical step in initiating systematic clinical trials to determine the diagnostic accuracy of Raman spectroscopy in Barrett's esophagus.

With respect to studies in the colon, Molckovsky and colleagues [83] have reported studies on the use of Raman spectroscopy for differentiation between normal colon and hyperplastic and adenomatous polyps. Here, *in vivo* Raman spectra, collected with specially designed Raman probes, have been subjected to a variety of spectral analysis algorithms (i.e. artificial neural networks and principal components analysis) to determine the optimal diagnostic values. Furthermore, this group has begun work on characterizing the microdistribution of Raman-emitting sources in colonic tissues using *ex vivo*-based Raman microscopy. Such important studies may contribute to a better understanding of the mechanisms involved in which Raman scattering differentiates normal from abnormal gastrointestinal tissues.

Although Raman microscopic imaging can be done *ex vivo*, the weakness of the signals may never allow

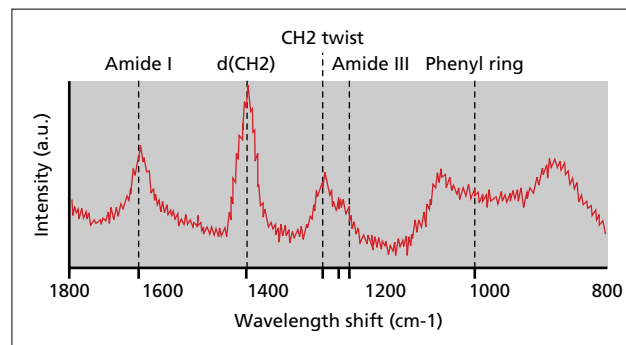


Fig. 44.10 Typical example of Raman spectra collected *in vivo* from normal colon. Note the peak-assignment of specific molecular bonds. (Data courtesy of Dr Louis Michel Wong Kee Song, Mayo Clinic, Rochester, MN, USA.)

real-time endoscopic *in vivo* Raman imaging. In addition, despite the potential for detecting very early biochemical changes in tissues associated with neoplastic transformation, to date there have been no correlative mechanistic studies to identify “pathologic stage-specific” molecular Raman markers. Such mechanistic studies remain overdue.

Light-scattering spectroscopy

Light-scattering spectroscopy (LSS) is based on white light reflectance, whereby photons incident on tissue are back-scattered without a change in their wavelength, and provides structural information about tissue *in situ*. LSS measurements are performed with visible light (400–700 nm) using fiberoptic probes placed at the tissue surface through the endoscope, and detect the relative intensity of back-scattered photons. These measurements have been shown to be sensitive to both endogenous tissue scatterers (i.e. cell nuclei and mitochondria) and tissue absorbers (i.e. hemoglobin). Since the optical probe detects scattered photons from as deep as the submucosa, information about the mucosal layer must be obtained by separating the contribution of multiply scattered light from deep in the tissue. Methods for doing this include spectral subtraction or the use of cross-polarization. In this way, singly scattered photons originating primarily from the mucosa can be obtained. Tissue transformation is associated with changes in the density and/or size of endogenous scatterers within the mucosal layer. These can be measured from the fine structure in the spectra and correlated with histopathology. One of the hallmarks of dysplastic change is that nuclei enlarge and become crowded and LSS is able to measure the size distributions of epithelial cell nuclei. In this way, direct quantitative measurement of nuclear enlargement, crowding, hyperchromaticity, and amount of chromatin is provided that aids in clinical diagnosis. LSS is a noninvasive method which does not require expensive laser light sources but instead is performed with white light that yields a strong signal in real time (< 1 s for a spectroscopic reading) [23,84,81]. Despite the advantages of requiring a simplified and less expensive spectroscopic detection system, LSS has the same disadvantage as point fluorescence spectroscopy, namely that the optical probe has a limited sampling volume. However, while technically difficult, LSS is currently being evaluated to facilitate *in vivo* imaging.

Clinical evaluation

To date, the potential of using LSS *in vivo* to detect epithelial nuclear crowding and enlargement in the human colon has not been reported. The ability to detect changes in nuclear size and density could potentially be

useful in identifying dysplastic lesions in the colon, despite the limited sampling volume. Unlike its use in identifying dysplasia in Barrett’s esophagus [84,86], clinical studies of LSS for detection of dysplastic lesions in the colon are awaited.

Optical coherence tomography

Optical coherence tomography (OCT) is a novel biomedical imaging technique based on the principle of low-coherence interferometry and enables cross-sectional imaging in near real time with high spatial resolution (~ 10–20 μm). OCT is analogous to B-scan ultrasonography but unlike the latter, which detects back-scattered sound waves, OCT images are formed by detecting light that is back-reflected from subsurface tissue microstructures. Briefly, low-coherence infrared light is split by a 50/50 beam-splitter, with half of the light directed toward the tissue and the other half toward a moveable mirror whose exact location is known. Light reflected from the mirror and tissue are recombined with the beam-splitter and directed to a sensitive detector. Using a light source with limited coherence length, an interference signal is produced only when the light that returns from the tissue travels the same distance as the light returning from the mirror. The amplitude of interference signal depends on the magnitude of back-reflected light intensity from tissue microstructures at that particular depth. By using an interferometric technique, the distance of the mirror is varied to allow scanning at varying depths of the tissue to produce an axial scan (A-scan). The optical probe can be scanned across the tissue surface to repeat the A-scan measurements at different lateral positions, resulting in a two-dimensional image (B-scan) (Fig. 44.11). Current endoscopic OCT prototypes have an axial (depth) resolution of about 10 μm that is determined by the coherence length of the light source, whereas the lateral resolution is about 25 μm and is determined by the focusing beam optics. Compared with high-frequency endoscopic ultrasound (EUS) that have resolutions of ~ 100 μm , current OCT systems have resolutions of ~ 4–20 μm , thereby permitting identification of microscopic features such as villi, glands, crypts, lymphatic aggregates, and blood vessels. Despite this high resolution, OCT has a limited imaging depth (~ 2 mm) compared with EUS (~ 5 cm).

Similar to EUS catheter probes, current *in vivo* endoscopic OCT probes typically have a diameter ranging between 2 and 2.4 mm, and varying designs allow either end-on scanning, linear scanning (along the longitudinal axis of the esophagus), or 360° radial scanning. Working distances smaller than 1 mm from the tissue surface provide adequate focus, and some compression artifacts may be seen with probe tissue contact. Although OCT

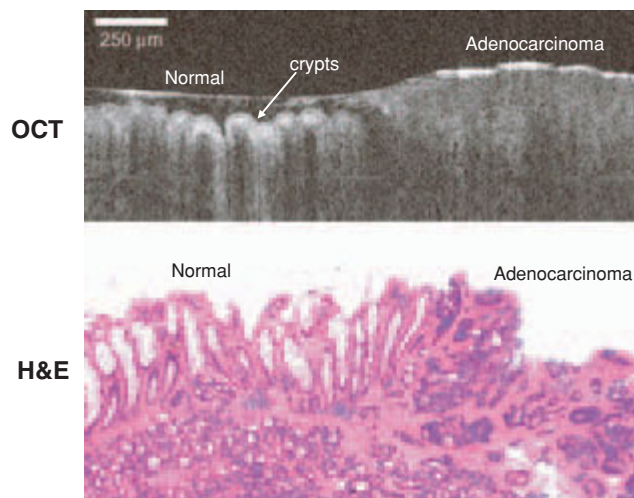


Fig. 44.11 Typical example of optical coherence tomography image collected from *ex vivo* colonic tissue samples showing normal mucosa on the left and a moderately differentiated tubulovillous adenocarcinoma on the right (upper figure). The lower figure is the corresponding H&E stain. Note the crypt structures in the normal mucosa. (Data courtesy of Dr Alex Vitkin, Department of Medical Biophysics, University of Toronto, Canada.)

images can be obtained as fast as four frames per second, avoiding motion blurring, in principle real-time OCT imaging is possible and development is in progress.

The majority of publications about OCT in the gastrointestinal tract have involved *ex vivo* tissue studies. Tearney and colleagues [87] investigated the ability of OCT to differentiate *ex vivo* the architectural morphology of normal and diseased gastrointestinal tissues, including esophagus and colon, collected post mortem. Images were compared with corresponding histology to confirm tissue identity and suggest the possible mechanisms that produce tissue contrast. This group reported that microstructure was delineated in different tissues at $16 \pm 1 \mu\text{m}$ resolution, higher than any clinically available cross-sectional imaging technology available. They determined that differentiation of tissue layers, such as mucosa, submucosa, and muscularis, were achieved because of their different optical properties.

In a similar *ex vivo* study, Kobayashi and colleagues [88] also used OCT to examine human gastrointestinal tissues from surgical resection and autopsy. Specimens were imaged within 5 h of resection or snap-frozen in liquid nitrogen. When compared with histology, OCT images demonstrated clear delineation of the mucosa and submucosa in most specimens, and clearly showed microscopic structures such as crypts, microvasculature, or esophageal glands in the submucosa and lymphatic nodules.

Sivak and colleagues [89] evaluated a prototype OCT system by imaging *ex vivo* tissues from various segments

of the gastrointestinal tract from 38 patients. Here, the 2.4-mm diameter OCT probe was inserted through an endoscope (tissue contact is not required) and provided a 360° radial scan. At ~ 1 mm above the mucosal surface, the OCT probe produced images of mucosal structures such as colonic crypts, gastric pits, and duodenal villi. However, when held against the wall, the OCT image revealed several layers, interpreted as mucosa, muscularis mucosae, and submucosa (and blood vessels were evident in the submucosa). This study concluded that OCT imaging provided interpretable high-resolution images of mucosa and submucosa, and therefore would be diagnostically useful.

Doppler OCT is a recent extension of OCT that acquires both morphologic images of the tissue and local blood flow velocities *in vivo* [90,91]. Reflectivity within the tissue provides contrast for the morphologic image while blood velocity maps the distribution of moving scatterers. Doppler OCT provides noninvasive functional imaging of microcirculation in tissue blood vessels, which are too small to be imaged by conventional Doppler ultrasound.

Clinical evaluation

Pitris and colleagues [92] examined the feasibility of using OCT for high-resolution imaging of gastrointestinal malignancies with *ex vivo* imaging of normal squamous esophagus, Barrett's esophagus, squamous carcinoma, UC, normal colon, and colonic adenocarcinoma. The columnar epithelial morphology as well as other mucosal structures in normal colon were also distinct. In contrast, disorganization of the normal mucosal layers and ulcerative lesions were identified in UC and colon adenocarcinomas. The ability of OCT to image tissue microstructure at high resolutions showed that it may be useful for minimally invasive assessment of the gastrointestinal tract and evaluation of early neoplastic changes.

Das and colleagues [93] reported an *in vivo* comparative study of OCT and catheter probe EUS (CPEUS) to determine their potential clinical roles. These techniques were used to evaluate normal-appearing portions of the gastrointestinal tract at the same sites (44 histologically confirmed normal sites in 27 patients). CPEUS was performed with 20-MHz or 30-MHz catheter probes. Mucosa and muscularis mucosa were clearly seen at all sites with OCT. Except for stomach, OCT demonstrated the submucosa in all sites. The penetration depth of OCT ranged from 0.7 to 0.9 mm. Microscopic structures such as esophageal glands, intestinal villi, colonic crypts, and microvasculature were easily identified. CPEUS penetration ranged from 10 to 20 mm, and five to seven distinct layers were discernible. However, both mucosa and submucosa were seen as thin layers without microscopic

detail. This important study demonstrated that OCT resolution is superior to high-frequency CPEUS, but depth of penetration is limited to mucosa and submucosa. In addition, OCT images major structural components of the mucosa and submucosa whereas CPEUS does not. Potentially, OCT and high-frequency CPEUS may be complementary for clinical imaging.

In its current form and resolution, OCT will likely localize areas displaying architectural distortion for biopsy, but will be limited to staging dysplasia. However, one can speculate that OCT may determine tumor invasion through muscularis mucosa into the submucosa better than conventional EUS and hence improve upon T-staging for selection of patients for endoscopic cure. Improvements in both axial and lateral resolutions are expected with the development of better light sources and focusing beam optics, respectively. Currently, these sources are cumbersome and expensive but are a starting point for the development of high-power, compact, and affordable lasers. Newer prototype designs may improve axial resolution to subcellular levels ($< 5 \mu\text{m}$), which may allow dysplastic cells to be resolved. One drawback of the linear-scanning OCT technique is its small sampling area and limited depth, similar to point spectroscopy. The placement of the OCT probe at a specific site, amid peristaltic motion, also appears challenging, so that contact with tissue (with potential compression artifacts) may be necessary.

OCT is not likely to replace biopsy and histopathology soon, but it may bring endoscopy and histopathology together in a single technology. The future "OCT endoscopist" will need to be familiar with histopathologic changes accompanying tissue transformation, which may initiate a new breed of endoscopic pathologists.

Confocal fluorescence endoscopy

Conventional fluorescence microscopy is an essential tool for the identification of cellular and subcellular microstructures, and has been especially popular in recent years with the development of physiologically and functionally specific fluorescent stains. However, unlike conventional epifluorescence microscopy, where thick specimens appear somewhat blurry due to the detection of out-of-focus light, confocal fluorescence microscopy (CFM) offers a clear advantage by reducing this out-of-focus light from above or below the focal plane. To achieve this clarity, confocal fluorescence instruments use pinholes placed confocally at the source and detector to minimize out-of-focus light, producing an image point-by-point by scanning laser beam across the sample in a raster pattern. High-resolution fluorescent optical "slices" through the sample are the result; by varying the axial position of the focal plane through the depth of the specimen, a stack of optical sections can

be collected without physical sectioning of the tissue sample. From this stack of images, a complex three-dimensional fluorescence structure of the sample can be created.

CFM may be used to image endogenous and exogenous fluorophores within cells of tissue sections as well as light reflected from these samples. Generally, CFM of tissue biopsies ($\sim 1\text{--}3 \text{ mm}^3$ in volume) can image as deep as $100\text{--}300 \mu\text{m}$ using 488-nm excitation light, the maximum interrogation depth depending on the excitation wavelength, the tissue's optical properties, and the collection efficiency of the detection optics.

We have demonstrated the use of three-dimensional CFM imaging of *ex vivo* normal and diseased colonic biopsies, optically sectioning these from the luminal surface, yielding three-dimensional rendered volumes of the mucosa. With this method, surface topologies are shown to be very different for each tissue type. In addition, differences in the autofluorescence emission patterns and the surface microarchitectural details of each tissue types can be visualized.

In other studies, we used blue-light excitation ($\sim 458 \text{ nm}$) CFM to compare the tissue fluorescence sources and microdistributions within each tissue layer of normal colon, hyperplastic polyps, and adenomatous polyps, and to compare the differences between these tissue types (Fig. 44.12). In normal colonic mucosa, the arrangement of crypts could be seen, despite the weak green fluorescence intensity of the normal epithelia, while strong green fluorescence from collagen fibers was observed in the submucosa. Hyperplastic mucosa was characterized by epithelia with weak green fluorescence, but increased collagen in the lamina propria produced increased green fluorescence. In contrast, the mucosa of adenomatous polyps was characterized by a marked increase in red fluorescence in the dysplastic epithelia and numerous small red fluorescent "granules" in the lamina propria. These were shown by immunohistochemistry to be macrophages and endocrine cells. The submucosal layer was highly green fluorescent due to structural collagen. Submucosal collagen was the most intensely fluorescent tissue component. CFM has shown that normal colonic mucosa, hyperplastic mucosa, and adenomatous mucosa differ significantly in autofluorescence features, while the submucosal layers of each tissue type are similar. This suggests that a fluorescence imaging device sensitive to "mucosal autofluorescence" alone may differentiate between these tissue types and be able to identify early intramucosal lesions. Preliminary studies on *ex vivo* tissue biopsies demonstrated that it was possible to achieve superior image quality and depth resolution in the mucosal layer of the upper and lower gastrointestinal tract [52]. Additionally, high-resolution CFM with special immunohistologic staining and transmission electron microscopy were used

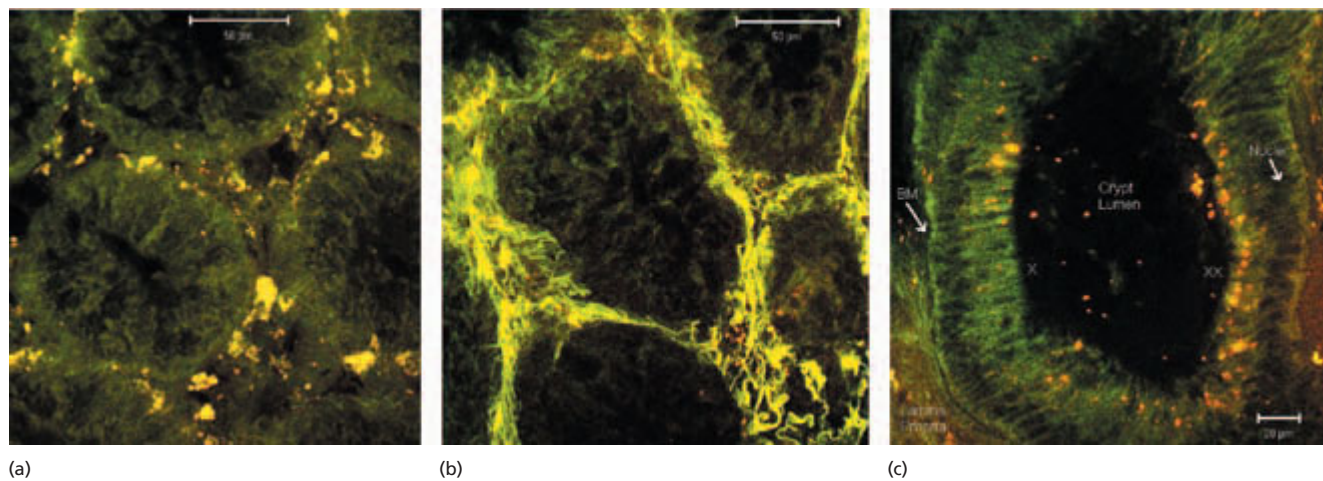


Fig. 44.12 Confocal fluorescence micrographs of frozen transverse thin sections of (a) normal colon, (b) hyperplastic polyp, and (c) adenomatous polyp mucosa illustrating significant differences in the autofluorescence sources and microdistributions in each type of mucosa.

in combination to characterize the cellular origins of whole living colonic crypts, and isolated living colonic epithelial cells derived from primary cell cultures of normal, premalignant, and malignant gastrointestinal tissues [53].

Inoue and colleagues [94] reported the use of CFM to obtain microscopic images from fresh specimens of gastrointestinal mucosa. Briefly, untreated mucosal specimens from the esophagus, stomach, and colon (obtained by endoscopic pinch biopsy, polypectomy, or endoscopic mucosal resection) were fixed in normal saline and examined by CFM with 488 nm excitation in reflectance mode. Images were compared with conventional hematoxylin and eosin staining, analyzing the nucleus-to-cytoplasm ratios. The overall diagnostic accuracy of CFM for cancer was 89.7%. The obvious advantages of “blur-free” fluorescence imaging and three-dimensional optical sectioning of *ex vivo* biologic tissues have made CFM an attractive concept for *in vivo* fluorescence endoscopic imaging.

Recently, a number of prototype confocal endoscopic devices have been described. Optiscan Inc. (Victoria, Australia) introduced a fiberoptic confocal imaging (FOCI) for subsurface microscopy of the colon *in vivo* [95]. In combination with topically applied fluorescent dyes, optical sections of the mucosal surface of the rat colon were made *in vivo*, with the colon surgically exposed. A miniaturized scanning mechanism sweeps a 488-nm excitation laser beam across the tissue surface. Images, with scanning speeds of up to 16 frames per second, have a field of view ranging between ~ 13 and $100 \mu\text{m}$, with optional zoom capabilities. The latest version of the FOCI device was used by the same group in

an experimental rat model of inflammatory bowel disease for imaging changes in the mucosal architecture of living colonic tissue *in vivo*. Morphologic changes associated with disease activity were detected microscopically *in vivo* using FOCI but were not evident on visual inspection of the colonic surface. Acridine orange enabled imaging of the colonic crypts at the surface of the mucosa. Morphologic changes associated with colitis, including inflammatory cell infiltrate, crypt loss, and crypt distortion, were also detected using this fluorescent dye. Application of fluorescein and eosin enabled subsurface imaging of the lamina propria surrounding the crypts [96]. This prototype may be the predecessor to a true CFM endoscopic imaging device.

Several groups have focused on miniaturizing conventional optics to achieve an instrument capable of passing through the accessory channel of standard endoscopes. For example, Liang and colleagues [97] reported the development of a miniaturized microscope objective for endoscopic confocal microscopy. The miniature water-immersion microscope objective is about 10 times smaller in length than a typical commercial objective. Used in a fiber confocal reflectance microscope, the miniature objective offers a field of view of $\sim 250 \mu\text{m}$ with micrometer-level resolution.

Advances in silicon-based microelectronic micromachined systems (MEMS) may allow further miniaturization of the confocal scanning mechanisms for endoscopy. Laser-und Medizin-Technologie GmbH, Berlin, Germany, have developed a miniaturized confocal laser scanning microscope using a two-MEM scanning unit to produce a two-dimensional scan with a field of view of $0.7 \times 0.7 \text{ mm}^2$, an optical resolution of $\sim 2 \mu\text{m}$. Other developments in MEMS-based confocal endoscopy are in progress [98–100].

The research group led by Dr Arthur Gmitro, at the University of Arizona, has developed a catheter-based real-time confocal fluorescence endoscopic imaging device using 488-nm light from an argon laser. This

uses a fiberoptic imaging bundle and a miniature microscope objective and focusing mechanism at the distal end of the catheter. This device achieved a field of view of $\sim 430 \mu\text{m}^2$ and a lateral resolution of $2 \mu\text{m}$. Focusing is accomplished via a hydraulic mechanism that moves the distal end of the fiber relative to the lens. Unpublished preliminary imaging results, performed in cell cultures, *ex vivo* tissue samples, and *in vivo* animal models with fluorescent contrast dyes, are impressive (<http://www.optics.arizona.edu/gmitro/>).

Despite the promise of CFM technologies and continual technical advances that permit further miniaturization, this technology has yet to be demonstrated *in vivo* in human endoscopic trials. The necessity of topically applied fluorescent dyes for optimal contrast, lack of control of probe placement in the colonic lumen affected by peristalsis, respiration, and aortic pulsation may limit its clinical role. This modality is capable of producing histologic-grade images and may have an important role in differentiating between hyperplastic and adenomatous polyps. CFM technologies may be used to histologically define areas detected by wide-scanning technologies such as autofluorescence endoscopic imaging. It will not be useful in the screening of broad areas of mucosa for occult dysplasia.

Immunophotodiagnostics

Conventional immunohistochemistry permits microscopic imaging of biopsied tissues on a “molecular” level by routinely combining chromogenic and fluorescent dyes with the specificity of monoclonal antibodies directly against tumor-related or tumor-specific antigens. Recently, this idea has been extended to *in vivo* endoscopic imaging as a means of enhancing the contrast between tumors and surrounding normal tissue by targeting tumors with monoclonal antibodies.

For the past 20 years radiopharmacology has relied on the highly specific reactivity of the antigen–antibody complex. For example, radiotherapeutic agents are commonly conjugated to monoclonal antibodies directed against tumor-associated antigens. These are used to selectively target tumor cells for destruction based on the inherent overexpression of a particular tumor-associated antigen relative to normal tissues [101]. Adapting this principle for fluorescence endoscopy involves the conjugation of a fluorophore dye to a monoclonal antibody or other tumor-targeting moiety, thereby producing a “fluorescent contrast agent.” Typically, these dyes are excited in the red range ($> 600\text{--}700 \text{ nm}$) and emit NIR fluorescence efficiently. They have adequate stability for labeling *in vivo* and produce fluorescence that is detectable through millimeter thicknesses of tissues [102]. Recent improvements in monoclonal antibodies and their derivatives (i.e. frag-

ments), the development and commercial availability of NIR-emitting fluorophores, and the availability of high-sensitivity digital cameras in this spectral region have made tumor localization using fluorescence contrast agents practical and attractive. Optimal fluorescent dyes can be selected based on their photophysical and spectral properties independent of their tumor-localizing properties [103].

Recent animal studies have demonstrated that fluorophore labeling of monoclonal antibodies produces adequate sensitivity and improved image contrast [104,105]. In a study in mice by Gutowski and colleagues [106], monoclonal antibody–dye conjugates were prepared using the monoclonal antibody against carcinoembryonic antigen (CEA) (35A7) labeled with indocyanine and ^{125}I . This study demonstrated the detection of very small nodules ($< 1 \text{ mm}$ in diameter) but noted a sensitivity decrease with decreasing tumor mass (100% for nodules $> 10 \text{ mg}$ vs. 78% for nodules $\leq 1 \text{ mg}$). Tumor nodules occult to the naked eye were also detected, and very low conjugate quantities ($< 1 \text{ ng}$) were sufficient for tumor nodule visualization. However, the authors also noted false-negative findings with some deep small tumor nodules producing very weak fluorescence that was not detected due to tissue scattering and absorption and the relative insensitivity of their detection camera.

To determine the binding of such fluorescently labeled contrast agents *in vivo*, Kusaka and colleagues [107] used Balb/cA nude mice grafted with human gastric cancer (St-40) and colorectal cancer (COL-4-JCK) cell lines, and the unconjugated antihuman anti-MUC1 mucin antibody to show that specific tumor labeling can be achieved in live mice at the tumor surface, thereby demonstrating that *in vivo* administration of a fluorescence-labeled monoclonal antibody for fluorescence detection is possible. However, many difficulties remain with this approach. For example, until recently most monoclonal antibodies were raised in nonhuman hosts (i.e. mice), resulting in a host immune response against them when used in patients. This not only causes the antibodies to be quickly eliminated but also forms immune complexes that damage the kidneys [108]. However, “humanized” monoclonal antibodies have become available recently. In addition, whole antibodies bound in human tumors do not exceed 10^{-5} of the administered dose per gram of tumor, hence requiring large amounts of injected conjugated monoclonal antibody, long exposure times, and high sensitivity to achieve adequate tumor brightness and contrast. This limitation is due to the pharmacokinetic properties of conjugated whole antibodies. The production of antibody fragments, smaller than the whole antibody, has resulted in some improvements in pharmacokinetics and tissue labeling. In a mouse xenograft model, Ramjiawan and

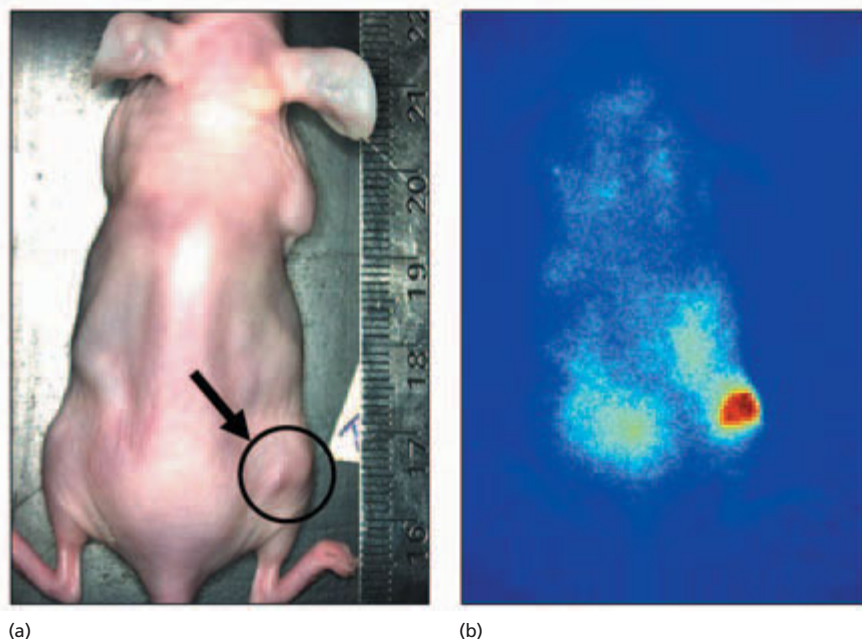


Fig. 44.13 Example of *in vivo* tumor targeting with a fluorescence contrast agent. This was achieved by administering a fluorescence-conjugated antibody directed against a tumor-associated glycoprotein (TAG72) in a xenograft nude mouse model of human colon cancer. (a) White-light image of dorsal side of mouse indicating tumor site (arrow). (b) Whole-body fluorescence image shows significant enhancement of tumor-to-normal contrast, thereby allowing the tumor to be detected easily with fluorescence 48 h after administration of tumor-targeted fluorescence probe.

colleagues [109] conjugated an NIR-emitting dye (Cy5.5) to a fragment of antihuman antibody with broad cancer specificity to demonstrate specific binding. Here, the peak fluorescence intensity was detected with a high-sensitivity CCD camera 2 h after injection. The presence and distribution of the conjugated fragment revealed that about 16 and 73% was located in the tumor and the kidneys respectively. Use of smaller antibody fragments produced rapid tumor uptake, better penetration (at the expense of reduced circulation time), more homogeneous tumor penetration, and reduced immunogenicity [110].

Fluorescent dyes can also be targeted to tumor tissues by means other than monoclonal antibodies. For example, Weissleder and colleagues [111] coupled an NIR fluorophore to a biocompatible polymer. This was administered to tumor-bearing mice and was taken up by tumor cells via pinocytosis. The intracellular release of the fluorophore by the protease cathepsin D resulted in a fluorescence signal detected *in vivo* in subnanomolar quantities and at depths sufficient for clinical imaging. The authors demonstrated that specific enzyme activity in a tumor could be imaged by fluorescence contrast agents *in vivo*. In addition, Marten and colleagues [112] studied the expression of the protease cathepsin B in dysplastic adenomatous polyps. Cathepsin B was consistently overexpressed in adenomatous polyps. When mice were injected intravenously with the reporter probe, intestinal adenomas became highly fluorescent, indicating high cathepsin B activity. Even microscopic adenomas undetected by white-light imaging were readily detected by fluorescence, the smallest lesion being ~ 50 μm in diameter. Control animals were either

noninjected or injected with a nonspecific NIR fluorescent probe (indocyanine green, ICG); in these, adenomas were only barely detectable above the background. This impressive study demonstrated the potential of using fluorescently labeled enzyme-sensing probes to detect such gastrointestinal lesions against adjacent normal mucosa.

Currently, work in our laboratory is assessing the utility of colonic mucins as a possible target for colonic adenomas and adenocarcinomas. Preliminary results have demonstrated distinct contrast enhancement of the tumor compared with surrounding normal tissues using the labeled cc49, which recognizes a tumor-associated glycoprotein antigen, in comparison with control autofluorescence images. Tumor visualization was apparent as early as 2 h with the fluorescence-conjugated cc49 probe, while maximum contrast was at 48 h after injection (Fig. 44.13). Hence, this demonstrated the selective *in vivo* targeting of fluorescence dye to tumor-associated mucins, resulting in the enhanced fluorescence detection of small (~ 4–5 mm diameter) xenografted human colonic tumors [113].

Clinical evaluation

Preliminary *in vivo* evaluation of fluorescence contrast agents in patients has been reported in a very limited number of studies. Early vascular changes were assessed in Crohn's disease in a prospective endoscopic study of 10 asymptomatic patients using unconjugated 10% sodium fluorescein [114]. Fluorescence endoscopy was used to evaluate the mucosal microcirculation of the neoterminal ileum in relation to endoscopic recurrence

in patients who had undergone ileocolonic resection for Crohn's disease. The fluorescence observed may reflect vasodilation associated with inflammation or genuine microvascular lesions. Correlation with histology suggested that these early vascular lesions were secondary to the inflammatory process.

In another study with *ex vivo* human tissues, Bando and colleagues [109] developed an NIR-excited fluorescent dye, ICG-sulfo-OSu, conjugated to antisulfomucin and anti-MUC1 antibodies in paraffinized tissue sections from 10 patients with esophageal cancer, 30 patients with gastric cancer, and 20 patients with colorectal cancer. They found that antibody staining patterns varied depending on the organs, histologic types, and depth of the cancers. Generally, staining on the mucosal surface of cancer tissues was retained and images of cancer cells were obtained by infrared fluorescence observation using the labeled anti-MUC1 antibody. These authors noted the difficulty of adapting this staining method to *in vivo* conditions, where the antibody agent would be administered to the luminal surface because of such problems as surface mucus and pH. Hayashi and colleagues [116] performed similar studies of immunostaining of ICG-conjugated antiepithelial membrane antigen antibodies on nonfixed freshly excised tissue samples by eliminating these factors under various conditions. Results suggested that vital immunohistochemical staining is possible under optimized conditions. Ito and colleagues [117], in a study of only three patients, confirmed that such immunofluorescent staining using ICG derivative (ICG-sulfo-OSu) conjugated to anti-CEA antibodies could be performed *in vivo* to detect small gastric cancers.

Tatsuta and colleagues [118] labeled anti-CEA monoclonal antibodies with fluorescein isothiocyanate (FITC) to study *ex vivo* human gastric lesions. FITC has a high fluorescence efficiency and excitation and detection wavelengths (~ 488 nm excitation, ~ 520 nm emission). The conjugated antibody was applied topically. Of 30 tumors, 27 (90%) showed positive fluorescence after 60 min with no false positives, whereas only 2 of 5 cancers (40%) could be detected earlier than 60 min. To remove gastric mucus and improve the binding of the tumor with the labeled antibody, pretreatment with a mixture of proteinases, sodium bicarbonate, and dimethyl-polysiloxane was used. *In vivo*, this would add another 90 min to the endoscopic examination. No significant relationship between positive fluorescence and tumor type or stage was found. However, positive fluorescence could also not be demonstrated in benign gastric lesions.

In 1998, Keller and colleagues [119] coined the term "immunoscapy" in a report on the detection of colorectal carcinomas and villous adenomas in surgically resected tissue samples. Fluorescence from FITC-labeled anti-CEA antibody was detected using a sensitive filtered

photographic camera in 27 of 28 cancers and 1 of 2 adenomas, as well as in 6 of 18 normal controls, giving a sensitivity of 93% and specificity of 67%.

There are two published reports of the use of fluorescence-conjugated monoclonal antibodies in humans *in vivo*. The first study used a monoclonal fluoresceinated anti-CEA conjugate to detect human colon carcinoma [120]. Upon laser irradiation, clearly detectable heterogeneous green fluorescence from the dye-antibody conjugate was visually observed on all six tumors; minimal fluorescence was detectable on normal mucosa. Tissue autofluorescence from both tumor and normal mucosa was subtracted by real-time image processing. In the second *in vivo* study of 27 patients with colonic polypoid lesions, Keller and colleagues [121] used a locally administered fluorescein-labeled anti-CEA monoclonal antibody for *in vivo* fluorescence endoscopic detection of colorectal dysplasia and carcinoma. During conventional WLE colonoscopy, the conjugated monoclonal antibody was applied directly to the mucosal surface. Specific fluorescence was visualized with a conventional fiber endoscope modified for fluorescence imaging with fluorescence bandpass filters (520 nm). Here, fluorescence was present in 19 of 25 carcinomas and 3 of 8 adenomas. Interestingly, the technique failed in the presence of mucosal ulceration or bleeding. One fluorescence-positive villous adenoma showed high-grade dysplasia, while another fluorescence-positive polypoid lesion was diagnosed as carcinoma in adenoma. Normal-appearing mucosa was fluorescence negative in all cases. In all cases (without ulceration or bleeding), the specificity of fluorescence endoscopy was 100%, the sensitivity was 78.6%, and the accuracy was 89.3%. Subsequent immunohistochemistry on biopsied tissues revealed that endoscopic fluorescence significantly correlated with CEA expression of luminal epithelial cells. Larger trials to demonstrate the value of this technique for differential diagnosis are currently underway.

However, despite these encouraging initial results, several important issues must be resolved. Selection of the best tumor-associated targets (i.e. monoclonal antibodies, peptides, enzymes) is not clear, and the possibilities are seemingly endless. For example, antigens expressed on the cell surface, such as growth factor receptors, mucins, and cell adhesion molecules, can be targeted by their respective fluorescence-conjugated antibodies, as can intracellular markers such as enzymes [122,123]. Biomarker studies continue to be reported in the literature for each segment of the gastrointestinal tract, in which a variety of molecular markers are evaluated in large tissue archives for their potential as diagnostic and/or prognostic indicators (CEA, mucin epitopes, etc.). It is possible that each segment of the gastrointestinal tract will have its own specific diagnostically relevant markers. Additionally, simultaneous

localization of multiple reagents is made possible by labeling multiple NIR fluorophores; thus background subtraction and differential labeling of multiple tumor-associated components can be performed. Difficulties in using the fluorophore labels are mainly related to light scattering and absorption in tissues, although detection of small tumors at depths of several millimeters should be feasible. Given the limitations in current fluorescence endoscopic imaging in detecting very early gastrointestinal lesions or preventing false positives due to confounding concurrent conditions (i.e. inflammation), these developments significantly complement existing fluorescence endoscopy.

An overview: the optimal technique

Several new optically based techniques are being evaluated with a view to enhancing the diagnostic capability of clinical gastrointestinal endoscopy. The ideal system should function in real time and combine excellent diagnostic accuracy with wide mucosal area surveillance. A major issue is how the detection of dysplasia and intramucosal cancer will ultimately fit into the treatment algorithm. For example, who and/or what should be treated with endoscopic ablation, chemoprevention, or resective surgery? Treatment will be markedly affected by accurate staging of lesions, via super high-resolution ultrasound or OCT. Short of replacing conventional biopsy, such technologies should provide guidance in locating optimal sites for targeted biopsy and be able to monitor ablative therapies such as photodynamic therapy. In this regard, fluorescence endoscopic imaging, with its wide field of view, has already detected early lesions, scars, and demonstrated reliability in differentiating hyperplastic vs. adenomatous polyps *in vivo*, and so appears most appealing and practical for screening. Additionally, fluorescence endoscopy does not require dye spraying and is relatively fast. However, many issues, such as optimal excitation and emission wavelength(s), confounding background fluorescence from metaplasia or inflammation (false positives), and artifacts due to motility, remain unresolved. Additionally, it is not clear if exogenous fluorophores (e.g. pro-drugs like ALA) will be necessary to achieve clinically useful sensitivity and specificity.

Despite its very high molecular specificity, Raman spectroscopy suffers the same weakness as all point spectroscopies, in that its clinical use is limited by practicality. This is also the case for LSS, which has shown promise in differentiating dysplasia (low and high grade) in Barrett's esophagus for example, based on nuclear size and density. However, used adjunctively with imaging techniques that survey large tissue surfaces for targeting suspicious lesions, the molecular specificity of Raman spectroscopy or the sensitivity to

subcellular scattering features of LSS may be useful for *in situ* diagnosis. These combinations are yet to be attempted.

OCT is attractive, although current OCT prototypes have several limitations that prevent their use as a stand-alone technique for surveillance. The main clinical advantage of OCT is the ability to stage mucosal disease as a means of identifying those patients where dysplasia and intramucosal cancer does not penetrate into the submucosa, and therefore would be ideal for curative endoscopic therapy. Although it has the potential to yield histologic details, this resolution has not yet been achieved in a real-time endoscopic system. Additionally, OCT will only be applicable for viewing small areas of the gastrointestinal tract. However, with anticipated improvements in resolution (subcellular level) and speed, OCT may become the technique of choice for surveillance and staging in the future. Furthermore, Doppler OCT may offer an additional endoscopic capability for imaging blood flow in mucosal and submucosal microvasculature, and may be of use in assessing changes in microcirculation resulting from *in situ* therapies.

At the moment, CFM has only been demonstrated on *ex vivo* human gastrointestinal tissues, including normal, metaplastic and preneoplastic lesions in the esophagus, stomach, and colon. Distinct fluorescence differences have been found between normal and abnormal mucosal tissues in each organ, yet this is likely not to be diagnostically useful in endoscopic fluorescence imaging, since the already weak mucosal fluorescence is overwhelmed by very strong fluorescence from deeper gastrointestinal tissue layers. To date, CFM techniques have been used primarily *ex vivo* to study and explain the origins of both tissue autofluorescence and the microdistribution of photosensitizers. The role of CFM *in vivo* may exploit the subtle differences in mucosal (auto)fluorescence between normal and abnormal colonic tissues by interrogation of only epithelia and lamina propria, hence reducing contribution from the collagen-rich submucosa. However, at present, CFM involves the use of fluorescent contrast dyes, which make the process more labor intensive. Currently, limitations in available technology prevent the clinical utility of "confocal microendoscopy."

All point spectroscopic techniques, as well as magnification endoscopy, are inherently limited by the small tissue area they sample. However, they contain more detailed information about tissue than any imaging system, which may translate into more accurate tissue differentiation. Rather than competing with an imaging system, the "best" instrument for surveillance may combine imaging and spectroscopy. For instance, a lesion could be detected by fluorescence imaging or OCT and its dysplastic nature characterized by Raman spectroscopy. However, in this era of cost containment, such an approach may be cost-prohibitive. Moreover, all

these expensive optical modalities will need to be compared against cheaper and equally promising alternatives such as chromoendoscopy, for which the dye is cheap and colonoscopes are readily available. However, dye spraying is labor intensive.

By far the least reported method to date is the use of immune-related fluorescence contrast agents. A limited number of *ex vivo* studies have demonstrated relative gastrointestinal tumor selectivity with highly fluorescent conjugated antibodies to well-known tumor-associated biomarkers. Such contrast agents have also been evaluated in a very limited number of patients with encouraging enhancement of tumor contrast. There are important technical issues to be resolved, such as finding the optimum site- and pathology-specific biomarkers, conjugate design, false positives associated with inflammatory conditions, optimizing relative tumor uptake, cost, and safety. However, advances in our understanding of cancer biology, tumor-associated gastrointestinal biomarkers, conjugation biochemistry, safety assessments, and fluorescence imaging hardware and software continue. This technology also offers a means of improving our fundamental understanding of disease processes in the gastrointestinal tract on a molecular level. It is conceivable that in the future molecular-targeted fluorescence endoscopic imaging will allow earlier detection and characterization of gastrointestinal disease, and may offer *in vivo* noninvasive monitoring of the functions of a variety of proteins as well as assessment of treatment effects.

Conventional endoscopy has relied strongly on the detection of subtle topographic and morphologic changes associated with the evolution of dysplasia through to invasive cancer, which may only become apparent at an advanced stage. However, the future of diagnostic endoscopy will certainly involve “molecular imaging,” whether fluorescence, Raman, or immunophotodetection. This may translate into a truly early detection of preneoplastic changes, when therapeutic intervention can result in cure.

“Optical biopsy” refers to tissue diagnosis based on *in situ* optical measurements, which would eliminate the need for tissue removal. The above-mentioned optical techniques are striving toward this goal but none are likely to replace conventional biopsy and histopathologic interpretation in the near future. Future implementation of these optically based methods for endoscopic detection of colonic neoplastic disease will likely involve a combination of more than one technique. Although they demonstrate potential for better diagnosis, these modalities are still in their infancy, with future technological refinement and large-scale clinical trials needed to assess their utility and limitations. To date, there have been no publications regarding the assessment of any commercial systems in multicenter comparative clinical

trials in the gastrointestinal tract. Ultimately, whether these optical techniques will become part of standard clinical endoscopic practice or remain on the sidelines can be summed up in two questions: how much better will they perform and at what cost?

Summary

Gastrointestinal malignancies continue to be the second leading cause of cancer-related deaths in the developed world. With regard to colonic neoplasms, early detection and therapeutic intervention have been demonstrated to significantly improve patient survival. Conventional screening tools include standard WLE, which has no trouble in detecting polypoid lesions in the well-prepared colon. Well-defined endoscopic surveillance biopsy protocols aimed at the early detection of dysplasia and malignancy have been undertaken for groups at high risk. Unfortunately, the relatively poor sensitivity associated with WLE is a significant limitation. In patients with diffuse chronic inflammatory bowel disease (i.e. UC and Crohn’s disease) the detection of dysplasia is a recurring problem even with multiple random biopsy protocols. In these and other diseases, major efforts are underway in the development and evaluation of alternative diagnostic techniques that may be used adjunctively with conventional endoscopy to improve detection of colonic neoplastic disease.

This chapter has focused on notable developments made at the forefront of research in novel optically based endoscopic modalities that rely on the interactions of various wavelengths of light with tissues. A condensed introduction to the biophysical interaction between light and biologic tissues is followed by a “state-of-the-art” review of fluorescence endoscopic spectroscopy and imaging, Raman spectroscopy, LSS, OCT, confocal fluorescence endoscopy, and immunophotodiagnosics. For each topic, background information is discussed, followed by a report on the most relevant clinical evaluations of the respective technique. The final section “An overview: the optimal technique” discusses whether these new developments offer significant improvement in the endoscopic diagnosis of early dysplastic lesions in concert with the traditional approach of targeted biopsies or submucosal resection.

The modality that will most appeal to the traditional endoscopist will be fluorescence endoscopic imaging, where the whole mucosal surface will be seen on a monitor similar to that seen with WLE, but with a simultaneous computer-generated colored fluorescent image where dysplastic areas will stand out against normal tissue. In contrast, point-directed methods such as Raman and fluorescence spectroscopy, LSS, confocal fluorescence endoscopy, and OCT will not likely play an important role in screening for dysplastic lesions because of

the immense surface area of the colon. These additional optically based procedures may play an ancillary role in the histologic or molecular interrogation of abnormal areas detected by other means, such as fluorescence imaging or dye spraying/chromoendoscopy. In the future, histologic or molecular grade interpretations may be possible without the need for tissue removal, the true "optical biopsy." This enhancement of the endoscopist's ability to detect subtle neoplastic changes in the colonic mucosa in real time and improved staging of lesions could result in curative endoscopic ablation of these lesions, and in the long term improve patient survival and quality of life.

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Chapter 45

Endoscopic Ultrasonography of the Colon

Joris W. Stubbe and Paul Fockens

Introduction

Imaging of colon, rectum, and surrounding tissues is a difficult task and colonoscopy, conventional barium studies, and computed tomography (CT) all offer only limited information about the local staging of rectal, perirectal, and colonic neoplasms. Magnetic resonance imaging (MRI) seems promising as an imaging modality but is still in its infancy. Endoscopic ultrasonography (EUS) was developed in the early 1980s to overcome the limitations of standard transabdominal ultrasound, whose use is limited due to interposed structures (e.g. air). With EUS it is possible to visualize the individual layers of the rectal and colonic wall and to detect adjacent lymph nodes. Using frequencies between 5 and 20 MHz provides an optimal resolution of around 0.1 mm and adequate penetration (> 5 cm for 5 MHz, 1 cm for 20 MHz).

Early in its development, EUS was limited to imaging rectal lesions since only rigid probes were available. However since the introduction of flexible fiberoptic echocolonoscopes and through-the-scope ultrasound catheter probes, numerous studies have been published dealing with indications for colonic EUS proximal to the rectum. The first report of (rigid) endorectal endosonography came from Wild and Reid in 1956, when they were able to diagnose a recurrence of rectal cancer after previous surgery [1]. However, it was not until 1983 that the first studies were published on endosonography of rectal cancer with the new flexible instruments [2–4].

This chapter discusses indications, achievements, and shortcoming of colorectal EUS as performed with flexible instruments using either through-the-scope probes or dedicated echoendoscopes. We do not discuss the important role endosonography has in imaging the pelvic floor and its musculature in incontinence nor the perirectal complications of inflammatory bowel disease.

Instruments

Dedicated echoendoscopes

Dedicated echoendoscopes are flexible instruments equipped with dual imaging modalities: endoscopy and

ultrasonography. About a decade ago, a special instrument was developed for use in the colon (CF-UM3/CF-UM20; Olympus Optical Co., Tokyo, Japan). It was a forward-viewing, 160-cm long echocolonoscope with a frequency of 7.5 or 12 MHz. It was not a complete 360° radial scanning instrument as the fiber bundles necessary for endoscopy blocked about 60° of the ultrasonographic image; this endoscope is no longer in production. A 45° oblique-viewing echoendoscope is now available, equipped with two switchable frequencies (7.5 and 12 MHz or 7.5 and 20 MHz). Extreme caution is warranted with these side- or oblique-viewing instruments in the colon since forward viewing is not an option, and the large intestine may have sharp turns especially in the presence of diverticulosis [5,6]. A forward-viewing instrument is now available from Pentax (EG-3630UR; Pentax Precision Instruments, Tokyo, Japan).

Miniprobes

High-frequency ultrasound (HFUS) generally uses through-the-scope catheter probes that can be advanced through the biopsy channel of a standard colonoscope. At the tip of these miniprobes, a small single-crystal transducer rotates at 10 cycles per second. This gives a 360° image with depth of penetration dependent on the frequency chosen (up to 2 cm for 12 MHz, diminishing to less than 1 cm for frequencies of 20 MHz or higher). The miniprobes are quite durable and can provide at least 50 examinations without loss of function. The miniprobes are manufactured by the Fuji and Olympus companies.

Patient preparation

For rectal lesions an enema is adequate preparation. Higher up in the colon a complete standard bowel preparation is necessary. The patient is usually examined in the left lateral decubitus position. If the lesion is seen endoscopically in the rectum, water can be instilled to see whether it is possible to place the entire lesion under water. Changing the position of the patient is of paramount importance in order to obtain a good-quality EUS image. If submersing the lesion is successful, the

rest of the EUS examination is usually relatively easy. If the lesion cannot be submersed, a balloon around the miniprobe or echoendoscope may be used. When examining a narrow segment of the colon, extreme caution is necessary when using a side- or oblique-viewing instrument. Advancing the echoendoscope blindly across a stenotic tumor may disturb interpretation of the lesion by distorting the shape of the tumor as well as causing pain and possible perforation.

Standard transrectal ultrasound examination is best performed with a 360° radial scanning transducer and starts just above the rectosigmoid junction in order to look for enlarged lymph nodes near the iliac vessels. Additional information can be obtained about suspicious lymph nodes by using a linear-array probe, where the imaging plane is parallel to the rectal axis instead of perpendicular. Flexible instruments are preferred for this investigation because fine-needle aspiration biopsy (FNA) can be obtained under direct EUS guidance.

When using HFUS miniprobes, a colonoscope provides visual evaluation and description of the lesion. The colon is then filled with 200–300 mL deaerated water and the miniprobe is inserted through the working channel of the colonoscope. Using the “picture-in-picture” modality, the lesion can be evaluated under direct endoscopic guidance to permit corrections in positioning (Fig. 45.1).

Sedation for rectal EUS application is generally not necessary. For colonic evaluation, using either a colonic echoendoscope or miniprobe, the same sedation is employed as for colonoscopy, i.e. intravenous short-acting benzodiazepine (midazolam), with or without pethidine, or propofol. Standard patient monitoring is mandatory.



Fig. 45.1 Monitor image during miniprobe endoscopic ultrasound examination of rectal polyp using the picture-in-picture function.

Anatomy

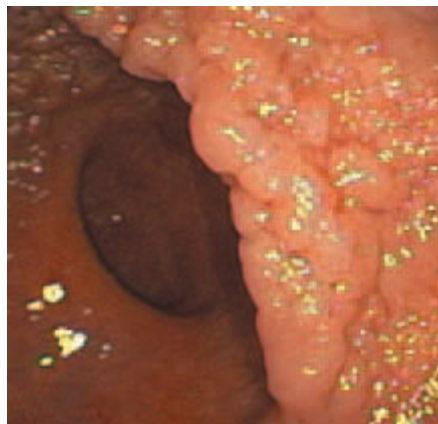
Endosonographic images of the colorectal wall are a composite of surface reflections and actual layers of the wall. Typically, a five-layer pattern is described, although higher ultrasound transducer frequencies allow more layers to be discriminated. Each layer is represented by either a hypoechoic (dark or echo-poor) or hyperechoic (bright or echo-rich) band. Crucial to accurate staging is the identification of the muscularis propria, the fourth (hypoechoic) layer. Controversy still exists as to the anatomic correlation of each layer of the imaged rectal wall. The first model, described by Hildebrandt and Feifel, states that the three hyperechoic lines correspond to interfaces, while the two hypoechoic lines represent actual anatomic layers. The first white line is the interface between the balloon and the mucosa, followed by the second interface between the submucosa and muscularis propria, and finally the interface between the muscularis propria and perirectal fat. The first hypoechoic layer in this theory corresponds to the mucosa and submucosa, making differentiation between a mucosal and submucosal tumor impossible. In contrast, in the model depicted by Beynon and colleagues [7] the middle three lines correspond to the specific layers of the rectal wall.

- 1 First (hyperechoic) layer: the interface between the water/balloon and the mucosal surface.
- 2 Second (hypoechoic) layer: combined image produced by the mucosa and muscularis mucosae.
- 3 Third (hyperechoic) layer: the submucosa.
- 4 Fourth (hypoechoic) layer: the muscularis propria.
- 5 Fifth (hyperechoic) layer: the interface between the muscularis propria and perirectal fat.

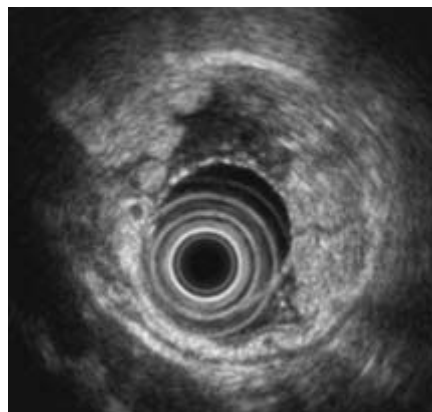
The sonographic layers of the normal colonic wall are similar to those described for the rectal wall, taking into account that the colonic wall is not surrounded by hyperechoic perirectal fat but by a serosal layer.

Some authors have further subdivided the fourth (hypoechoic) layer into three layers: two hypoechoic layers representing inner circular and outer longitudinal muscle layers and a thin hyperechoic layer that represents the connective tissue between the two muscle layers [4,7–12].

Using HFUS probes, it is possible to image the colorectal wall as a structure of nine layers, where the first three echo layers are considered to correspond to the mucosa, the fourth (hypoechoic) layer to the muscularis mucosae, the fifth (hyperechoic) layer to the submucosa, the (sixth) hypoechoic layer to the inner circular muscle, the seventh (hyperechoic) layer to the intermuscularis propria layer, the eighth (hypoechoic) layer to the outer longitudinal muscle layer, and the ninth (hyperechoic) layer to the subserosa and serosa (or perirectal fat). These categories are not absolute, as shown in a study using a 20-MHz ultrasound probe, where imaging the normal



(a)



(b)

Fig. 45.2 (a) Endoscopic and (b) endosonographic images of a flat villous adenoma in the distal rectum imaged with a dedicated echoendoscope at 12 MHz. The endosonographic image shows a normal five-layer wall pattern at the bottom of the image (5–7 o'clock) and thickening of the second (hypoechoic) layer between 2 and 5 o'clock. The area between 12 and 2 o'clock is not completely in focus. The ultrasound image is compatible with a mucosal lesion; no infiltration in deeper layers is detected.

colorectal wall as a nine-layered structure succeeded in only half the cases [13].

Colorectal adenocarcinoma

The preoperative staging of colorectal malignancies is one of the most important indications for EUS. Because less invasive treatments have been developed for early stages and since neoadjuvant therapy is increasingly used for more advanced stages, the findings of colorectal EUS influence treatment, i.e. endoscopic vs. surgical treatment (transrectal local excision, laparoscopic surgery, terminal sphincter-sparing procedures, neoadjuvant chemotherapy and/or radiotherapy). EUS has shown to alter clinical decision-making in up to one-third of patients with advanced T-stage rectal lesions [14,15]. In colonic cancer proximal to the rectum, preoperative T and N determination, although helpful for prognosis, is not of major significance since surgical resection is the major treatment modality [16].

EUS assessment of T-stage

Colorectal carcinoma is seen by EUS as an intraluminal or transmural mass altering parts of the wall structure. Most of the time, the tumor is a mainly hypoechoic mass with different types of penetration according to its T-status. Irregular thickening of a layer with a hypoechoic mass is interpreted as the presence of invasion into that corresponding layer. Disruption of a layer by a hypoechoic mass is interpreted as invasion through that corresponding layer. Therefore, destruction or disappearance of one or more of the normal layers is a reliable indication of depth of tumor invasion, although it is possible for normal hyperechoic layers to disappear because of inflammatory infiltration around a tumor mass [17–21].

The infiltration depth of a colorectal malignancy is based on the TNM classification, with the prefix “u” added indicating endosonographic staging [4]. uT1 is diagnosed when the lesion is limited to either the sec-

ond or third layer (Figs 45.2–45.5). Complete disruption of the middle echogenic layer, with invasion of the lesion into the fourth hypoechoic layer (representing the muscularis propria), is interpreted as uT2; uT3 is diagnosed when the lesion infiltrates through the muscularis propria. In this case the border between the outer hypoechoic layer and the outer hyperechoic layer (interpreted as serosa or perirectal fat) is irregular or serrated with some pseudopodia (Fig. 45.6). Continuity between the hypoechoic tumor and adjacent structures or organs is indicative of a uT4 tumor. Because of the difficulty of differentiating between a uT2 and uT3 tumor, an alternative criterion has been postulated whereby an irregular outer border of the muscularis propria is still interpreted as representing a T2 tumor as long as the outer hyperechoic layer (interface between muscle layer and perirectal fat) is not disrupted. Only complete disruption of this hyperechoic layer is in concordance with a T3 tumor. Although this view leads to less overstaging of T2 tumors, it does understage some T3 tumors, which can lead to undertreatment [17,22,23].

Several reports have shown EUS to be superior to digital rectal examination, CT, and MRI in staging rectal cancer, although use of endorectal coil MRI shows a similar accuracy rate compared with endorectal EUS in T-staging as it is also capable of evaluating the depth of wall invasion [24–27]. Even with the use of an endorectal coil, it is difficult to differentiate between a T1 and T2 lesion. Accuracy reported for standard CT and MRI ranges from 33–77% for CT to 59–95% for MRI [28]. It has to be stated that most patients included in studies using CT had advanced disease and only few studies classified wall penetration according to TNM classification. In addition, the number of patients included in studies using MRI was very limited, usually less than 40 patients. Most of the initial studies in endosonography were performed with blind rigid probes but more recent data using echoendoscopes show similar results [29].

In comparing the ability of all the imaging modalities for T-staging accuracy there is a large variability, rang-

Fig. 45.3 (a) Endoscopic and (b) endosonographic images of a slightly more elevated lesion imaged with a miniprobe with 20 MHz frequency. The ultrasound image shows the lesion as a thickened second layer with intact submucosa and muscularis propria. No infiltration can be detected.

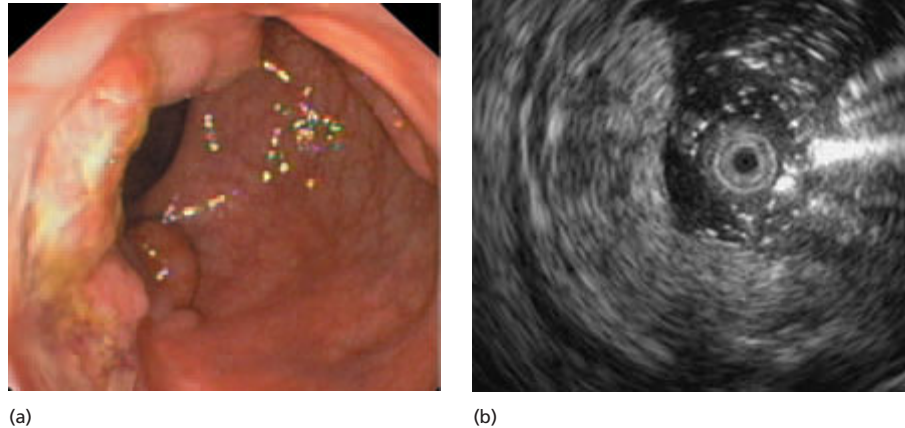
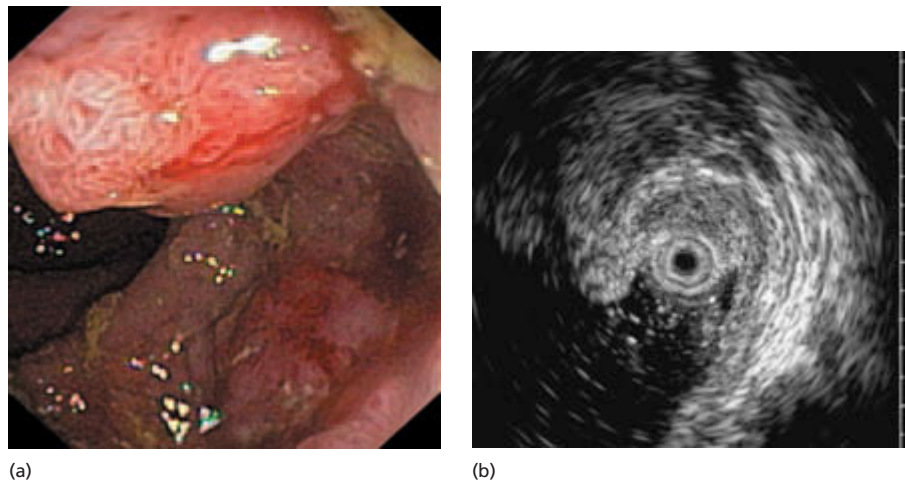


Fig. 45.4 (a) Endoscopic and (b) endosonographic images of a polypoid tubulovillous adenoma of the rectum. The examination is done with a 12-MHz miniprobe and the probe is maneuvered close to the edge of the lesion in order to delineate the transition between the normal wall and the lesion, which is limited to the second (hypoechoic) layer.



ing between 52 and 100%. Pooled data show accuracy for determining wall penetration of 79% for CT, 82% for MRI, and 84% for MRI with endorectal coil. The pooled sensitivity, specificity, and accuracy for colorectal EUS are 93, 78, and 87%, respectively. Accuracy is correlated with T-stage, with accuracies of 80, 68, 94, and 89% for stages T1–T4, respectively [25,27,30,31]. Two recent large ($n > 400$) studies showed a lower accuracy of, respectively, 69 and 64%, which might be due to the exclusion of advanced tumors because of preoperative radiotherapy, and possibly from lack of experience in one of these studies [32,33].

In general, overstaging is twice as common as understaging, a particular problem with T2 tumors. This is caused by peritumorous inflammation (inflammatory infiltrate or even abscesses), which cannot be distinguished from malignant tissue, desmoplastic changes, or hypervascularity. Understaging is caused by microscopic invasion beyond the resolution of EUS or tumor location close to the anal canal or on the valves of Houston. Less accurate staging in the lower rectum is

caused by difficulty in achieving an optimal (perpendicular) imaging of all sites of the ampulla recti, especially with a rigid probe. Interpretative errors can also affect accuracy, especially the tendency to overestimate a malignant lesion because of concern for undertreatment [14,34–39]. Staging postpolypectomy also seems to affect accuracy, mainly due to focal edema and/or postpolypectomy hematoma (21,40–43).

In large sessile adenomas the incidence of malignancy is postulated to be 20%. Since EMR techniques or surgical transanal excision has enabled the removal of superficial colorectal neoplasms, much attention has been directed to the depth of invasion of these lesions. Overstaging of adenomas is more likely in the evaluation of villous lesions than nonvillous lesions, especially when large (≥ 20 mm) lesions are taken into account. It was suggested by Mosnier and colleagues [44] that overstaging of villous tumors is due to the difficulty in demonstrating the interface between mucosa and submucosa using low-frequency endosonography [12, 20,45]. Understaging in early rectal cancer seems to be an

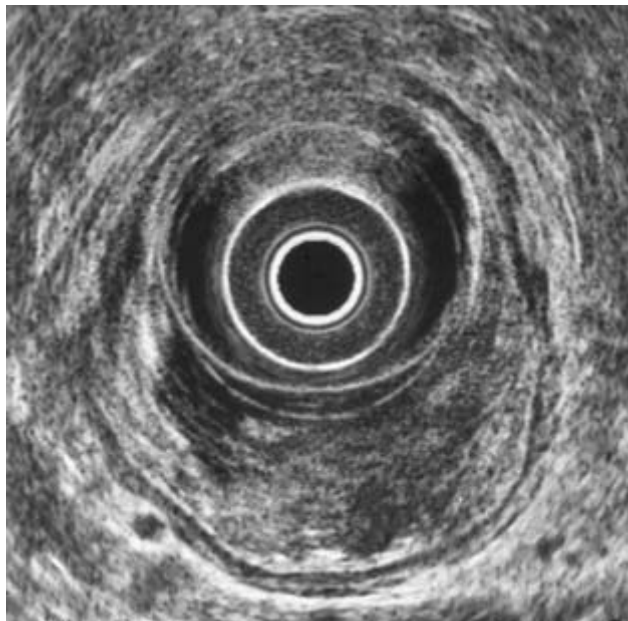


Fig. 45.5 Endosonographic image of a large polypoid lesion in the rectum, biopsies of which showed villous adenoma with high-grade dysplasia. The center of the hypoechoic lesion is located at 6 o'clock and there is a darker area visible consistent with a focus of malignancy infiltrating into the third (hyperechoic) layer, the submucosa.

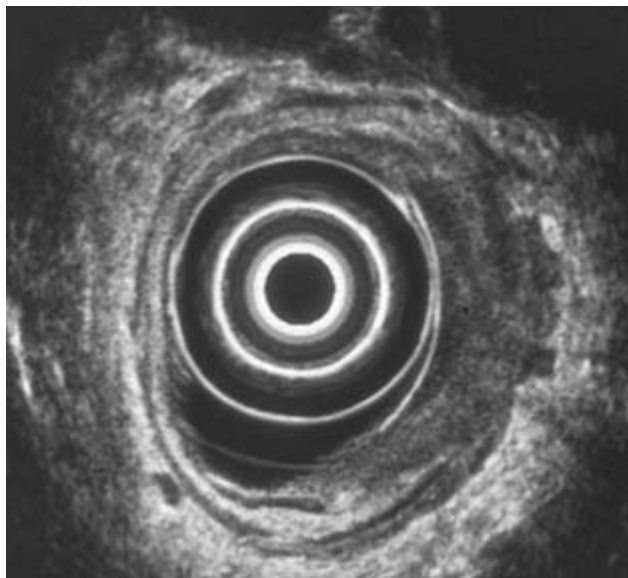


Fig. 45.6 Endosonographic image of an infiltrating rectal cancer with extension of the hypoechoic mass outside the muscularis propria. The irregular outer margin is indicative of a uT3 lesion.

even greater problem, as it might lead to undertreatment. In one series, up to 20% of investigated mucosal lesions showed invasion to the submucosa or deeper. It can be concluded that the resolution of conventional

EUS is not always sufficient to provide absolute accuracy in order to determine the appropriate treatment [46,47].

In locally advanced rectal cancer, preoperative irradiation has resulted in a reduction of local recurrence rate and an increase of disease-free survival. Preoperative radiotherapy also causes changes in echogenicity of the ultrasound image (tumor as well as rectal wall) due to inflammation and/or fibrosis, resulting in a significant decrease in accuracy, ranging from 29 to 75% [48–53]. After irradiation, the rectal wall is thickened and more hypoechoic, allowing a less clear visualization of the different layers, especially the outer limit of the rectal wall, as a result of fibrosis. The tumor itself might reveal three different echo features after radiotherapy:

- 1 hypoechoic pattern as observed before radiation, with possible changes in both morphology and size;
 - 2 more hyperechoic and nonhomogeneous pattern; and
 - 3 reappearance of the typical five-layer structure (although thickened) at the site of the tumor, which might correlate with a complete sterilization of the lesion [54].
- Due to the lower accuracy, EUS is considered to be unsatisfactory for predicting treatment response.

EUS assessment of N-stage

In colorectal cancer, not only depth of penetration but also involvement of peritumoral lymph nodes is a major determinant of prognosis, giving an indication of the risk for disseminated disease. Moreover, identification of metastatic lymph nodes plays an important role in decision-making, as the absence of lymph nodes in T1 and T2 disease makes them suitable for local resection. However, no single imaging modality shows sufficient accuracy to allow confident determination of metastatic involvement. Determination of lymph node involvement is less accurate than T-staging [11,26,55]. Accuracy by EUS ranges between 44 and 87%. Pooled data show an accuracy of 66% for CT, 74% for EUS, 74% for MRI, and 82% for MRI with endorectal coil [31,56]. Although CT does not allow discrimination between involved and noninvolved nodes, because the internal structure of the nodes cannot be depicted, a diameter of 1 cm is considered the cut-off value for differentiating between metastatic and inflammatory nodes [57].

Overstaging is mainly due to the difficulty of discriminating between inflammatory lymph node and metastatic lymph nodes. In contrast to T-staging, where Doppler ultrasonography has no proven benefit, Doppler has been suggested as useful in differentiating hypoechoic lymph nodes from blood vessels, especially when the vessel is running perpendicular to the scanning plane, in which case a normal vessel is difficult to assess [58,59].

Understaging is due to the presence of metastasis in extra-mesorectal nodes (out of reach of the endosonographic probe), micrometastasis in small nodes, lymph nodes too small to be visible, and inadequacy of criteria for involved nodes [60]. The normal criteria used elsewhere in the gastrointestinal tract (round in shape, hypoechoic with a distinct border and size) cannot be applied in N-staging for colorectal cancer [61]. Initially, suspicious lymph nodes were described as rounded, echo-poor, with their short-axis diameter greater than 5 mm [27,36]. Most of the normal lymph nodes cannot be seen, as they are isoechoic with perirectal fat. Lymph nodes are found by EUS in less than 50–66% of patients [55,62,63]. Detection increases with their size, and invasive cancer is associated with larger diameters of nodes.

Node size itself is a bad indicator of metastatic disease. Although lymph nodes that harbor malignant deposits are usually larger than nonmalignant ones, size alone cannot distinguish reactive hyperplasia from metastatic involvement. Lymph nodes smaller than 3 mm are beyond the resolution of EUS and up to 20% of lymph node metastases in rectal cancer are smaller than 3 mm. In one series, up to 50% of the positive nodes were smaller than 5 mm [18,64–66].

EUS features of metastatic lymph nodes include short-axis diameter ≥ 9 mm (99% specificity), degree of heterogeneity, and presence or absence of a hilar reflection, although large interobserver variability makes accurate evaluation difficult. Echogenicity itself is not an objective criterion and depends on the tissue structure of the node, transducer frequency, gain, distance between lymph node and transducer, attenuation due to the overlying tumor, and choice of the reference tissue [67,68].

The addition of FNA raises the accuracy of staging lymph nodes [69]. Nevertheless, FNA is not frequently used because of the difficulty of gaining access to a lymph node without transgressing the primary tumor. In a recent series, FNA led to a change in management in only one patient, due to close agreement between the T and N stage, and the fact that visualization alone of perirectal lymph nodes has a much higher predictive value for perirectal lymph node metastasis than for nodes elsewhere in the gastrointestinal tract [15,70].

EUS detection of local recurrence

Local recurrence after curative surgery represents a significant problem in 15–25% of patients, with most of the recurrences appearing within the first 2 years after resection, a rate that has declined since the introduction of preoperative radiotherapy and also since new surgical techniques were introduced (total mesorectal excision). Although the percentage of local recurrence is still high, with huge implications for survival and quality of life, early detection is warranted to allow curative reinter-

vention or at least palliative prevention of tumor compression symptoms [15,71,72].

CT as well as MRI has been shown to be very useful in detecting local recurrence, although there are several limitations. For CT, lesions have to be at least 2 cm in diameter for accurate diagnosis and distinction between local recurrence and postoperative alterations remains difficult [73]. MRI gives better results for tumor characterization, with reported accuracy ranging from 75 to 93% [74]. Both CT and MRI have to be repeated frequently in order to permit early detection, which leads to high cost and (for CT) radiation exposure.

Since growth of local tumor recurrence is predominantly extraluminal, implying that it is undetectable for follow-up screening by colonoscopy, EUS can be used as the diagnostic method of choice. In one series, local recurrences of up to 3 mm could be detected. Because it is relatively cheap, well tolerated, readily accessible, and does not involve X-ray exposure, EUS appears to be an ideal technique for repeated use in the postoperative monitoring of (colo)rectal cancer. Although postoperative EUS incorporated in a follow-up program has not been proven to influence patient survival, some authors propose performing EUS every 6 months during the first two postoperative years [75,76]. The reported accuracy rate ranges from 80 to 85%, increasing to more than 90% using FNA. Improving accuracy by EUS-guided biopsy can avoid overtreatment of patients with suspicious lesions [72,75,77,78].

A baseline EUS is suggested by some authors within 3 months after surgery to facilitate the interpretation of later examinations. Because this interval is relatively short after primary resection, any hypoechoic mass must be differentiated from a pelvic floor abscess, hematoma, or fluid collection [71,73,79]. A normal anastomosis is visualized as an echo-mixed symmetric interruption of the typical five-layer structure. In the case of stapling, small localized bright echoes appear in the anastomotic wall, without creating a shadow. An extramural recurrence is identified as an oval or circular echo-poor lesion in the perirectal area. An anastomotic recurrence is often seen as a hypoechoic irregularly shaped area in the anastomotic region that may infiltrate the perirectal fat. Sometimes, it is visualized as an echo-mixed or hyper-echoic lesion, especially after radiotherapy. Peritoneal carcinomatosis is diagnosed when EUS shows small hypoechoic nodules (usually < 1 cm) surrounding the colonic serosa and a heterogeneous mass is detected in the omentum or can be suspected if ascites is present [74,76,80,81].

High-frequency ultrasound

As mentioned earlier, no accurate differentiation is possible between adenomas and uT1 carcinomas because

both manifest as a broadening of the second (hypoechoic) layer. Lesions expanding the second layer with invasion into the third layer (submucosa) have to be considered uT1 lesions [32]. Since the introduction of HFUS probes, accurate staging of more superficially located lesions became possible due to its higher resolution. An HFUS probe can be introduced through the working channel of a colonoscope, permitting its use in the same session of diagnostic colonoscopy and the evaluation of stenotic lesions is possible. It is suggested that HFUS could be the first choice for narrow strictures, early cancer, and submucosal lesions due to its higher resolution and for staging of proximally located lesions [82–85].

According to the Japanese Cancer Society Classification, the submucosa can be divided into three layers:

- 1 sm1: tumor limited to the upper third of the submucosa;
- 2 sm2: tumor limited to the middle third;
- 3 sm3: tumor involving the deep portion of the submucosa.

The risk for positive lymph nodes is considered to be 0–3% in T1m and T1sm1, whereas the possibility of lymph node metastasis in T1sm2 and T1sm3 is suggested to be as high as 22%, therefore necessitating surgical therapy [86–90]. To improve accuracy, a new technique called “enhanced EUS” has been created, in which deaerated saline solution is injected into the submucosa to lift the tumor. The saline-infiltrated submucosa is then visualized as a thickened hypoechoic layer, whereas an additional echoic layer is seen between mucosa and submucosa, allowing better distinction of invasion into the submucosa using HFUS [91].

Accuracy of HFUS in evaluating colorectal T-staging has been reported to be in the range of 80–93%. There seems to be no significant difference in staging between colonic and rectal lesions. Accuracy for staging lymph nodes varies between 63 and 87% [13,46,92,93]. Accuracy as low as 24% has been reported in a small number of patients [94]. Accuracy for T-staging is relatively less discriminate in T4-staging due to the limited depth of penetration, but accuracy is also related to tumor size (accuracy decreases as tumor size increases) and shape (lesser accuracy with protruded lesions). To enhance accuracy, it has been suggested that lower frequencies are used in elevated or large polypoid lesions [13,95–97]. Also, because of attenuation with limited depth of HFUS, deep lymph nodes cannot be detected, although the ability to detect lymph nodes is higher in rectal cancer because rectal lymph nodes are located closer to the rectal wall.

Preliminary data show that HFUS performs better than magnifying colonoscopy in predicting invasion depth in early colorectal cancer. Optical coherence tomography (see Chapter 44) offers a better resolution of mucosa and submucosa and could be more accurate in

evaluating superficial layers confined to mucosa and submucosa. The technique seems promising but is still in its experimental stage [94,98].

Mucosal and submucosal tumors

Because EUS is able to evaluate the five-layered structure of the bowel wall accurately, it has shown to be useful in differentiating submucosal growth from extraluminal compression in cases where endoscopy shows only bulging of the normal wall without visible mucosal defects. HFUS can also be used to define accurately the extent of the submucosal lesion before endoscopic mucosal resection [82,99].

Lipomas appear on EUS as hyperechoic lesions with regular borders in the third layer. EUS can be used to determine any extension into the muscularis propria before injection-assisted polypectomy of symptomatic lipomas [100]. Gastrointestinal stromal tumors (formerly designated as leiomyoma, leiomyoblastoma, and leiomyosarcoma) are the most frequent non-epithelial submucosal tumors in the gastrointestinal wall. Gastrointestinal stromal tumors are visualized as hypoechoic masses in continuum with the fourth (muscularis propria) layer, seldom deriving from the muscularis mucosae. Due to uncertainty about whether these lesions are malignant, several criteria have been proposed for distinguishing malignant from more benign forms, realizing that a definitive diagnosis is only made by immunohistochemistry. A mass of 40 mm or more in diameter, with irregular borders, cystic spaces (> 3 mm), and echogenic foci is depicted as a suspicious lesion. Echogenic foci might be due to fibrosis, cystic degeneration may be caused by cellular necrosis. Two or more features are present in most cases of malignant disease. Interpretation is difficult and is strongly dependent on interobserver variability. The accuracy of EUS for diagnosis of malignant gastrointestinal stromal tumors has been reported to be 78%; the accuracy of EUS-FNA, with the addition of Ki-67 labelling index, for diagnosis of malignant gastrointestinal stromal tumors is stated to be 100% [101–104].

Carcinoid tumors are mainly located in the third layer, although they may also appear in the second layer. They are visualized as oval or round lesions, generally slightly hypoechoic and homogeneous. EUS is also useful in determining the presence of local metastasis and lymph nodes [105]. A lymphangioma is visualized as a cystic lesion with septal structures in the third layer. Lymphomas are mostly seen as hypoechoic inhomogeneous masses, located in the second to fourth layer [106]. Rectal linitis plastica is characterized by diffuse circumferential thickening of the wall, especially in the submucosa and muscularis propria; extension into the perirectal fat may be visualized. In rare cases, complete

disappearance of the normal five-layer structure can be seen. No distinction is possible between primary and secondary rectal linitis plastica by EUS alone, although EUS-FNA can provide the diagnosis. EUS can be used in follow-up by measuring reduction of rectal wall thickening [107,108].

In portal hypertension, rectal varices appear as rounded, oval, or longitudinal echo-free structures, mainly in the submucosa or outside the wall. Rectal varices often have a diameter greater than 2 mm [109]. Endometriosis, which is predominantly located in the distal colon, may appear as either extrinsic compression or as an irregular hypoechoic mass mainly in the fourth layer, in continuity with the fifth layer. Metastases appear as hypoechoic heterogeneous masses and can potentially be encountered in all layers. Cysts are seen as anechoic, rounded, or ovoid lesions and must be differentiated from pneumatosis cystoides intestinalis and colitis cystica profunda [103,110].

Inflammatory bowel disease

Apart from the evaluation of perianal abscesses and fistulae in inflammatory bowel disease, EUS is also useful in the evaluation of colorectal wall involvement, although the impact of EUS on medical therapy is not yet clearly defined (80,111). Several parameters have been proposed for evaluation but no reliable criteria are available to make a clear distinction between Crohn's disease and ulcerative colitis. Involvement of the colorectal wall in Crohn's disease is characterized by thickening, mostly with hypoechoic changes of the submucosa or the whole wall, often with disappearance of the normal five-layer structure, with deep ulcerations and fibrosis of the serosa, correlating well with anatomopathologic findings. Thickening can be present in the absence of mucosal lesions [112,113]. Discontinuity of lesions on EUS suggests Crohn's disease, as in colonoscopy [20]. In ulcerative colitis there is mostly a thickening of the first three layers, with preservation of the five-layer structure, although involvement of the entire wall has been reported [114,115]. EUS has been used to assess the severity of inflammation and to predict relapse in ulcerative colitis due to persistent wall thickening during remission [116–118]. In collagenous colitis a broadening of the second layer, consistent with subepithelial collagen bands, and of the fourth layer are observed [119].

Summary

During the past decade, EUS has proven its reliability and accuracy in colorectal cancer staging, making it an essential and indispensable tool in the preoperative staging and follow-up of rectal cancer. Although there are limitations, especially in assessment of nodal disease,

there is no better, relatively inexpensive alternative available. With the development of HFUS probes providing more precise staging, a better selection of less invasive treatments in patients with early cancer became possible. EUS is clearly the best modality for the evaluation of submucosal lesions, especially with the addition of FNA. In inflammatory bowel disease the value of EUS seems rather limited apart from its diagnostic capabilities in perianal disease.

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Chapter 46

Virtual Colonoscopy in the Evaluation of Colonic Diseases

Michael Macari

Introduction

Virtual colonoscopy is an evolving noninvasive imaging technique that allows detection of colorectal polyps and cancers. Currently, most centers that perform virtual colonoscopy utilize computed tomography (CT) for image acquisition [1]. In Europe and several centers in the USA, some investigators are acquiring virtual colonoscopy data using Magnetic resonance imaging (MRI) [2]. A potential advantage of MRI is lack of exposure to ionizing radiation. However, using CT to acquire virtual colonoscopy data, the radiation dose to the patient can be substantially lowered when compared to routine abdominal and pelvic CT due to the high tissue contrast between the insufflated colonic gas and the wall of the colon [3]. Considerable progress in the procedure and understanding of fundamental aspects have developed since the first report of virtual colonoscopy appeared in the literature in 1994 [4].

The first question that needs to be asked and answered is “why consider virtual colonoscopy at all?” After all, there are other techniques available to evaluate the colon including fecal occult blood testing, sigmoidoscopy, barium enema, and conventional colonoscopy. After attempting to address this important question, issues related to patient preparation, data acquisition, and data interpretation for virtual colonoscopy will be reviewed. Finally, this chapter will attempt to address the current and future roles of virtual colonoscopy. Throughout this chapter the terms virtual colonoscopy and CT colonography will be used interchangeably to describe a combination of two-dimensional and three-dimensional CT images used to evaluate the surface of the colon.

Why use virtual colonoscopy?

Colorectal cancer is a curable disease if detected and treated early. Screening may decrease the morbidity and mortality associated with colorectal cancer by detecting and leading to the removal of premalignant adenomatous polyps before they become invasive cancers [5–12]. There is currently consensus among healthcare providers and policy-makers that screening for colorectal cancer is

justified [5]. The current options available for colorectal carcinoma screening include digital rectal examination, fecal occult blood testing, sigmoidoscopy, barium enema, fiberoptic colonoscopy, and combinations of these tests [12].

The following strategies have been recommended by the United States Agency for Health Care Policy and research for colon screening [7] (see Chapter 12). Fecal occult blood testing (FOBT) is recommended every year beginning at age 50. If this test is positive, a diagnostic examination should be performed including either colonoscopy or double-contrast barium enema (possibly in combination with sigmoidoscopy) [8]. In asymptomatic individuals, either flexible sigmoidoscopy is offered every 3–5 years, double-contrast barium enema every 5 years, or colonoscopy every 10 years for the detection of nonbleeding polyps and tumors [7,8].

Despite consensus on the need for colon cancer screening and the multiple current available options, there are 150 000 new cases of colorectal cancer diagnosed every year in the USA that result in approximately 55 000 deaths [6]. Since most colorectal polyps grow slowly from precancerous adenomas to invasive cancer, and screening can detect the precancerous adenomas, the high prevalence of cancer is preventable. However, there are many reasons for the continued high prevalence of colon cancer including patient reluctance to undergo screening, limitations of current screening options, and confusion about when to perform current screening options. Regarding patient reluctance to comply with current screening options, a survey in 1992 found that only 17.3% of patients over age 50 had undergone fecal occult blood testing within the last year, and only 9.4% had undergone sigmoidoscopy within the last 3 years [8]. Studies have also demonstrated that even healthcare professionals are reluctant to undergo colon screening [13].

In addition to poor patient acceptance of screening, all current screening options have important limitations. While the performance of yearly FOBT has demonstrated a mortality reduction from colorectal cancer, FOBT does not directly evaluate the colonic mucosa [14]. Many large adenomatous polyps do not bleed and occasionally colorectal carcinoma will not bleed. In addition,

there are many false-positive fecal occult blood tests for colon cancer, which can lead to further testing and expense. One study demonstrated that in greater than 50% of heme-positive stool examinations for occult blood, the source was from the upper gastrointestinal tract, thus leading to further unnecessary testing [15].

Screening sigmoidoscopy has been shown to decrease the mortality of colorectal cancer [16]. However, sigmoidoscopy fails to evaluate the entire colon and therefore complete colon screening is not obtained [17,18]. Two recent studies evaluating sigmoidoscopy and colonoscopy found similar results. If only sigmoidoscopy were performed for colon screening in an asymptomatic population, many advanced proximal carcinomas would be missed [17,18]. This is true even taking into account the fact that if a significant distal lesion were detected during sigmoidoscopy, it would prompt a complete colon examination with colonoscopy. In fact, half of all proximal carcinomas in these studies did not have a distal polyp that would have prompted colonoscopy. Moreover, it appears that the combination of FOBT and sigmoidoscopy does not result in a significant improvement in the efficacy of screening [19,20]. For example, a recent study showed that in a population of 2884 screening patients with a negative fecal occult blood test and who then underwent fiberoptic endoscopic evaluation of the distal colon (rectum and sigmoid), advanced colonic neoplasia was missed in 24% of patients [19].

There are currently two options available and reimbursed for a full colonic evaluation: colonoscopy and double-contrast barium enema. Both of these examinations evaluate the entire colon, yet they have limitations. The sensitivity of the double-contrast barium enema for polyp detection is unknown. One study has demonstrated a sensitivity of 81% for double-contrast barium enema when compared with colonoscopy in diagnosing polyps of at least 10 mm [21]. The sensitivity for smaller polyps was less. However, a recent study comparing double-contrast barium enema with colonoscopy in detecting polyps in patients with prior polypectomy (surveillance evaluation) demonstrated poor sensitivity of the double-contrast barium enema. In this study the barium enema missed over 50% of polyps larger than 1 cm [22].

The gold standard for colonic evaluation is flexible colonoscopy. Complete flexible colonoscopy allows the most thorough evaluation of the colon with the added benefit of biopsy or excision of suspicious lesions. However, there are certain limitations to the widespread use of colonoscopy for screening, including examination time, need for sedation, potential risk of perforation, and failure to complete the examination in up to 5–10% of patients [23,24]. Other significant limitations to colonoscopy as a screening test include the lack of sufficient numbers of trained endoscopists to perform screening

colonoscopy in all eligible patients and the expenses incurred. The median reimbursement charge in the USA for colonoscopy is US\$1736 [23,24].

Virtual colonoscopy is a new, evolving and relatively noninvasive technique, which allows evaluation of the entire colonic surface for polyps and cancers. Preliminary clinical evaluation of virtual colonoscopy shows promise in detecting polyps and cancers of the colon and rectum with sensitivity ranging from 75% to 100% for polyps 10 mm and greater [1,3,25–31]. In addition, a recent study showed that among potential patients for colon screening, 60.2% favored virtual colonoscopy, 25.7% preferred conventional colonoscopy, and 14.1% had no preference [32].

So returning to the original question; “why should we pursue the clinical evaluation of virtual colonoscopy?” As pointed out above, colorectal cancer is preventable if detected early. Yet there are limitations to the current available screening options and there is reluctance on the part of patients to undergo colorectal screening. This is manifested by the continued high prevalence and mortality of the disease. If virtual colonoscopy can prove effective in detecting precancerous lesions, it would aid in the ability to screen the large number of patients who are currently eligible for screening. In addition to evaluating virtual colonoscopy as a screening test, there are numerous other potential scenarios where virtual colonoscopy may have a clinical role, including evaluating the colon after an incomplete examination or proximal to an obstructing cancer, in elderly patients, those with significant medical comorbidity, and in those patients who are unable to tolerate sedation.

Patient preparation and data acquisition for virtual colonoscopy

Bowel preparation

Virtual colonoscopy continues to evolve in an attempt to increase the diagnostic value of the examination. Regarding patient preparation it is desirable to perform virtual colonoscopy in patients with “clean” colons [1,3,33–37]. While virtual colonoscopy is a relatively noninvasive imaging procedure, there are two aspects of the examination that may produce some anxiety and potential discomfort for patients. These include the need for bowel preparation and colonic insufflation with gas. Currently, the colon needs to be thoroughly cleaned and properly distended in order for interpretation to proceed.

The biggest limitation of virtual colonoscopy is bowel preparation. Like all other techniques that attempt to image and visualize the colon surface, the colon needs to be cleansed of residual fecal material. Many patients find this the worst part of the examination. There are three main bowel preparations available including cathartics

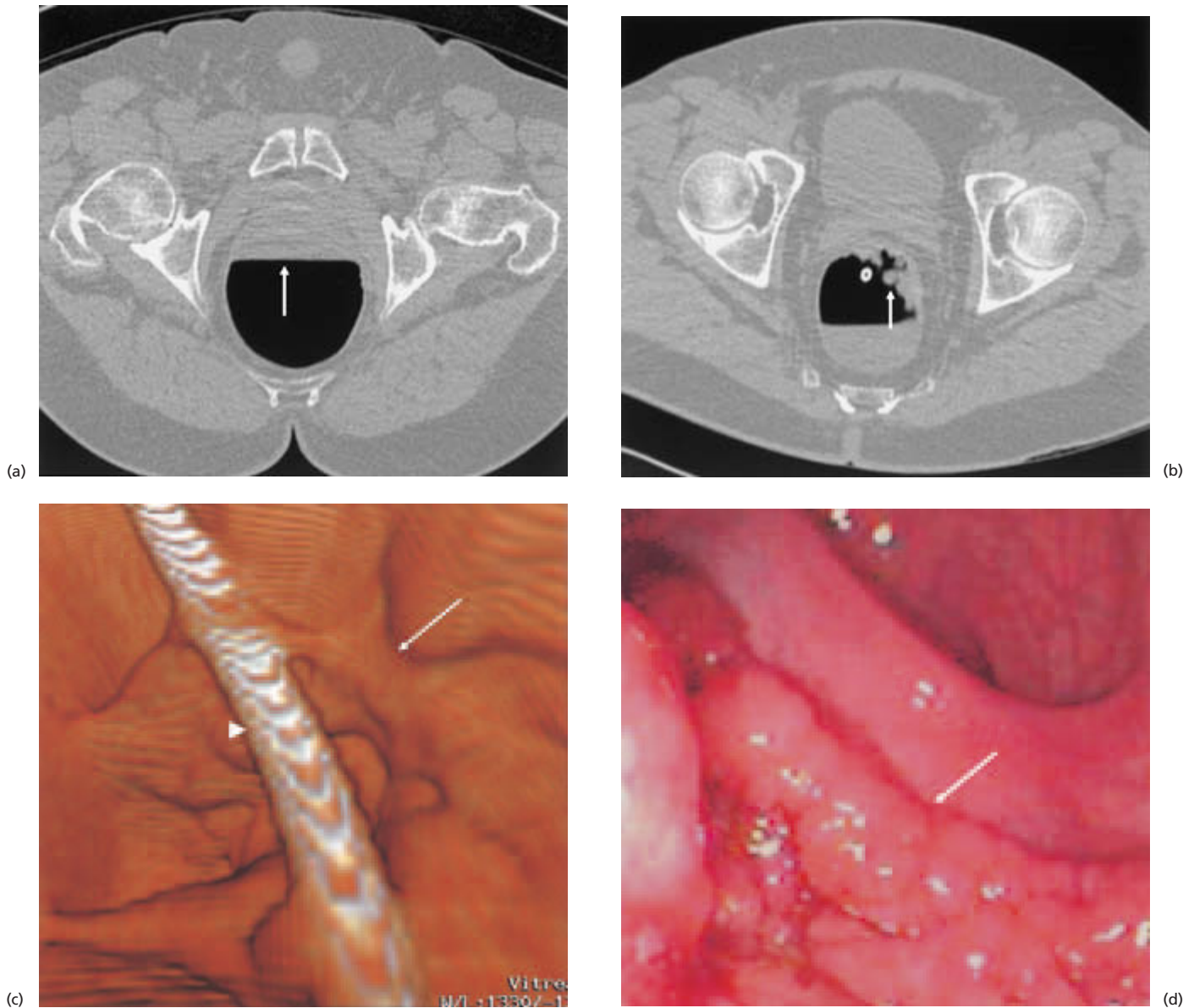


Fig. 46.1 Carpet-like filling defect in rectum. (a) Axial image in prone position shows large amount of residual fluid obscuring ventral wall of rectum. (b) Axial image in supine position shows redistribution of fluid and now irregular carpet-like filling defect (arrow) along ventral wall of the rectum. (c) three-dimensional endoluminal view of the area shows carpet-like irregular morphology of the surface of the

rectum (arrow). Note rectal tube (arrowhead). (d) View from conventional colonoscopy confirms irregular morphology of the wall of the rectum. Histological analysis revealed villous adenocarcinoma. Occasionally, very large amounts of fluid are present using a polyethylene glycol preparation and despite supine and prone imaging the entire colonic surface may not be seen.

such as magnesium citrate, oral phospho-soda, and colonic lavage solutions such as polyethylene glycol. In our experience, both magnesium citrate and phospho-soda provide acceptable bowel preparation. We have found the polyethylene glycol preparation frequently leaves a large amount of residual fluid [37]. While this preparation is adequate for colonoscopy, the potential limitation of large amounts of residual fluid at CT colonography is important (Fig. 46.1). At colonoscopy

residual fluid can be endoscopically aspirated out of the colon. During a barium enema examination, multiple different projections can be used to redistribute the fluid. With CT colonography, the examination is limited by only two projections, supine and prone. In this setting, the preparation that provides the least amount of residual fluid will theoretically provide the greatest opportunity to detect polyps by enabling evaluation of the entire mucosal surface of the colon.

Commercial preparation kits can be used for bowel preparation. The instructions are easy for the patient to follow and the kits are inexpensive. Two commercial preparation kits that we utilize are the 24 h Fleet 1 Preparation (Fleet Pharmaceuticals, Lynchburg, VA) or the LoSo Preparation (EZ-EM, Westbury, NY). The Fleet Kit utilizes a clear fluid diet the day prior to the examination as well as a single 45-mL dose of phospho-soda and 4 bisacodyl tablets the day prior to the examination, and a bisacodyl suppository the morning of the examination. The LoSo Preparation relies on magnesium citrate and 4 bisacodyl tablets the day prior to the examination, and a bisacodyl suppository the morning of the examination. In the past, these preparations have provided adequate bowel cleansing for the majority of patients undergoing double-contrast barium enema. It should be noted that the 24-h Fleet kit utilizes a single 45-mL dose of phospho-soda the evening prior to the examination. Most gastroenterologists who rely on phospho-soda for bowel preparation, utilize two 45-mL doses of the phospho-soda, one the day prior to the examination and one the morning of the examination.

These commercial preparation kits appear to provide a drier colon than a 4-litre electrolyte lavage solution [37]. However, these preparations do on occasion leave more fecal residue than a typical electrolyte preparation or a double dose, that is, two 45-mL doses of phospho-soda. Approximately 5% of patients who undergo bowel preparation with these commercial kits will have a poor preparation limiting interpretation.

Given this limitation, the idea of fecal and fluid tagging for virtual colonoscopy is currently being evaluated [38,39]. Fecal tagging can be performed without bowel cleansing [38] or with bowel cleansing [39]. Fecal tagging without bowel cleansing relies on having the patient ingest small amounts of iodine or dilute barium with low fat and fiber diets beginning several days prior to the examination. When the CT examination is performed residual fecal material will appear high attenuation (white). Utilizing computer-generated fecal subtraction techniques, the high-attenuation fecal material can be subtracted out of the dataset leaving only the colonic mucosa and any colorectal neoplasm or polyp. This technique is still experimental and has not been proven to be effective; however, research into this area is an important topic in virtual colonoscopy. As has been pointed out, if virtual colonoscopy could be effective in detecting colorectal polyps and not require a bowel preparation, it would become the screening test of choice [25].

A recent study evaluating the use of fecal tagging with dilute barium in conjunction with a less intense bowel cleansing agent to “tag” or “label” residual fecal material was reported (Fig. 46.2). Utilizing a magnesium citrate preparation with a fluid-restricted, low-fiber, low-fat

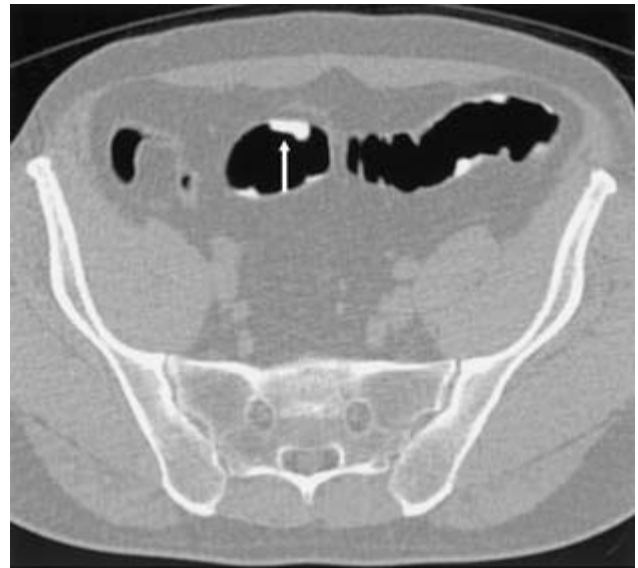


Fig. 46.2 Fecal tagging. Axial CT image shows retained fecal material is tagged with barium (arrow) and appears white.

diet as well as fecal tagging, a sensitivity and specificity of 100% for detecting polyps 10 mm and greater was found [39]. In this study, the fecal tagging preparation was compared with that of polyethylene glycol. The specificity of virtual colonoscopy in patients undergoing fecal tagging was improved when compared with those undergoing bowel preparation with a standard polyethylene glycol preparation without fecal tagging. Moreover, in this study patients preferred the fecal-tagging preparation to the polyethylene glycol preparation. The potential for virtual colonoscopy and fecal tagging without bowel preparation exists, and if shown to be reliable will decrease one of the main barriers to widespread colon screening with virtual colonoscopy.

Colonic distention

Once the colon has been prepared, the examination is ready to be performed. It should be noted that different institutions utilize different CT techniques. Outlined below is the New York University technique, which is easy to perform and provides excellent sensitivity and specificity for colorectal polyps measuring 10 mm and greater. Data acquisition is performed entirely by a trained technologist or a nurse. A radiologist is not on site, thus minimizing the commitment of radiologist time to data acquisition.

Immediately prior to the examination being performed, the patient is asked to evacuate any residual fluid from the rectum (easy access to a close bathroom is essential). For colonic insufflation, either room air or carbon dioxide (CO₂) can be used. The use of room air is easy, and inexpensive. Proponents of CO₂ argue



Fig. 46.3 Catheter used for insufflation. A small flexible rubber catheter is used to insufflate the colon. It is the size of a Foley catheter and patients do not feel it inserted into the rectum. No balloon is used.

that because it is readily absorbed from the colon it causes less cramping after the procedure than room air insufflation. In our experience CO₂ is associated with less delayed discomfort. While cramping may be a problem in some patients after room air insufflation, most find the examination to be quick and minimally uncomfortable.

A small rubber catheter is used to insufflate the colon with a hand-held bulb syringe (Fig. 46.3). This catheter is much smaller than a barium enema tip and a balloon is not used. We ask them to let the technologist know when they are just beginning to feel uncomfortable from the distention. Generally this signals that the colon is well distended. Patients are encouraged to keep the gas in. Approximately 40 puffs with a hand-held bulb syringe is sufficient to distend the colon. However, we do not use a set strict number of insufflations since the length of an individual colon is variable. Also, if the ileocecal valve is incompetent more gas will be required for optimal distension.

We do not use a bowel relaxant (glucagon) for CT colonography [35]. This minimizes cost and patient anxiety since no intravenous needles are used. After insufflation, the catheter is left in the rectum and a single scout CT image is obtained in the supine position to verify adequate bowel distention. If adequate bowel dis-



Fig. 46.4 Mobility as an indication of residual fecal material. (a) Supine image of rectum shows 15-mm homogeneously attenuating filling defect (arrow) on dorsal aspect of rectum. (b) Prone image in same patient shows that the filling defect (arrow) is now on the ventral aspect of the rectum indicating mobility. In general, mobility indicates residual fecal material.

tension is not achieved, additional air is insufflated into the rectum. Following air insufflation, CT colonography is performed first in the supine position in a cephalocaudal direction encompassing the entire colon and rectum. The patient is then placed in the prone position and several additional puffs of air are then administered. Supine and prone imaging doubles the radiation dose but is essential to allow optimal bowel distention, redistribution of residual fluid, and differentiation of fecal material from polyps, since visualization of mobility of a filling defect implies residual fecal material (Figs 46.4, 46.5). However, apparent mobility of a filling defect should not automatically signal that a lesion is a polyp since occasionally the sigmoid colon and cecum are on a long mesentery and the colon has actually changed position, simulating mobility of a colon lesion.

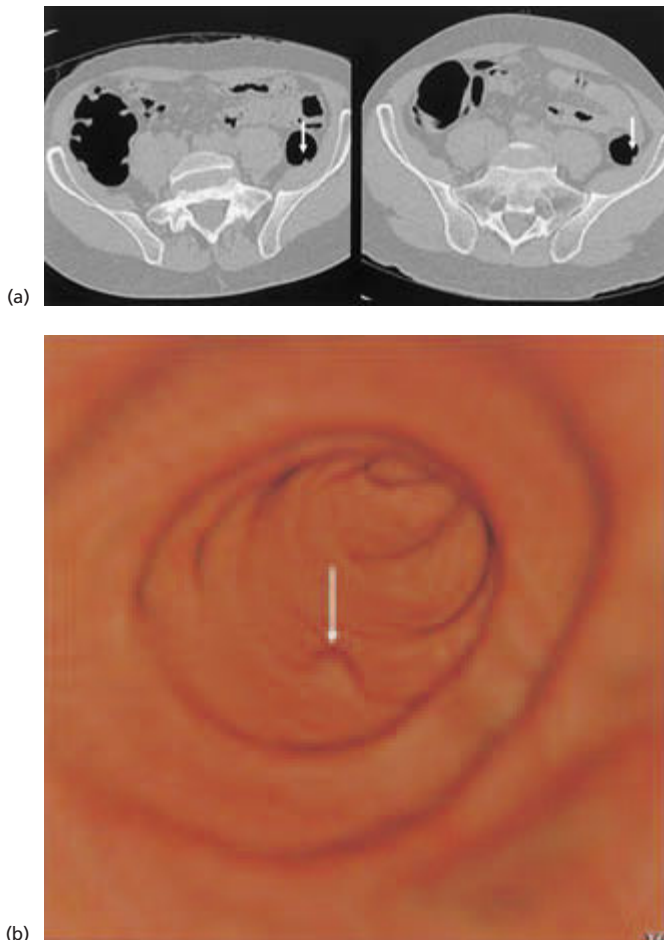


Fig. 46.5 Small nonmobile filling defect in descending colon, advantage of simultaneous supine and prone imaging. (a) Axial prone (left) and supine (right) images show 5-mm filling defect (arrow) in the descending colon, which does not move. (b) Endoluminal image confirms small polypoid lesion. At colonoscopy a 5-mm tubular adenoma was found.

There is some controversy about the use of intravenous contrast administration. One study found improved detection of polyps after the administration of intravenous contrast material [40]. Occasionally polyps may be obscured by residual fluid. After administering intravenous contrast a polyp will enhance and it may become visible despite the presence of fluid. However, the downside of the routine administration of contrast is cost, need for intravenous access, and risk of allergy from the iodinated contrast material. In the setting of a known colorectal lesion, the use of intravenous contrast may be justified since better delineation of the colonic abnormality, as well as improved tumor staging is possible.

Data acquisition

The single most important factor in the improvement of the performance of virtual colonoscopy has been the development of multidetector row spiral CT scanners (Fig. 46.6). These scanners allow between four and 16 slices to be obtained in a single rotation of the X-ray tube [3,41,42]. The advantages of these scanners are that they allow large volumes of data to be scanned with very thin sections in a single breathhold. As a result motion artifact from respiration and peristalsis is decreased or eliminated. Moreover, interpretation is not limited to evaluation with axial images only. Using improved computer workstations, coronal, sagittal, and endoluminal images can all be obtained from the single axial acquisition, thus facilitating differentiation of polyps, bulbous folds, and residual fecal material [3] (Fig. 46.7).

A 4×1 mm slice detector configuration, 120-kV, 0.5-s gantry rotation, and effective 50 mAs enables the entire colon to be covered within a 30-s breathhold. CT images are reconstructed as 1.25-mm-thick sections with a 1-mm

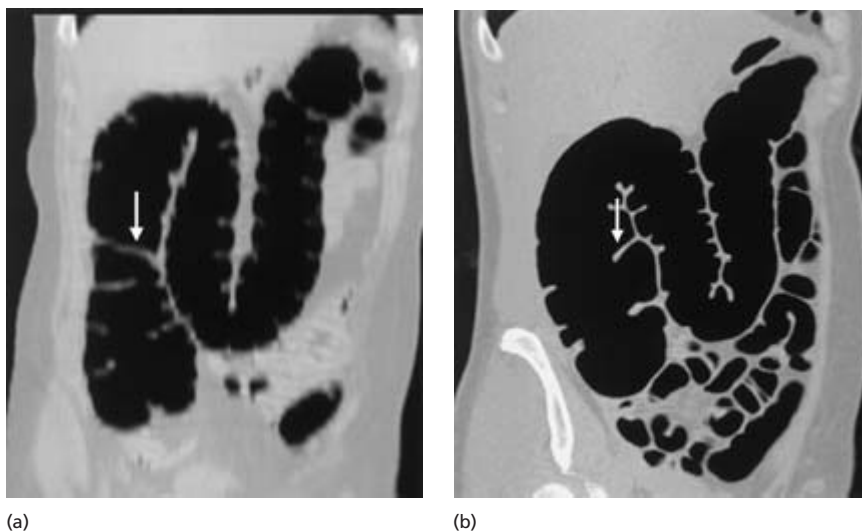


Fig. 46.6 Improved resolution with thin section multislice CT. (a) Coronal reformatted image from data acquired with 5-mm-thick sections on a single-slice helical CT scanner shows poor resolution. (b) Coronal reformatted image from data acquired with 1-mm-thick sections on a multislice helical CT scanner shows improved resolution when compared with (a) related to acquisition with thinner slice collimation.

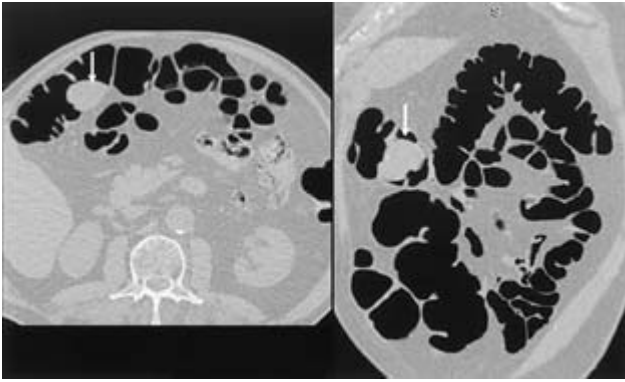


Fig. 46.7 Large lobulated filling defect in hepatic flexure. Axial and coronal CT colonographs show 4-cm lobulated mass (arrows) in hepatic flexure. Both images were acquired from a single axial acquisition. By using thin slice collimation the data can be viewed in any orientation (axial, sagittal, coronal, or endoluminal).

reconstruction interval. The examination is networked to a workstation where data interpretation can proceed.

Currently there is a radiation dose penalty using the thin-section multidetector row CT scanners. This is due to a penumbra effect of unused radiation that does not contribute to image formation [3,41,42]. However, for virtual colonoscopy examinations, there is the opportunity to decrease radiation dose by lowering the radiation exposure [3,43]. This is possible because of the very high contrast between the colon wall and the insufflated gas. Importantly, with new multidetector row CT scanners that acquire greater than four slices with each rotation (up to 16 slices with each gantry rotation), the radiation dose penalty is reduced. Moreover, most CT manufacturers are installing automated features on the scanners that allow the dose to be decreased when scanning relatively thinner areas of patient anatomy. In fact, as performed today, the effective dose that a patient receives from a virtual colonoscopy examination is lower than that from a conventional double-contrast barium enema [3,42].

When performing virtual colonoscopy examinations, there is the opportunity to evaluate more than just the colon. Incidental extracolonic findings may be detected [44]. These lesions may be difficult to detect and importantly difficult to characterize since a low radiation dose is used. In addition, patients do not routinely receive intravenous or oral contrast material during a virtual colonoscopy examination. Despite this, a routine check for incidental extracolonic findings is justified when interpreting virtual colonoscopy examinations.

Data interpretation techniques

Currently many sophisticated computer workstations are available to interpret virtual colonoscopy examina-

tions. These workstations allow fast processing of the data as well as an interactive ability to evaluate an abnormality in multiple projections as well as endoluminal views. There is some controversy regarding whether virtual colonoscopy examinations should be interpreted using a primary two-dimensional or three-dimensional viewing technique.

The three-dimensional viewing technique uses the computer to generate a centerline path through the colon that simulates the visualization of a conventional colonoscopy. The disadvantage of this technique is that large areas of the colon are obscured behind folds. To optimally evaluate data using a three-dimensional technique four fly-through navigations are required; antegrade and retrograde using both supine and prone acquisitions. Even using these time-consuming techniques, the entire colon surface may not be visualized.

Most investigators agree that a primary axial two-dimensional review is sufficient with the use of coronal and endoluminal imaging for problem solving [31,45]. Using these techniques the colon can be evaluated in approximately 5–15 min by an experienced reader. It is important to remember that whether one uses two-dimensional or three-dimensional as the primary review technique, both must be available to accurately differentiate folds, polyps, and residual fecal material (Figs 46.8–46.11).

Potential clinical role of virtual colonoscopy

Currently there are several clinical situations where virtual colonoscopy may play an important role in the evaluation of patients' colons. These include evaluation of the colon proximal to an incomplete conventional colonoscopic examination or to evaluate the colon proximal to an obstructing neoplasm [46–48]. Another potential indication for virtual colonoscopy is colonic evaluation in patients who are clinically unfit for conventional colonoscopy, such as those with chronic obstructive pulmonary disease, patients with a bleeding diathesis or those on coumadin, and patients with prior allergic reaction to sedation. Finally, in the future, virtual colonoscopy may contribute to colorectal screening by providing a safe, effective, and rapid examination that evaluates the entire colon.

Failed colonoscopy

An incomplete colonoscopy examination may occur in up to 5–10% of cases and may be due to patient discomfort, colon tortuosity, postoperative adhesions, or hernias (Figs 46.12, 46.13). Traditionally, double-contrast barium enema has been used to evaluate the colon in this setting. However, after an incomplete colonoscopy, a

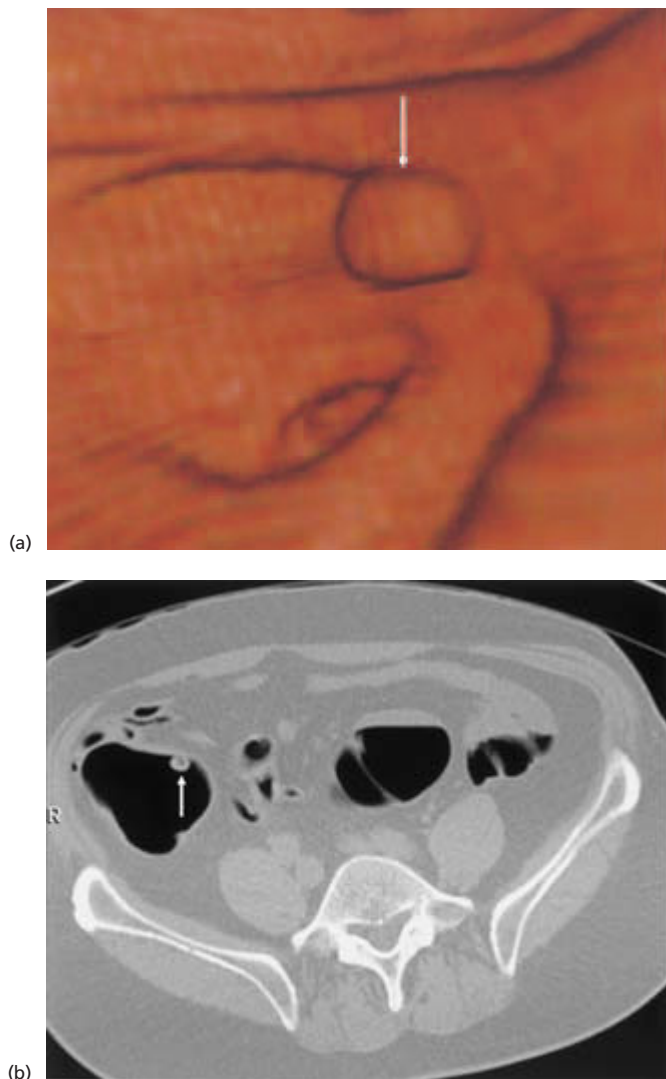


Fig. 46.8 Internal heterogeneity as an indicator of fecal material. (a) Endoluminal image shows round, well-circumscribed filling defect (arrow) in the cecum. (b) Prone image in same patient as (a) shows internal low density indicating gas within the filling defect. In small lesions, internal heterogeneity is an indicator of residual fecal material.

double-contrast barium enema may be difficult to perform related to air blockage from gas present from the recently performed colonoscopy. In addition, because of residual fluid from a polyethylene glycol preparation optimal coating of the colon wall with barium may not be obtained. Two studies have demonstrated the utility of virtual colonoscopy after an incomplete colonoscopic examination [46,47]. In one of these studies, CT was better able to evaluate the colon than was barium enema [46]. A virtual colonoscopy performed on the same day as an incomplete colonoscopy takes advantage of the single bowel preparation and the fact that the colon is often well distended from previous gaseous insufflation

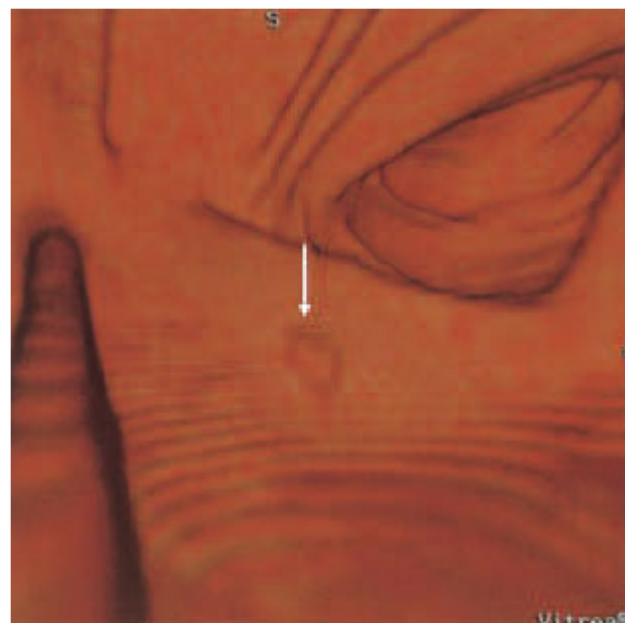


Fig. 46.9 Geometric morphology as an indicator of fecal material. Endoluminal image in transverse colon shows filling defect (arrow) with angled edges. This is not consistent with a polyp. Small polyps are round, oval, or lobulated, but do not contain geometric edges. Visualization on three-dimensional morphology is facilitated by thin-section multislice CT.

from colonoscopy, thus requiring only a small amount of gas insufflation. In this setting virtual colonoscopy has been shown to be useful in evaluating the more proximal colon for synchronous lesions [48].

Evaluation of the colon proximal to an obstructing lesion

Synchronous colon cancers occur in approximately 5% of cases of colorectal cancer and synchronous polyps are very common [48]. Occasionally, a cancer is identified in the distal colon that may prevent endoscopic evaluation of the more proximal colon. In this setting virtual colonoscopy has been shown to be useful in evaluating the more proximal colon for synchronous lesions [48]. A potential limitation of virtual colonoscopy in this setting is in getting the colon proximal to the tumor clean enough to allow optimum evaluation. However, in our experience an optimal evaluation is usually possible (Fig. 46.14).

Patients with contraindications to colonoscopy and patients who refuse other screening options

For a variety of reasons, a colonoscopist may be hesitant or unwilling to perform conventional colonoscopy in a patient with a high suspicion of having a colonic lesion based on clinical symptoms (bleeding, change in bowel

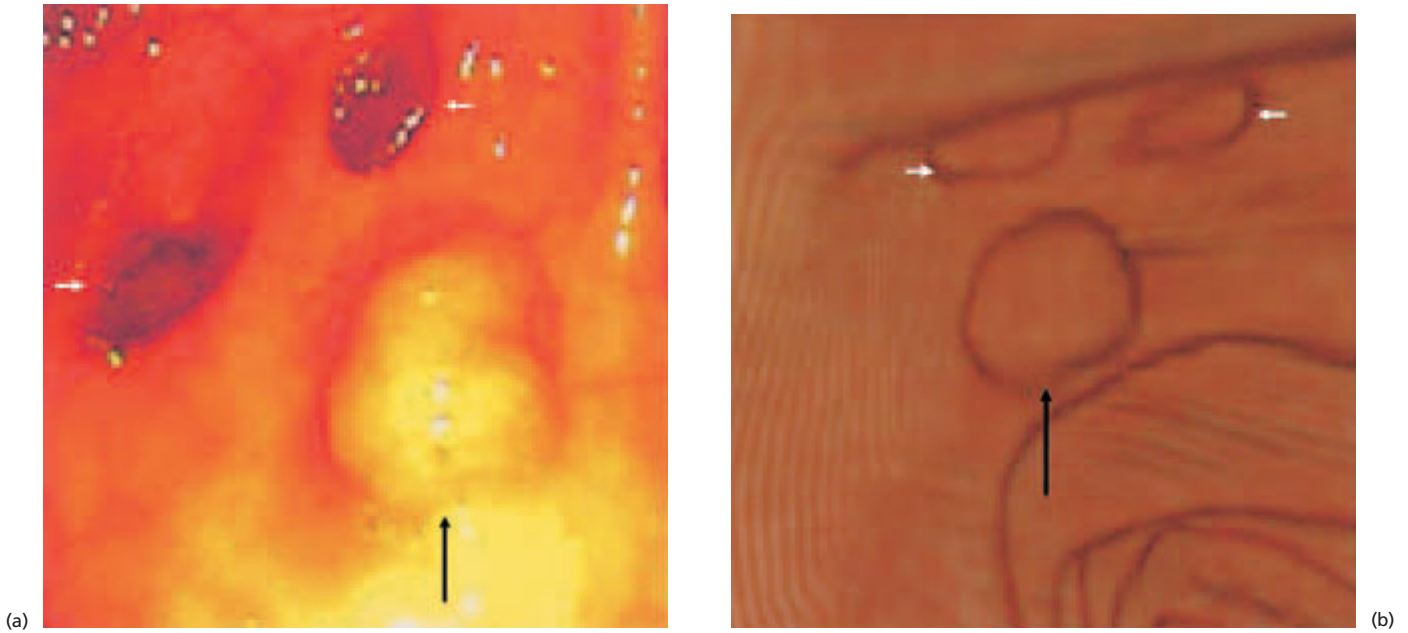


Fig. 46.10 Difference between polyp and diverticulum at virtual and conventional colonoscopy. (a) Conventional colonoscopy shows 7-mm polyp in cecum (black arrow) as well as two small adjacent diverticula (small white arrows). (b) Virtual colonoscopy in same patient shows same polyp

(black arrow) and small diverticula (small white arrows). Note that in general there is an incomplete border around a polyp and diverticula have a complete ring around the orifice. If there is uncertainty at endoluminal imaging axial images are very helpful in differentiating these entities.

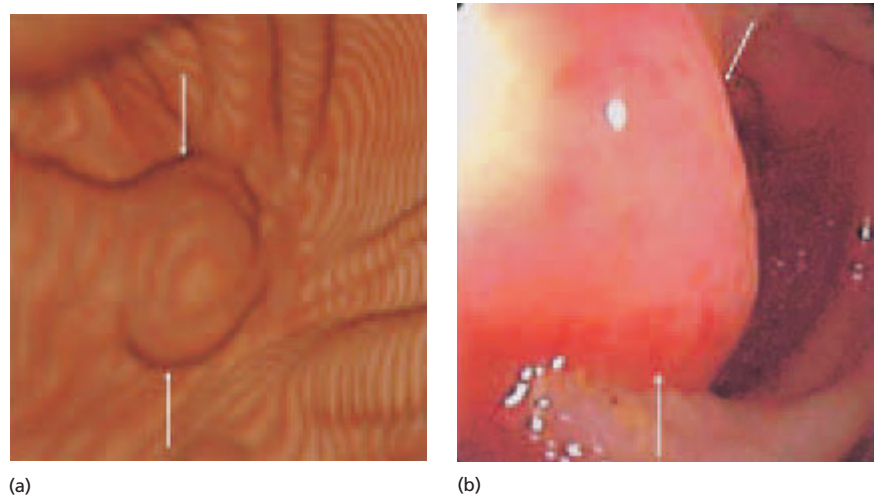


Fig. 46.11 Utility of multi window/level settings in evaluating filling defects. (a) Endoluminal image shows 11-mm filling defect in cecum of indeterminate etiology. (b) Conventional colonoscopy in same patient shows lesion in cecum. (c) Axial supine images window/level 1500/-200 (left) and 400/10 (right) shows indeterminate lesion on left (arrow), but shows lipoma on right (arrow). Recognizing adipose tissue in a filling defect confirms lipoma.



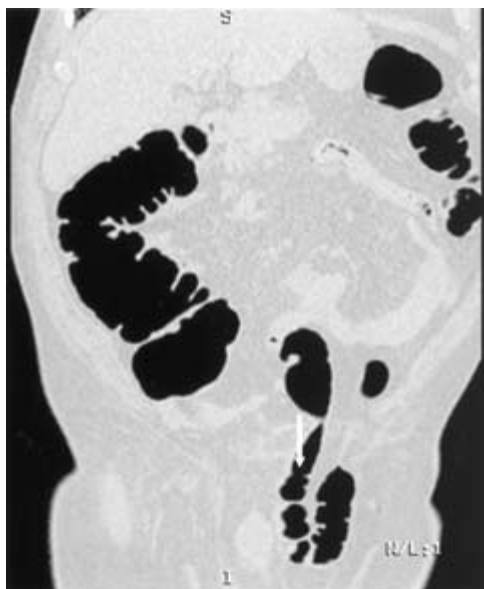


Fig. 46.12 Patient with incomplete colonoscopy. Coronal image from CT colonography shows sigmoid colon in inguinal hernia (arrow) as etiology of incomplete colonoscopy.



Fig. 46.13 Patient with incomplete colonoscopy. Coronal image from CT colonography shows large fibroid uterus (arrow) as etiology of incomplete colonoscopy.

habits, etc.). Reluctance to perform colonoscopy may be related to advanced patient age, severe pulmonary disease, bleeding diathesis, and prior allergic reaction to sedation during colonoscopy. In these cases, a virtual colonoscopy can be safely performed to exclude neoplastic disease.

For a variety of reasons (anxiety, fear, embarrassment, lack of education) people who should undergo screening are often reluctant. Although conventional colonoscopy is the current gold standard for pancolonic evaluation, it

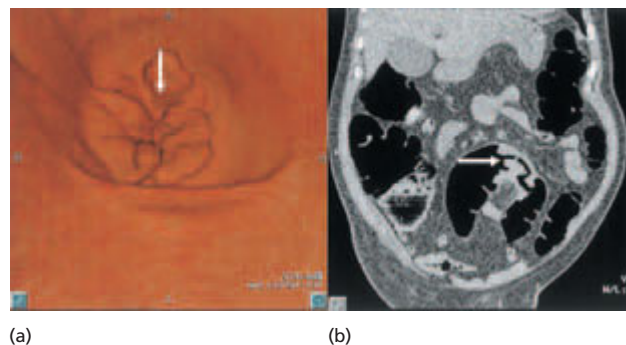


Fig. 46.14 Sigmoid cancer preventing more proximal evaluation at endoscopy. Endoluminal image (a) shows fungating carcinoma (arrow) in sigmoid. Coronal CT colonography (b) shows obstructing cancer (arrow) in sigmoid colon.

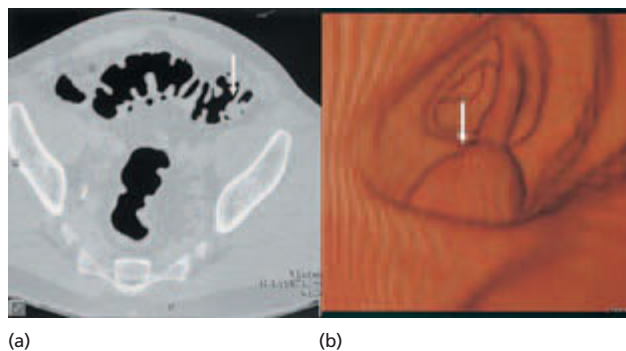


Fig. 46.15 Patient who was unwilling to undergo conventional colonoscopy. Axial image (a) shows pedunculated polyp (arrow) in sigmoid. Endoluminal image (b) confirms 13-mm pedunculated polyp on a stalk (arrow) in the sigmoid colon. When patient was told of the abnormality, he immediately requested endoscopy for removal of the lesion.

is useless if patients are unwilling to have the procedure performed. The concept of a relatively painless examination (virtual colonoscopy) that can image the colon and detect significant lesions is appealing to many patients. Once a suspicious lesion is detected, a patient will be more willing to undergo conventional colonoscopy and polypectomy (Fig. 46.15).

It should be pointed out that the concept of virtual colonoscopy being an entirely benign procedure is not entirely correct. Regarding patient satisfaction and comfort levels with the examination, there has been some controversy in the literature [49–51]. Our own data evaluating patient preferences for virtual and conventional colonoscopy is ongoing. The data for the first 45 patients that we questioned are presented in Table 46.1. When asked which procedure they preferred, 70.5% of patients chose virtual colonoscopy while 29.5% chose conventional colonoscopy.

Moreover, another recent study showed that in patients undergoing virtual colonoscopy followed by conven-

Table 46.1 Patient preference score (1 = least, 10 = greatest) for virtual and conventional colonoscopy at New York University.

	Virtual	Conventional	P value*
Satisfaction	8.9 ± 1.6	8.3 ± 2.1	0.12
Abdominal pain	3.3 ± 2.5	4.3 ± 2.9	0.07
Discomfort	3.8 ± 2.6	5.0 ± 2.9	0.03
Bloating	5.1 ± 2.8	4.2 ± 2.6	0.13
Embarrassment	1.7 ± 2.0	1.9 ± 2.0	0.59
Anxiety	3.8 ± 3.5	4.0 ± 3.4	0.83

* Wilcoxon matched-pairs signed ranks test.

tional colonoscopy, 82% preferred virtual colonoscopy [50]. Another recent study showed that 63.7% preferred conventional to virtual colonoscopy [51]. How can these differences be explained? Intravenous catheters or needles are not required for the procedure, but some may use bowel relaxants requiring intravenous access. Virtual colonoscopy can be performed with a small rubber catheter, considerably smaller than a barium enema tip catheter. The difference in the diameter between the two catheters is 10 mm (5 mm vs. 15 mm). In addition, when questionnaires are given to patients regarding the two procedures, outcomes need to be addressed as well as the therapeutic effect of conventional colonoscopy in being able to remove polyps as well as detect them. A patient may prefer virtual over conventional colonoscopy, but if the patient knows that a polyp can be removed when discovered during colonoscopy, it may increase the patient's acceptance of conventional colonoscopy.

Current clinical results of virtual colonoscopy

Ultimately, virtual colonoscopy may assist other current options in enabling widespread pancolonoscopic screening to be performed in a time-efficient manner. Colonoscopy is the current gold standard for pancolonoscopic evaluation, allowing visualization of the entire colon in most patients with the added benefit of biopsy and removal of polyps. As stated in the section "Why use virtual colonoscopy" above, there are several barriers to widespread colonoscopy screening including cost, need for sedation, potential complications of the procedure, and important manpower issues.

Within the gastroenterology community there are differing opinions as to the current role of virtual colonoscopy. It has been suggested that while virtual colonoscopy is an exciting imaging technique that has promise, it is not yet ready to be recommended for general screening [49]. Others have suggested that based on the current CT data performance, virtual colonoscopy could now legitimately enter clinical practice [25]. What are the data comparing CT and conventional colonoscopy?

Initial investigators evaluating virtual and conventional colonoscopy including those performed by Vining, Hara, and Dachman showed promise in the ability of CT to detect colorectal polyps and cancers [1,4,29,31]. In fact, most clinical studies evaluating virtual colonoscopy have demonstrated a sensitivity of over 90% for the detection of colorectal polyps measuring 1 cm and greater when correlated with conventional colonoscopy [1]. These results compare favorably with studies that have evaluated double-contrast barium enema with colonoscopy in detecting lesions of this size [22]. A study of 100 patients undergoing back-to-back virtual and conventional colonoscopy published in the *New England Journal of Medicine* showed a sensitivity of 100% for colorectal carcinoma, 91% for polyps that were 10 mm or more, and 82% for polyps that were between 6 and 9 mm [50]. However, not all studies have demonstrated a sensitivity for detecting 10-mm polyps at this level. In a cohort of 180 patients, Fletcher *et al.* [33] showed a sensitivity of 85% for polyps measuring 10 mm or larger. In 1997, a study by Hara *et al.* [27] showed a 75% sensitivity for detecting polyps in this range. In 2001, a follow-up study by Hara *et al.* [42] showed improved sensitivity ranging to 80–89% for the 10-mm polyps.

In the detection of small polyps (5 mm and less), the sensitivity for detection is lower. The clinical significance of these small (< 5 mm) raised polyps is questionable. Many represent hyperplastic polyps or normal elevations of the colonic mucosa [3]. However, some will represent small adenomas. These lesions are difficult to detect at virtual colonoscopy. What should an appropriate interval of follow-up be in a patient with a normal interpretation at virtual colonoscopy? What if a small 3-mm filling defect is detected at virtual colonoscopy? Should this patient undergo colonoscopy? These are difficult questions, somewhat related to patient age and underlying health status of the patient, but clearly questions that deserve further attention.

Perhaps of more concern than the small raised polyp is the truly flat adenoma that is almost impossible to detect at virtual colonoscopy [51]. A previous report pointed out the difficulty in detecting these lesions at virtual colonoscopy. In our experience, they are very difficult to see and even in retrospect are usually not detected (Fig. 46.16). However, these lesions appear to be relatively rare in western populations. The ability of CT to detect the vast majority of clinically significant lesions is still relative [52]. It should be pointed out that even colonoscopy has limitations in its ability to detect all colorectal polyps [53].

Screening

There have been few published series evaluating virtual colonoscopy and conventional colonoscopy in a screening

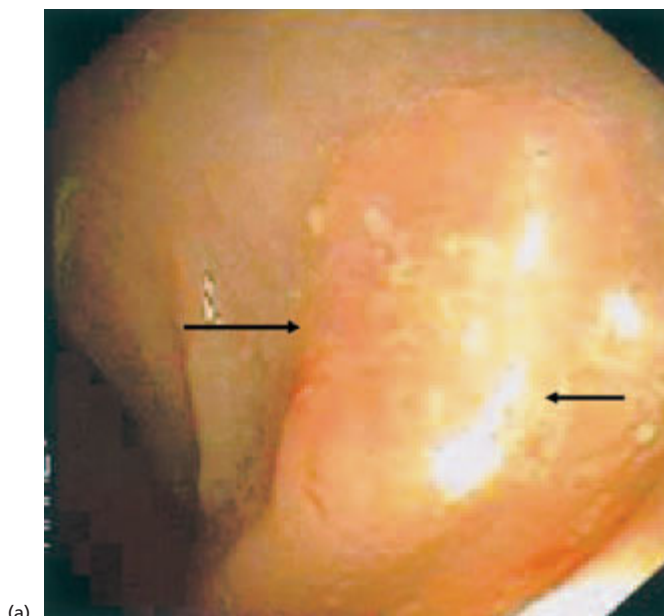


Fig. 46.16 Flat adenoma. (a) View from conventional colonoscopy in rectum shows slightly discolored area (arrows), which is not raised from the background mucosa. Biopsy revealed tubular adenoma. (b) Axial CT image of

rectum shows no abnormality. Even in retrospect this area could not be seen with either two-dimensional or three-dimensional imaging. These truly flat adenomas are impossible to visualize at CT colonography.

population [45,51,54]. In a series of 42 asymptomatic patients undergoing screening CT colonography and conventional colonoscopy, 4 of 6 (67%) polyps 6 mm or larger were detected at CT [45]. Sensitivity for polyps 5 mm or less was 20%. A report by Rex *et al.* on 46 patients undergoing screening CT colonography and colonoscopy demonstrated not only a low sensitivity of CT colonography in detecting small polyps (11% for polyps 5 mm or less) but also larger flat lesions as well [51]. In this study, only 1 of 4 flat adenomas measuring more than 2 cm that were present at conventional colonoscopy were detected at virtual colonoscopy. The results of this study seem to suggest that CT colonography may not be an accurate screening test for colorectal polyps. However, as pointed out in an associated editorial on this series of patients, it is too early to pass judgment on CT colonography based on this single report [52]. As with all new techniques, there is a learning curve and as experience with virtual colonoscopy increases, so will performance characteristics [25]. Importantly, in these screening studies, virtual colonoscopy was performed using single-slice helical CT scanners with 5 mm collimation.

Our recent data evaluating multidetector row virtual colonoscopy and screening comes from a cohort of 68 screening patients undergoing both CT and conventional colonoscopy [54]. In this study the vast majority of diminutive polyps were not seen. Fifty-six per cent of those between 6 and 9 mm were detected and 3 of 3 colorectal polyps measuring 10 mm were detected.

There was a flat lesion at the dentate line that could not be seen, even in retrospect, because this area cannot be distended at virtual colonoscopy. This is another important limitation of virtual colonoscopy and screening. Very low rectal/anal lesions frequently cannot be identified because these segments cannot be distended. Therefore, a digital rectal examination should be performed by an experienced clinician in conjunction with virtual colonoscopy.

Summary

There is already a role for virtual colonoscopy in evaluating those patients with failed colonoscopy and evaluating the colon proximal to an obstructing lesion. In addition, it may be the test of choice in patients with underlying medical problems as well as those with bleeding disorders and those who cannot undergo sedation. It is important to stress that currently only certain medical centers have expertise in the performance and interpretation of virtual colonoscopy examinations.

There are several technological developments that will improve the performance characteristics of virtual colonoscopy. Currently there is consensus in the radiology community regarding CT colonography that the colon needs to be cleaned and well distended to obtain adequate datasets. However, research into optimizing fecal tagging with subtraction techniques may, in the future, allow CT to be performed without a bowel preparation. In addition, there is much interest in com-

puter-aided detection (CAD) and diagnosis that may increase the ability of virtual colonoscopy to detect colorectal polyps [55]. The hope is that CAD will be used as a "second read," increasing the performance characteristics of virtual colonoscopy in polyp detection.

The future of virtual colonoscopy is very promising. However, we should proceed cautiously. Radiologist training in patient preparation, data acquisition and, perhaps most importantly, data interpretation is necessary if virtual colonoscopy is used in the general radiology community.

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Chapter 47

Colonoscopy and Severe Hematochezia

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Introduction

Hematochezia is the passage of bright red blood or maroon-colored blood, with or without clots, per rectum. Most often, hematochezia is low grade and self-limited and does not require hospitalization or urgent intervention. Such patients can be managed in an outpatient setting. A smaller group of patients experience severe hematochezia and require hospitalization because of the volume of blood loss or symptoms due to severe anemia or comorbidity [1,2]. In addition, another group of severely ill patients will develop severe hematochezia while in hospital for other medical or surgical conditions. These latter two groups require a systematic and expeditious approach to their resuscitation, preparation, diagnosis, and treatment. For more than a decade, our CURE-UCLA Hemostasis Group has recommended an aggressive diagnostic approach, with preparation of the patient with oral purge followed by urgent colonoscopy for diagnosis and treatment. This approach is similar to that used for patients with severe upper gastrointestinal hemorrhage. This approach changes outcomes of patients, particularly for those with severe or persistent hematochezia [1,2].

The purpose of this chapter is to review our approach to the patient with severe hematochezia, discuss the outcomes from this approach, and present the details of colonoscopic treatment of several specific colonic lesions that frequently cause severe colonic bleeding.

Resuscitation and initial evaluation

Patients who present with evidence of severe volume depletion, such as hypotension and tachycardia, require adequate intravenous access and vigorous replacement of intravenous fluids and/or blood. Patients with coagulopathies, i.e. prolonged prothrombin time or international normalized ratio (INR) due to either liver disease or anticoagulant therapy (warfarin), and ongoing hematochezia usually require administration of fresh frozen plasma. Those with severe thrombocytopenia or severe chronic renal failure may require platelet transfusions to help control ongoing hematochezia. Treatment of comorbidities and close monitoring in an intensive care

Table 47.1 Resuscitation and management of patients with severe hematochezia.

Establish one or preferably two large-bore intravenous lines
Assess intravenous volume and replace vigorously
Evaluate degree of blood loss and replace with packed red blood cells
Evaluate coagulation and correct with fresh frozen plasma, platelets, and/or desmopressin acetate (DDAVP)
Place a nasogastric tube to check for a possible upper gastrointestinal source of blood or bile
Treat comorbid conditions

unit (ICU) or a telemetry unit by skilled nurses is highly recommended (Table 47.1).

The patient should be evaluated with a careful history and physical examination. The history in particular may give the physician a clue as to the source of the bleeding. Elderly patients with heart disease who present with abdominal pain and hematochezia may have ischemic colitis. A history of cirrhosis might suggest varices, most often esophageal or gastric but rectal varices or anastomotic varices can also present as severe hematochezia. Severe heart disease (valvular in particular) or chronic renal insufficiency are associated with gastrointestinal angiomias. A history of inflammatory bowel disease, peptic ulcer disease, diverticulosis, or internal hemorrhoids might indicate potential bleeding sites. A history of recent polypectomy, particularly of a large sessile polyp, should suggest delayed bleeding from a postpolypectomy ulcer. Abdominal pain, weight loss, fever, diarrhea, or vomiting are important in the differential diagnosis of inflammatory, infectious, or malignant lesions.

As part of medical history, it is also important to elicit and list all medicines, including over-the-counter drugs and herbal medications, that the patient has taken acutely or chronically. Some of these drugs may either cause gastrointestinal lesions or aggravate gastrointestinal bleeding by interfering with intrinsic coagulation parameters. Aspirin (in any dose, including 81 mg/day), nonsteroidal antiinflammatory drugs (NSAIDs), anticoagulants, antibiotics, inflammatory bowel disease drugs, or antiarrhythmics may cause either gastrointestinal

lesions or gastrointestinal hemorrhage. Herbal medications such as ginkgo and ginseng may also be associated with hemorrhage from a preexisting gut lesion.

Diagnostic evaluation

When severe, ongoing hematochezia and marked blood loss are evident; however, if there is no history or signs of frank hematemesis or coffee-ground emesis, a nasogastric (or orogastric) tube should be placed for diagnosis of a potential upper gastrointestinal source. Gastric lavage should be performed to help exclude the possibility of an upper gastrointestinal bleeding source. When bile is obtained in the presence of ongoing hematochezia, there is continuity with the duodenum and an upper gastrointestinal lesion is unlikely as the source of the hematochezia. When clear lavage fluid returns and no bile or blood is noted, continuity with the duodenum is not ascertained and the study is nondiagnostic. However, when blood, clots, or coffee grounds return from the lavage, a panendoscopy must be performed to exclude an upper gastrointestinal lesion as the cause of the gastrointestinal hemorrhage and hematochezia (Table 47.1).

Bowel preparation

In order to perform a complete colonoscopy in the presence of hematochezia, it is imperative that the colon be adequately cleansed. Cleansing the colon is the major rate-limiting step prior to urgent colonoscopy. After considering an upper gastrointestinal site of hemorrhage and after nasogastric aspiration, we administer polyethylene glycol balanced electrolyte purge (Golytely R or Colyte R) either orally or via a nasogastric tube. Since some of these patients already have a nasogastric tube in place to check for upper gastrointestinal bleeding, it is easier to leave it in place for the purge. A liter of solution is administered every 30–45 min until the rectal effluent clears of solid matter and clots. In our experience, 6–8 L of fluid over 3–6 h are usually needed to achieve this goal. Metoclopramide 10 mg i.v. may be administered 5–30 min prior to starting the purge for its prokinetic and antiemetic effects (Table 47.2).

For patients with congestive heart failure, ascites, or chronic renal failure on hemodialysis, a very careful assessment of volume status is recommended prior to starting the purge. An increase in third-space fluid and intravascular volume should be treated preemptively. If there is clinical evidence of congestive heart failure, diuretics are indicated. In patients with chronic renal failure on dialysis, hemodialysis concurrent with the purge should be considered. In patients with tense ascites, therapeutic paracentesis should be performed to diminish the risk of respiratory compromise during colonoscopy.

Table 47.2 Colon preparation prior to urgent colonoscopy in patients with severe hematochezia.

Metoclopramide (if no contraindications) 10 mg i.v. or i.m. 5–30 min prior to starting purge
Polyethylene glycol balanced electrolyte purge (Nulytely R or Colyte R) orally or via nasogastric tube at 1 L every 30–45 min until effluent is clear of clots, stool, and blood. Usually, 6–8 L are required over 3–5 h to clean the colon
In patients with tense ascites, perform therapeutic paracentesis to prevent respiratory compromise during colonoscopy
If patient is in congestive heart failure, treat with intravenous diuretics
If patient is in renal failure, use concurrent hemodialysis

Endoscopes and other equipment

It is imperative to consider all the equipment that may be needed for the control of hemorrhage during emergency colonoscopy so that it is readily available for the endoscopist. A cart with all necessary equipment can then be taken to the bedside (such as in the ICU). We prefer to use a colonoscope that is 13 mm or less in diameter, with a 3.8-mm suction channel and separate port for water-jet irrigation. The water jet facilitates target irrigation and the large suction channel allows for simultaneous rapid clearing of water, blood, and liquid stool. The addition of simethicone to the irrigation water is helpful in reducing the formation of bubbles, which interfere with visualization particularly in the presence of blood.

For bleeding angiomas, postpolypectomy ulcers, or colonic diverticula, a bipolar probe is preferred for coagulation due to its limited depth of coagulation. Epinephrine injection prior to coagulation is useful for postpolypectomy and diverticular bleeds but is not used for angiomas. A sclerotherapy catheter with retractable needle is needed for epinephrine injection or India ink labeling of lesions. A medium-sized slotted anoscope is useful for diagnosis of bleeding internal hemorrhoids, which can be controlled using a rubber-band ligator. Small- and large-capacity forceps should be available for tissue biopsies. Standard and rotatable mini, medium, and large polypectomy snares are needed for polypectomies, submucosal resections, and cold guillotining (shaving down) of adherent clots or lesions. A small-bowel enteroscope should be available in case colonoscopy (including examination of the terminal ileum) and anoscopy fail to reveal a bleeding site. Dieulafoy lesions, diverticula, or ulcerated small-bowel tumors that may need repeat endoscopy for recurrent bleeding or that may require surgical resection are tattooed with India ink or a sterile carbon-particle suspension after endoscopic treatment. India ink injection facilitates localization on repeat endoscopy for rebleeding or finding the lesion at surgery (Table 47.3).

Table 47.3 Equipment needed for emergency colonoscopy.

Video colonoscope with > 3.8-mm suction channel and separate irrigation port
Hemostasis probes (bipolar or heater probe), size 7F and 10F, and respective power units
Mini, medium, and large polypectomy snares, jumbo forceps, and fixatives for histopathology
Needle catheter and epinephrine (1 in 10 000), India ink, and sclerosant
Slotted anoscope and hemorrhoid treatment accessories
Therapeutic video panendoscope and/or push enteroscope

Coagulation probes

The heater probe (Olympus Corporation) and bipolar coagulation (Gold probe, Microvasive/Boston Scientific) have gained popularity with therapeutic endoscopists because of their efficacy, safety, easy portability, and low cost. The power units and catheters should be on the mobile endoscopy cart that is taken to the bedside. The CURE Hemostasis Research Group has studied the technical parameters related to endoscopic coagulation in the laboratory [3,4] and in clinical studies [1,2,5,6]. Table 47.4 lists the various parameters recommended for the use of either coagulation probe for treatment of selected colonic lesions. For most actively bleeding lesions or those with adherent clots in the colon, except angiomata and internal hemorrhoids, combination epinephrine injection and thermal coagulation (with bipolar or heater probe) are used. Small or large probes may be used depending on the size of the lesion being treated. The probe is placed directly on the bleeding point with moderate pressure and low power settings and coagulation is applied until complete hemostasis is achieved. In contrast to coagulation of bleeding ulcers in the upper gastrointestinal tract, only moderate pressure is used

and shorter pulse duration is sufficient to achieve good hemostasis in the colon.

Study results

Patients admitted for hematochezia

The CURE Hemostasis Research Group reported on 291 consecutive patients who were admitted to the hospital because of significant hematochezia [2]. The patients included both those with persistent bleeding and those who stopped bleeding after hospitalization. The approach to diagnosis in these patients was the same as with the group of persistently bleeding patients, i.e. resuscitation, placement of a nasogastric tube to exclude an upper gastrointestinal bleeding site, colonic purge, and urgent colonoscopy. Upper endoscopy was performed in those patients who had evidence of an upper gastrointestinal bleeding site. Push enteroscopy was performed in patients who had a negative colonoscopy and negative nasogastric aspirate. Urgent colonoscopy and the other examinations were performed within 6–12 h of gastrointestinal consultation.

For the 291 patients, colonic bleeding sites were found in 77.7%. An upper gastrointestinal source of hematochezia (e.g. ulcers, varices, or angiomata) was diagnosed in 14.8% of the patients. A small-bowel source was present in 0.7% and no source was found in 6.9% (Fig. 47.1). The most common colonic sources of bleeding were diverticulosis (29.6%), internal hemorrhoids (14.2%), and ischemic colitis (12.4%) (Table 47.5). Less common lesions included rectal ulcer, postpolypectomy ulcer, colon polyp or cancer, colon angiomata, and ulcerative colitis. Identification of stigmata of hemorrhage and endoscopic treatment were possible in patients with focal lesions. Low-risk patients without stigmata of hemorrhage and/or severe comorbidities could be

Table 47.4 CURE Hemostasis Research Group parameters for heater probe and bipolar coagulation of bleeding colonic lesions.

	Bipolar probe			Heater probe	
	Pressure	Power (W)	Pulse (s)	Pressure	Power (J)
Diverticula, delayed bleeding*, ulcers					
Active†	Moderate	12–16	1–2	Moderate	10–15
Nonbleeding visible vessel	Moderate	12–16	1–2	Moderate	10–15
Clott‡	Moderate	12–16	1–2	Moderate	10–15
Angioma	Light	10–16	1–2	Light	10–15
Cancer/polypst‡	Moderate	16–20	1–2	Moderate	20–25

* Delayed bleeding from a postpolypectomy ulcer.

† For active bleeding, inject 1 in 10 000 epinephrine in 1–2 mL aliquots within 2–5 mm of the bleeding site or clot before thermal coagulation.

‡ For adherent clots on lesions, inject 1 in 10 000 epinephrine around the pedicle, use cold guillotine removal of clot, and then coagulate the small clot of nonbleeding visible vessel at the point of clot attachment.

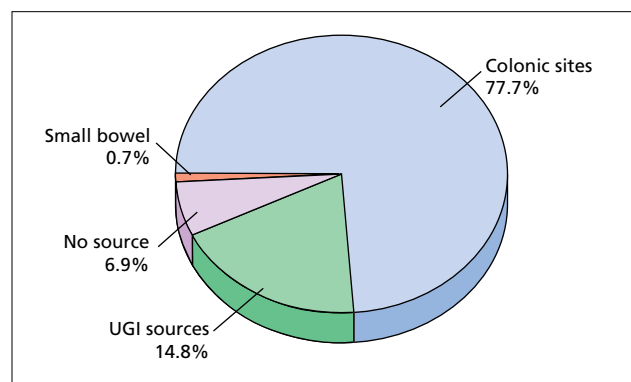


Fig. 47.1 The final sites (location) of hemorrhage are shown for 291 patients hospitalized for severe hematochezia.

Table 47.5 Colonic sources of severe hematochezia (expressed as percentage of all colonic sources of bleeding). (From Jensen *et al.* [2].)

Diverticulosis	29.6%
Internal hemorrhoids	14.2%
Ischemic colitis	12.4%
Rectal ulcers	9.3%
Ulcerative colitis or other colitis	8.8%
Postpolypectomy ulcer	8.0%
Colon angiomas	5.7%
Colon polyp or cancer	6.2%
Other lower gastrointestinal	7.0%

triaged to a less intensive level of care as well as to earlier discharge. In a cost analysis, a comparison of the urgent colonoscopy approach with the traditional approach to hematochezia was previously reported from our group [7]. The urgent colonoscopy group had fewer hospital days, surgeries, and diagnostic tests. The cost savings based on 1990 estimates was a mean of \$10 000 per patient.

Specific lesions

Diverticular hemorrhage

Diverticulosis is the most frequent colonic lesion responsible for severe hematochezia. Diverticular bleeding is due to the erosion of a small arteriole, most commonly at the neck of the diverticulum or in the base. Therefore, diverticular bleeding is usually sudden and significant. Diverticular bleeding was the cause (including definitive diverticular or presumptive diverticular hemorrhage as defined below) of severe hematochezia in 30% of all patients admitted with severe hematochezia in our study (and 29.6% of colonic sources). However, of all the patients with colonic diverticulosis who were admitted with severe hematochezia, 50% were found to have bleeding from nondiverticular colonic sources.

“Presumptive diverticular bleeding” was diagnosed when no source or other potential source of hemorrhage was found. “Definitive diverticular bleeding” was diagnosed when there were stigmata of recent hemorrhage, such as active bleeding (Fig. 47.2), a nonbleeding visible vessel (Fig. 47.3), or an adherent clot (Fig. 47.4), on a diverticulum at urgent colonoscopy. Identification of stigmata of hemorrhage on a diverticulum was possible only with adequate colonic cleansing and target water-jet irrigation during urgent colonoscopy.

In prospective studies of patients with definitive diverticular hemorrhage, we compared medical–surgical to medical–colonoscopic management [8]. Medical–surgical treatment was given to the initial 17 patients to define the natural history of definitive diverticular hemorrhage. These patients underwent emergency colonoscopy for diagnosis but did not receive any colonoscopic treatment. The second group of 17 patients with definitive diverticular hemorrhage received medical treatment and endoscopic hemostasis at the time the stigmata were diagnosed at urgent colonoscopy. Treatment consisted of epinephrine injection or bipolar cautery or both. The treated diverticulum was labeled with India ink injection to facilitate localization at repeat colonoscopy or surgery. Both groups were comparable in terms of age, comorbid conditions, recent aspirin and/or NSAID ingestion, and blood transfusion requirements prior to colonoscopy (Table 47.6).

Ongoing or recurrent hemorrhage requiring transfusion of 2 units or more of packed red blood cells was observed in 53% of the medical–surgical patients in contrast to 6% of the medical–colonoscopic group. Surgery for control of bleeding was required in 35% of the medical–surgical group and in 6% of the medical–colonoscopic group. No complications occurred in any of the patients who received colonoscopic treatment. The median time to discharge was longer (5 days) for the medical–surgical patients than for the medical–colonoscopic patients (2 days) (Table 47.7). None of the patients in either group had recurrent bleeding on long-term follow-up (mean 36 months).

The long-term treatment recommended was fiber, control of constipation, and avoidance of aspirin, NSAIDs and anticoagulants.

Internal hemorrhoids

Internal hemorrhoids were responsible for severe hematochezia in 11% of our patients who were admitted to hospital (and 14.2% of colonic sources). Most gastroenterologists do not include internal hemorrhoids in the differential diagnosis of severe hematochezia because the majority of internal hemorrhoidal bleeding is intermittent, low grade, and self-limited. However, some patients with hemorrhoids have sudden severe bleeding. Bleeding internal hemorrhoids constitute a

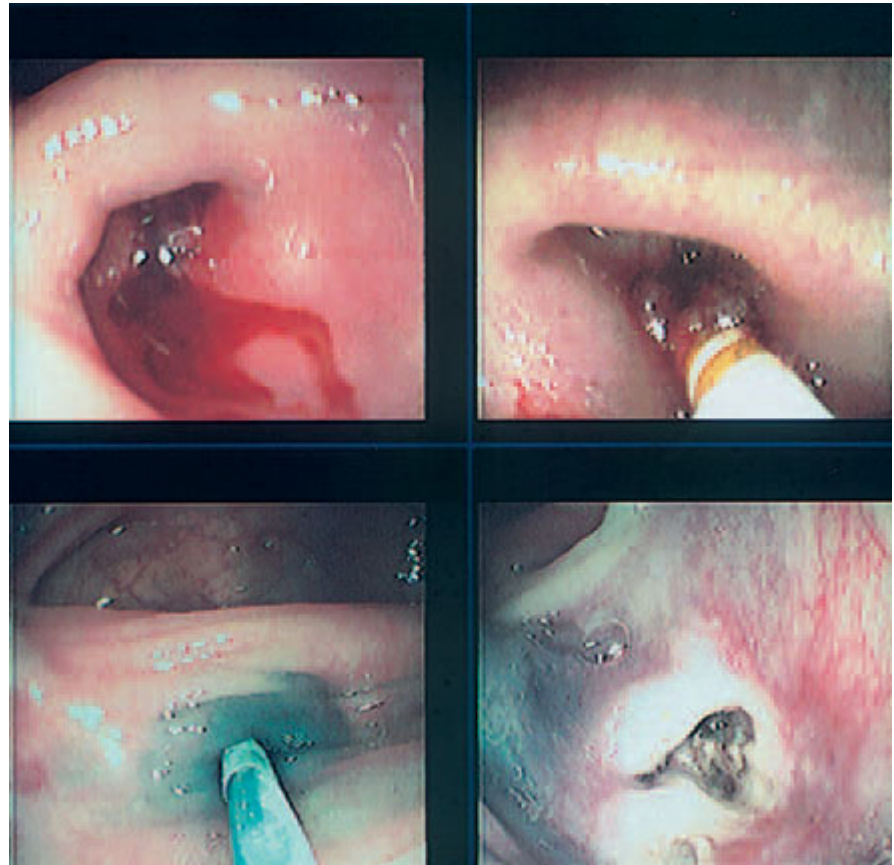


Fig. 47.2 Patient with severe hematochezia and a definitive diverticular hemorrhage (active bleeding) in descending colon. Initially, the diverticulum was injected with epinephrine (1 in 10 000 in saline) in three sites near the bleeding point. Then a 10F Gold probe (power setting 14 W and 2-s pulses) gently tamponaded the bleeding site and coagulated it to flatten the visible vessel. India ink tattooing and appearance at the end of the procedure are shown. No complications or rebleeding occurred.

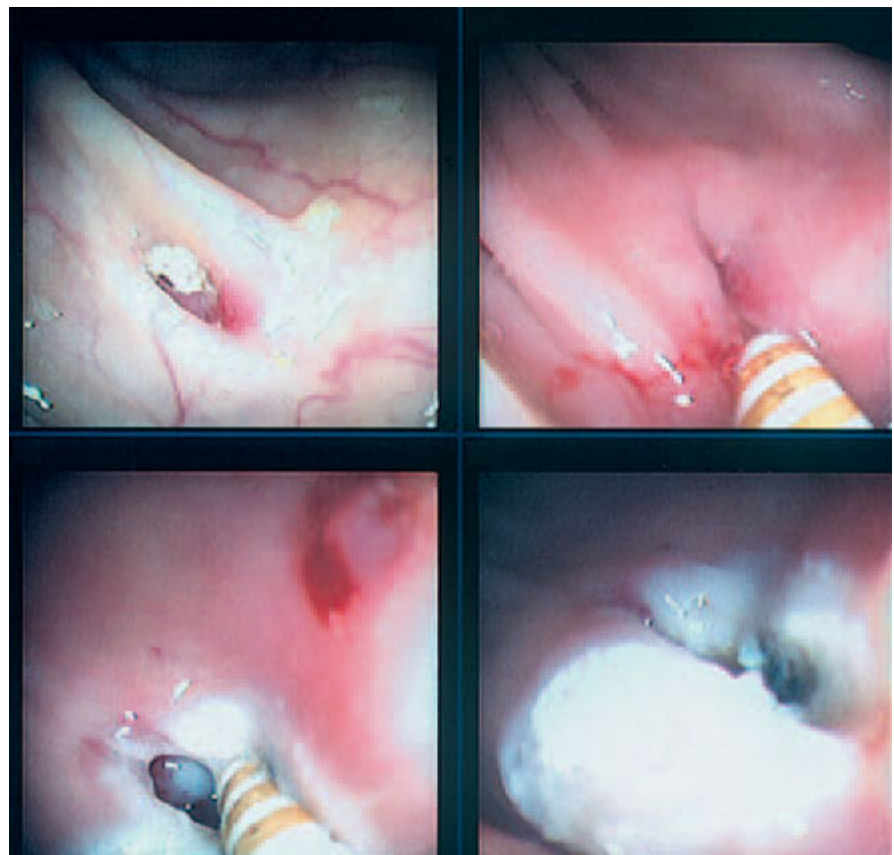


Fig. 47.3 A nonbleeding visible vessel on the right side of a splenic flexure diverticulum was identified during urgent colonoscopy in a patient with severe hematochezia. This was coagulated with a Gold probe.



Fig. 47.4 An adherent clot in a right colonic diverticulum indicates this was the site of hemorrhage. The patient had severe hematochezia and severe anemia, requiring transfusion with 3 units of red blood cells. Patient was treated with combination therapy: epinephrine injection, cold guillotining of the clot, and thermal coagulation of the residual small clot at the pedicle.

significant public health problem: it is estimated that approximately 10.4 million people suffer from hemorrhoidal symptoms annually, prompting 3.5 million physician visits per year [9]. We grade internal hemor-

rhoids with a slotted anoscope on a scale from 1 to 4 (Table 47.8), depending on the degree of prolapse through the anal sphincter. Although bleeding may occur from any grade of hemorrhoid, severe bleeding causing anemia and hospitalization is most often due to grade 3 or 4 internal hemorrhoids. Following enemas to clear the distal colon (disposable enema or tap water), bleeding hemorrhoids can be diagnosed with a flexible sigmoidoscope, although more often the hemorrhoids can be better visualized with the use of a medium-sized slotted anoscope.

While outpatients with bleeding from internal hemorrhoids often have cessation of hemorrhage with medical therapy, in our experience [10] those with severe hematochezia require endoscopic therapy or surgery. In the past, we used sclerotherapy or anoscopic coagulation (such as bipolar or heater probes) for patients with internal hemorrhoids and hematochezia [11,12]. Recently, rubber-band ligation has been found to be faster and more efficient particularly for control of severe hematochezia [10] (Fig. 47.5). Concomitant medical therapy with fiber, stool softeners, and avoidance of aspirin, NSAIDs and anticoagulants is also highly recommended. Outpatient follow-up and further treatment to completely control bleeding and to reduce the internal hemorrhoids to grade 1 or less should also be considered.

Surgical intervention is indicated for those patients who would prefer to have a single procedure despite

	Medical-surgical (n = 17)	Medical-colonoscopy (n = 17)
Age (years)	66 ± 3	67 ± 4
Comorbidity	100%	100%
Recent ASA/NSAID use	18%	29%
Initial units RBC before colonoscopy	6.0 ± 1.2	5.1 ± 1.2
Endoscopic findings, number of patients (%)		
Active bleeding	6 (35%)	7 (41%)
Nonbleeding vessel	4 (24%)	6 (35%)
Adherent clot	7 (41%)	4 (24%)

ASA, aspirin; NSAID, nonsteroidal antiinflammatory drug; RBC, red blood cells.

* Definitive diverticular bleeding is finding major stigmata of hemorrhage on a diverticulum during urgent colonoscopy for patients with severe hematochezia [1,2,8].

	Medical-surgical (n = 17)	Medical-colonoscopy (n = 17)
Endoscopic hemostasis	0	17 (100%)
Additional bleeding	9 (53%)	1 (6%)*
Severe bleeding	6 (35%)	1 (6%)*
Emergency surgery	6 (35%)	1 (6%)*
Median time to discharge after colonoscopy (days)	5	2
Complications	2 (12%)	0

* $P < 0.05$.

Table 47.6 Clinical and endoscopic findings in 34 consecutive patients with definitive diverticular bleeding*.

Table 47.7 Outcomes of treatment of 34 consecutive patients with definitive diverticular hemorrhage.

Table 47.8 Grades of internal hemorrhoids.

Grade 1	No prolapse below the dentate line
Grade 2	Prolapse during defecation with spontaneous reduction
Grade 3	Prolapse during defecation requiring manual reduction
Grade 4	Nonreducible prolapse below the dentate line

discomfort and those patients who have failed medical and endoscopic therapy. Surgical hemorrhoidectomy is highly effective in controlling bleeding and eradicating internal hemorrhoids as well as external hemorrhoids [13–15]. However, surgical hemorrhoidectomy is not free of complications [16–18].

Ischemic colitis

Colonic ischemia was responsible for severe hematochezia in 12.4% of colonic sources for our patients hospitalized with hematochezia [2]. Other series report an incidence of 3–9% of severe lower gastrointestinal bleeding being caused by ischemic colitis [19–21]. There is usually no identifiable precipitating cause for the acute onset of colonic ischemia. However, most patients with ischemic colitis have underlying atherosclerotic cardiovascular or peripheral occlusive disease. Patients

usually present with the acute onset of crampy abdominal pain that can be localized in the right lower quadrant, epigastrium, or left lower quadrant depending on the segment of colon involved. However, the pain tends to radiate throughout the entire abdomen. The splenic flexure and sigmoid colon, which have poor collateral blood flow (watershed areas), are most often involved. When present, abdominal pain is usually associated with bloody diarrhea. Occasionally, nausea, vomiting, and fever are present. Signs of hypovolemia, tachycardia, and hypotension may be seen in severe cases of ischemic colitis. Physical examination of the abdomen may be normal or there may be diffuse abdominal tenderness and hyperactive bowel sounds. No localized peritoneal signs are usually present unless there is frank colonic infarction with involvement of the serosa. Thumbprinting may be observed on plain abdominal radiographs or barium enema but this is not a frequent finding. In many cases, ischemic colitis in elderly patients can present with painless hematochezia and no other symptoms. The physical examination may reveal only mild tenderness or may be normal.

Flexible sigmoidoscopy or colonoscopy is the best way to make the diagnosis [1,2]. There is usually segmental involvement consisting of mucosal edema, erythema, friability, mucosal hemorrhages, mucosal necrosis and

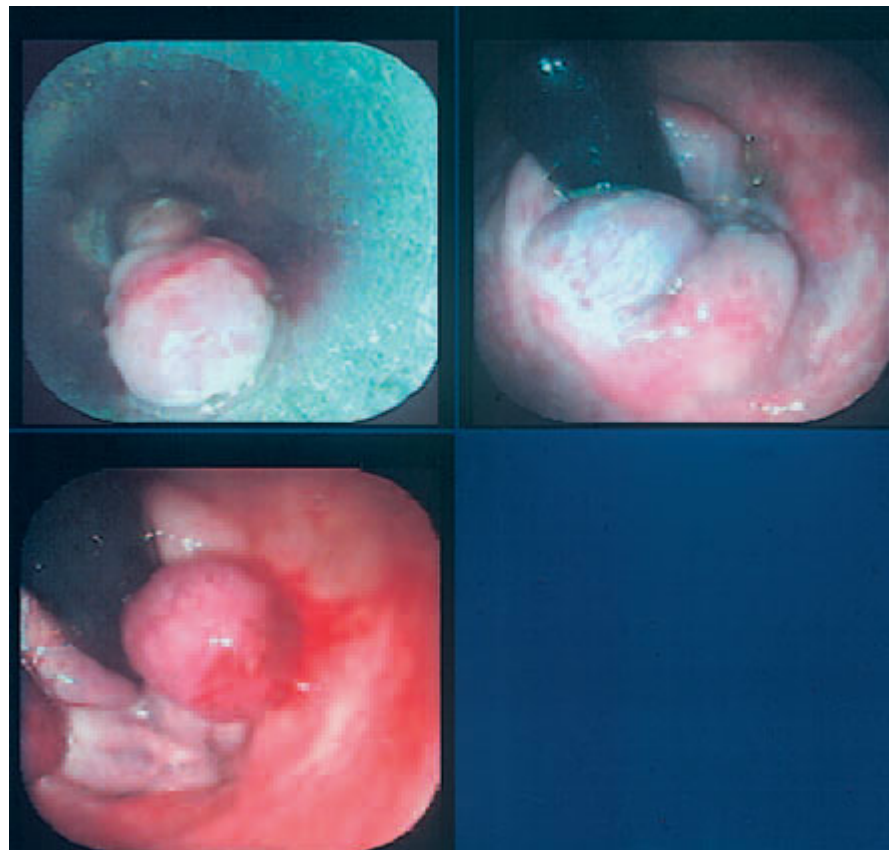


Fig. 47.5 A 62-year-old patient was hospitalized for anemia and severe hematochezia requiring transfusion with 2 units of red blood cells. No colonic lesions were found on urgent colonoscopy and anoscopy, except for grade 3 internal hemorrhoids without active bleeding. These were treated with rubber-band ligation, using a diagnostic panendoscope and a multishot ligator in retroflexion in the rectum.

ulcerations. Colonic biopsies from the affected as well as unaffected areas are usually definitive for ischemia. Colonoscopic and histopathologic findings are useful for differentiating colonic ischemia from inflammatory or infectious colitis.

Medical treatment is supportive, with intravenous fluids and/or blood transfusions to improve tissue perfusion. Urgent treatment of comorbid conditions is warranted, including peripheral or central vascular disease, cardiac arrhythmias, or severe anemia that may have contributed to bowel ischemia. Antibiotics are indicated if fever or sepsis is present. If there is clinical deterioration of the patient with development of peritoneal signs, fever, leukocytosis, or evidence of bowel perforation, surgical intervention with segmental colon resection is indicated. Therapeutic colonoscopy plays no role in these patients unless a focal ulcer with stigmata of hemorrhage is found at colonoscopy, which usually is not the case [22,23].

Solitary rectal ulcer syndrome

Solitary rectal ulcers were responsible for 9.3% of colonic sources for the patients presenting with severe hematochezia, making it the fourth most common diagnosis in this large study [2]. In contrast to previous series which have reported that this syndrome occurs in younger patients (third and fourth decades) [24,25], our patients were in the sixth and seventh decades of life [23]. This syndrome is more common in women and is characterized by rectal bleeding and mucous discharge in 56–89% of patients [25,26]. These patients usually present with symptoms of severe constipation and often fecal impaction. The etiology of this disorder is not completely understood, but prolapse-induced rectal mucosal trauma or ischemia appear to contribute [27]. Pressure-induced mucosal necrosis in elderly patients with fecal impaction must also be considered. On endoscopy, one or more well-demarcated ulcerations are seen with edematous, erythematous, and nodular borders [28]. Active bleeding or stigmata of recent hemorrhage were found at urgent colonoscopy in most patients with severe hematochezia in our recent study [28].

Colonoscopic therapy consists of coagulation with a large-contact thermal probe with or without preinjection of epinephrine. For actively bleeding ulcers or ulcers with an overlying clot, injection of 1 in 10 000 epinephrine is recommended circumferentially around the bleeding point or pedicle of the clot in four quadrants prior to coagulation. In actively bleeding ulcers, after epinephrine injection irrigation is used to expose the bleeding vessel and then subsequently coagulate the bleeding point to completely flatten the vessel. For those ulcers with an overlying clot, following epinephrine injection the clot is removed by cutting it off with a

cold polypectomy snare thereby exposing the vessel. Subsequently, the vessel is cauterized as before until completely flattened. Rectal ulcers with a nonbleeding visible vessel can be coagulated without preinjection of epinephrine. The large thermal probe is placed directly on the visible vessel and cauterized until flattened. Recommended power settings for the bipolar probe are 12–16 W for 5–10 s pulses or, for the heater probe, 10–15 J.

Delayed postpolypectomy hemorrhage

Hemorrhage after an endoscopic polypectomy may occur immediately or may be delayed hours, days, or rarely weeks. In this section, we focus on delayed severe postpolypectomy hemorrhage resulting in hospitalization for severe hematochezia. This is defined as occurring one or more days after discharge of the patient from the endoscopy unit after the polypectomy. The incidence of delayed postpolypectomy hemorrhage is reported at 1–6% [29,30]. The variation in these reported rates is most likely a function of study design, patient population (i.e. age, comorbid conditions, use of antiplatelet drugs or anticoagulants), and configuration and size of polyps. Because of changes in colonoscopy practices and with resection of larger sessile colonic polyps in the last decade, including piecemeal resection or following submucosal saline injection, delayed postpolypectomy hemorrhage appears to be occurring more frequently. Severe postpolypectomy bleeding was the cause of severe hematochezia in 8.0% of patients in a recent study [2]. The mean diameter of the polyps was 20 mm, and most were sessile polyps without carcinoma on histopathology. Delayed hemorrhage occurred a median of 9 (range 2–73) days after polypectomy. Most patients (77%) were men, with a mean age of 69 years. The majority (77%) were also consuming aspirin or warfarin after polypectomy for comorbid cardiac or vascular conditions. All patients required hospitalization because of severe hematochezia. After colonic purge, urgent colonoscopy revealed ulcerations with a mean diameter of 11 mm. Stigmata of hemorrhage on the ulcers included active bleeding in 23%, nonbleeding visible vessel in 23%, clot in 38%, spot (a single small red flat lesion) in 8%, and clean ulcer in 8%. Endoscopic treatment was performed in 92% of patients, and only one patient rebled. One patient with cancer had surgery, while the remainder were treated medically.

Bleeding occurring immediately following polypectomy is thought to be due to inadequate cauterization of the polyp vessels during polypectomy, whereas delayed postpolypectomy hemorrhage is thought to be due to sloughing of the necrotic cauterized tissue in the induced ulcer, with erosion into underlying blood vessels. The predominance of visible vessels with or without active bleeding or clots indicates an underlying

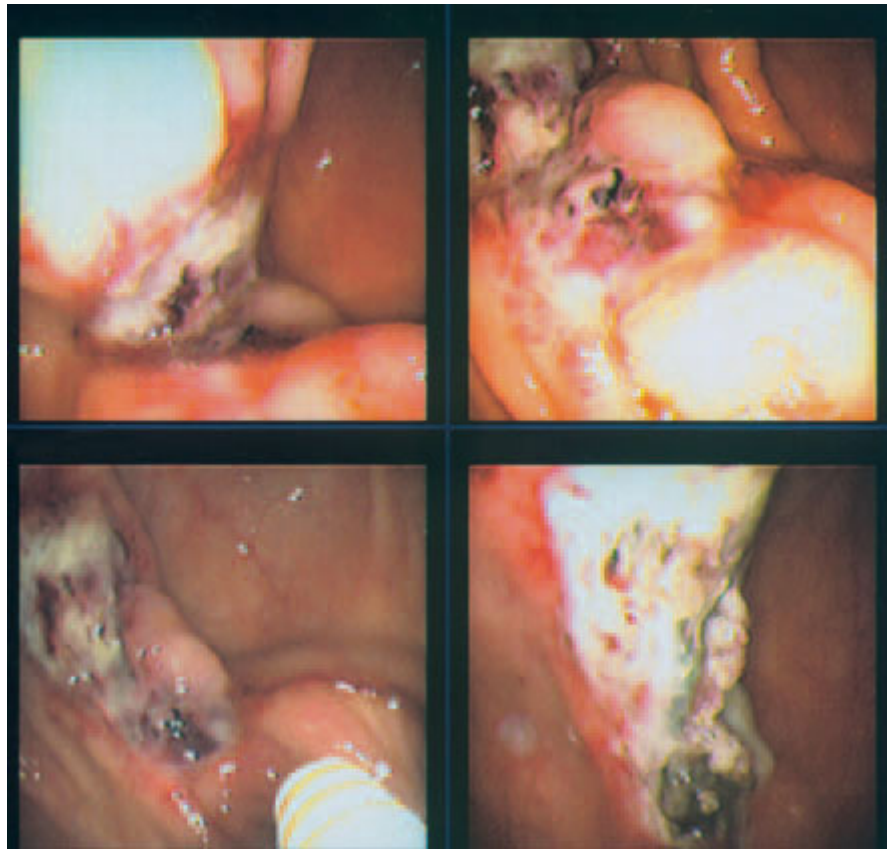


Fig. 47.6 A 77-year-old patient on aspirin for coronary prophylaxis was hospitalized 8 days after saline-assisted piecemeal polypectomy of a large (benign) sessile right colon polyp. At urgent colonoscopy a large ulcer with a small adherent clot was found and treated with a 10F Gold probe. The settings were 16 W with 2-s pulses. Moderate tamponade pressure was used to coagulate and flatten the clot and underlying visible vessel.

vessel, probably similar to the anatomy of peptic ulcers as defined by Swain and colleagues [31]. However, to date there have been no studies reporting on the histology of stigmata of hemorrhage for delayed post-polypectomy ulcers.

There are several effective methods for controlling bleeding from a postpolypectomy ulcer. We use techniques similar to those employed for chronic peptic ulcers to treat major stigmata of hemorrhage. In a post-polypectomy ulcer with active bleeding, epinephrine (1 in 10 000) is injected to slow or control the hemorrhage and then thermal coagulation is applied with the bipolar probe or heater probe on the bleeding vessel. For an adherent clot on the ulcer, we inject epinephrine around the pedicle of the clot in the ulcer base and then shave down the clot using a cold polypectomy snare. Rotatable snares facilitate this type of clot removal. Once the visible vessel is exposed, it can be coagulated with a thermal probe (for an example see Fig. 47.6). With a bipolar probe, we use a low power setting of 12–16 W with 2–4 s pulses. For the heater probe, power settings of 10–15 J/pulse are used. For a nonbleeding visible vessel, thermal coagulation alone is used. We also label the segment of the colon with India ink.

Colonic angiomias

Colonic angiomias (or angiectasias) were responsible for severe bleeding in 5.7% of our patients admitted to hospital for severe hematochezia. In contrast, the majority (70%) of patients we have seen with bleeding angiomias presented with self-limited intermittent bleeding or occult blood-positive stools and iron-deficiency anemia. These patients are usually hemodynamically stable and can undergo elective colonoscopy in the outpatient setting [32]. A smaller group (30%) of patients with colonic angiomias present with severe persistent hemorrhage, possibly hemodynamic instability, and/or severe anemia, and require hospitalization, blood transfusions, and emergency evaluation.

The CURE Hemostasis Research Group randomized 108 prospective patients with bleeding colonic angiomias to colonoscopic treatment with bipolar coagulation (57 patients) or heater probe (51 patients). Most of these patients were elderly (> 65 years) and suffered from one or more comorbid conditions (Table 47.9). The mean follow-up of these patients was 2 years, which was compared with the 2 years prior to endoscopic treatment in terms of number of bleeding episodes, number of blood

Table 47.9 Comorbid conditions for patients with hemorrhage from colonic angiomata ($n = 108$).

Severe heart disease (46%)
Valvular heart disease (29%)
Aortic stenosis (16%)
Aortic regurgitation (5%)
Mitral regurgitation (8%)
Chronic renal failure: hemodialysis (16%)
Cirrhosis (16%)
Collagen vascular disorder (5%)
Osler–Weber–Rendu syndrome (5%)

transfusions, and hematocrit while on iron and not acutely bleeding.

At colonoscopy most angiomata (85%) were in the right colon. The majority of angiomata (80%) were 5–10 mm in size, 18% were 11–20 mm, and 2% were greater than 20 mm (Fig. 47.7). The mean number of colonoscopies to control bleeding during the follow-up period was 1.4, with a range from one to four.

The techniques of the CURE Hemostasis Group for coagulating angiomata in the colon include using a small probe (2.4 mm diameter) for angiomata under 5 mm or a large probe (3.2 mm) for angiomata larger than 5 mm. Overdistension of the colon should be avoided during colonoscopic coagulation. Light pressure is applied with the probe directly on the angioma. For bipolar coagulation, we use a 50-W generator and coagulate with a setting of 10–16 W and 1- or 2-s pulses. For heater probe coagulation, we use a setting of 10–15 J. Whitening of the entire angioma is the desired endpoint of treatment (Fig. 47.8). All angiomata that are visualized during the course of the examination are coagulated. However, we caution against coagulation of large colonic angiomata in patients who have never had severe gastrointestinal hemorrhage (such as hematochezia), because of the potential for complications.

We found that 70% of patients had a good outcome

with colonic coagulation, experiencing fewer bleeding episodes, requiring fewer blood transfusions, and maintaining a higher hematocrit during follow-up (Fig. 47.9). Partial colectomies were performed in 18% of patients who had multiple colon angiomata (usually more than 25 in one segment such as the right colon). However, 38% of these operated patients continued to have recurrent bleeding after hemicolectomy. Complications from colonoscopic coagulation were observed in 5% of patients, consisting of delayed hemorrhage due to ulceration (four patients) or postcoagulation syndrome due to full-thickness coagulation (two patients). No perforations occurred. Two of the patients with delayed hemorrhage who had coagulopathies required surgery.

Summary

Severe lower gastrointestinal bleeding is now a more frequently encountered medical–surgical problem. The prevalence appears to be increasing because of recent colorectal cancer screening practices and the aging of referral patient populations. Our recommended approach to these patients is for vigorous resuscitation with intravenous fluids and blood transfusions, close monitoring in an ICU or monitored bed unit, bedside evaluation with nasogastric lavage for possible upper gastrointestinal bleeding source, and urgent colonoscopy (or upper endoscopy or small-bowel enteroscopy if colonoscopy is negative) following thorough colonic cleansing with oral or nasogastric purge. Definitive diagnosis of the bleeding site can be made with this approach in over 93% of cases. In patients with severe hematochezia, a colonic bleeding site is found in 77% of cases. Endoscopic treatment of focal bleeding lesions in the colon is highly effective and safe, diminishing the need for surgical intervention. In patients who have a recent bleed but no stigmata of hemorrhage or low-risk stigmata, early diagnosis may facilitate downgrading the intensity of medical care and early discharge.

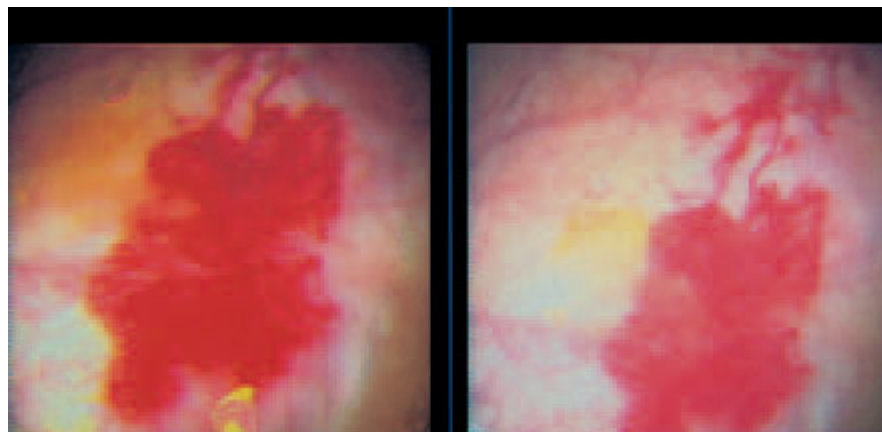


Fig. 47.7 A large right colonic angioma (angiectasia) was determined to be the cause of severe hematochezia when no other colonic or foregut lesions (by push enteroscopy) were found.

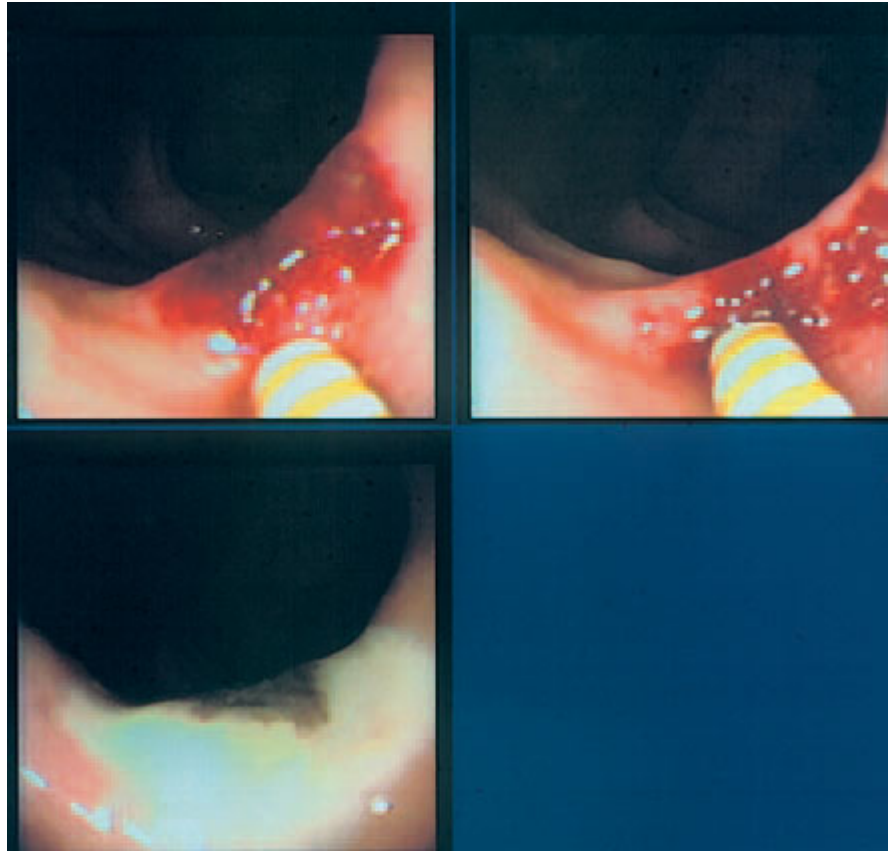


Fig. 47.8 During urgent colonoscopy, a right colon angioma was found to be bleeding. This was coagulated with a 7F Gold probe (power setting 14 W and 2-s pulses) using gentle tamponade pressure. No complications or rebleeding occurred.

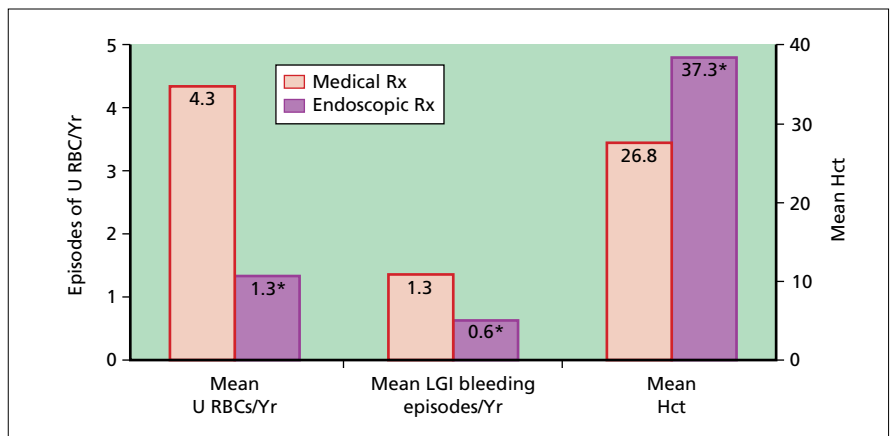


Fig. 47.9 Outcome results of 108 consecutive patients referred to and treated by the CURE Hemostasis Research Group for recurrent gastrointestinal bleeding from colonic angiomas. The outcomes for the 2 years before referral on medical therapy were compared with outcomes after colonoscopic treatments. * $P < 0.05$.

Acknowledgments

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to continue to perform urgent colonoscopies for severe hematochezia, after all these years.

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Chapter 48

Endoscopy in Inflammatory Bowel Diseases

Geert D'Haens and Paul Rutgeerts

Introduction

The widespread availability of gastrointestinal endoscopy has changed the management of inflammatory bowel disease (IBD) to an important extent. The need for an unpleasant bowel preparation, the high cost, and the discomfort sometimes caused by endoscopic procedures should nonetheless force the clinician to limit the indications. In this chapter we describe the most characteristic lesions of Crohn's disease and ulcerative colitis, the value of endoscopy in the initial assessment and monitoring of IBD, and therapeutic endoscopic interventions (see Chapter 27 for a discussion of surveillance biopsy in IBD).

Characteristic endoscopic findings in IBD

The nature and distribution of the mucosal abnormalities often allow an experienced endoscopist to diagnose IBD with a good level of confidence. However, in some instances the endoscopic picture may have features of both Crohn's disease and ulcerative colitis and then the term "indeterminate colitis" is more appropriate. Biopsies will confirm the suspected endoscopic diagnosis in the majority of cases, with signs of nonspecific idiopathic inflammation and chronicity. Only in a minority of cases is the diagnosis of Crohn's disease ascertained by the presence of granulomas.

Crohn's disease

Crohn's disease can affect any part of the gastrointestinal tract, including the oropharynx and the anorectum. Once the disease has become established, the extent and location tends to stay the same in most patients, although exceptions do occur, especially following surgical resections [1]. The most common involvement is ileocecal, observed in 41–55% of patients with Crohn's disease. Colonic Crohn's disease without small bowel involvement is less common (5–25%). Crohn's disease is confined to the small bowel alone in approximately 30% of cases [2,3].

The aphthous ulcer is the earliest and most characteristic endoscopic finding in Crohn's disease (Box 48.1). It can be found throughout the gastrointestinal tract. An

Box 48.1 Typical endoscopic findings in active Crohn's colitis.

- Aphthous (or aphthoid) ulcerations
- Deep irregularly shaped ulcerations
- Longitudinal ulcerations
- Cobblestones
- Discontinuous involvement (patchiness/skip areas)
- Luminal narrowing
- Fistulae

aphthous ulcer represents a small (maximum 5 mm) superficial ulcer surrounded by a characteristic tiny rim of erythema (Fig. 48.1). Aphthous ulcers can appear in a single segment or be spread throughout the colon [3–7]. They are often seen in groups, tend to enlarge concentrically, and give rise to larger and deeper ulcerations. Larger and deeper ulcers are also commonly observed [8]. They have clear margins and are often surrounded by normal colonic mucosa with very little reactive

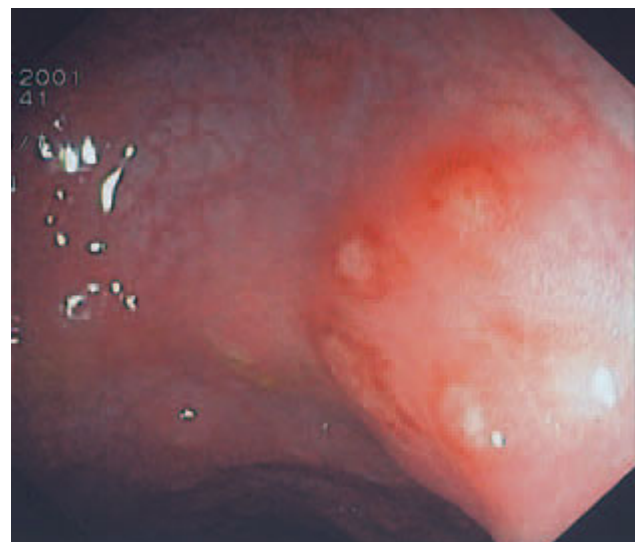


Fig. 48.1 Array of aphthous ulcers: small hyperemic nodules with central erosions are the first manifestations of Crohn's disease.



Fig. 48.2 Typical longitudinal ulcers interspersed with nodularity (cobblestoning) in severe active Crohn's colitis.

change (Fig. 48.2). The ulcers can be of various size and shape, including deep punched-out ulcerations, stellate ulcers, or longitudinal, tortuous or serpiginous ulcerations. The mucosa lying between long linear ulcerations can be normal or very edematous, reddish, and hyperplastic, almost polyp-like. This is referred to as the "cobblestone appearance" (Fig. 48.2) [7]. Different areas of the colon can be involved within a specific patient and larger areas can be completely spared from disease (i.e. patchiness). An example of this is the typical "rectal sparing," which has been reported in up to half of the cases. However, if the whole rectum is involved (5–10% of colonic Crohn's disease), the inflammatory activity in this area is not indicative of the severity higher up [9].

In the prospective European Cooperative Crohn's Disease Study (ECCDS), fissure or cleft-like ulcerations and aphthous lesions were the most common abnormalities followed by pseudopolyps, cobblestone lesions, and stenosis. A segmental pattern was the most common form of ulceration, whereas only 14% of patients had a continuous pattern of ulcerations [10].

Where the inflammation is deep and extensive, luminal narrowing or strictures can occur (Fig. 48.3) [6,7]. Strictures virtually always arise in areas of severe ulceration. Both length and width of the strictures can vary considerably, ranging from less than 3 to more than 10 cm in length and to less than 5 mm in width [2,9]. Features that suggest possible malignancy within a stricture include rigidity, nodularity at the margins, and an eccentric lumen [12]. The inflammation and ulcerations in Crohn's disease are often transmural and can lead to perforation, inflammatory mass, and/or fistula formation, reported in up to 8% of patients with Crohn's colitis. Fistulae are most often seen proximal to strictures and



Fig. 48.3 Ulcerated stricture in an area of severe Crohn's inflammation in the colon with surrounding ulcerations. Biopsies should always be taken to exclude malignancy.



Fig. 48.4 Healing of colonic ulcers may lead to extensive scarring due to fibrosis.

are frequently surrounded by extensive inflammatory changes [3].

When the active disease becomes quiescent, signs of chronic inflammation often remain visible, with a diminished or disturbed vascular pattern (Fig. 48.4). In patients with more extensive disease, healing may be more irregular and hypertrophic zones may alternate with areas of atrophy. This gives rise to the so-called "pseudopolyps" (Box 48.2).

When Crohn's disease involves the upper gastrointestinal tract, it is almost invariably accompanied by small bowel or colonic disease [13]. The prevalence of upper gastrointestinal tract involvement is much higher in prospective studies of both symptomatic and asymptomatic patients (17–75% for upper endoscopy) than in retrospective series (0.5–13%) [14]. In retro-

Box 48.2 Endoscopic findings in chronic or quiescent Crohn's colitis.

- Attenuated or loss of vascular pattern
- Mucosal bridging
- Pseudopolyps
- Stricture formation

spective series oral lesions were more frequent (6–9%) than gastroduodenal (1.8–4.5%) and esophageal (1.8%) involvement.

Esophageal involvement is usually seen in seriously ill patients, presenting with dysphagia, odynophagia, heartburn, and chest pain. Characteristic endoscopic features in the esophagus include hyperemia, granularity, friable mucosa, erosions or aphthoid lesions, ulcers, nodular thickening, cobblestones, and stenosis [15]. The true incidence of gross gastroduodenal involvement by Crohn's disease is unclear. Reported incidence ranges from 2 to 49% of patients with Crohn's ileocolitis [16–19]. Many patients, however, do not have endoscopically detectable lesions in the stomach and duodenum, although examination of biopsies does reveal histopathologic changes suggestive of Crohn's disease [19–23]. Gastroduodenal involvement often leads to symptoms similar to peptic ulcer disease or nonulcer dyspepsia, such as epigastric pain, anorexia, and sometimes signs of gastric outlet obstruction. In isolated duodenal disease any part of the duodenum can be involved but the second part is most frequently affected, with typical mucosal defects on top of the Kerckring's folds, called "notching." In the duodenum stricturing may also occur.

Ulcerative colitis

In ulcerative colitis the inflammation typically extends from the anal verge upward to a variable distance, which can change during the course of the disease. Since the rectum is virtually always involved in this disease, rigid proctoscopy is often sufficient for evaluation during follow-up. In patients whose disease is limited to the left colon, flexible sigmoidoscopy may suffice for evaluation. However, when topical treatment is being used the rectum may appear relatively normal despite the fact that more proximal segments remain inflamed. In patients with more extensive involvement a full colonoscopy with ileoscopy is advised to help differentiate from Crohn's colitis [24]. It is generally accepted that one should be cautious about performing endoscopic examinations in patients with fulminant colitis, given the increased risk of perforation and toxic megacolon.

Ulcerative colitis may involve the rectum (proctitis, approximately 30%), rectosigmoid area (proctosi-

Box 48.3 Characteristic endoscopic findings in ulcerative colitis.

- Continuous involvement
- Erythema
- Friability
- Granular appearance
- Microulcerations, shallow ulcerations
- Cecal patch

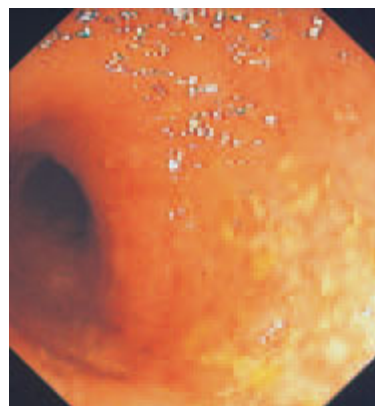


Fig. 48.5 Active ulcerative colitis: mucosa with disappearance of vascular pattern and presence of mucopus and friability.

moiditis or distal ulcerative colitis), left colon (left-sided colitis in 30–40%), or the entire colon (total colitis, approximately 30%) [25]. During follow-up, a large Scandinavian cohort study showed that up to 40% of patients had extension of their disease. Patients with initial extensive colitis showed regression over time in 44% [26].

The endoscopic appearance of ulcerative colitis is quite characteristic (Box 48.3). Unlike Crohn's disease, the inflammation is continuous and circumferential from the anal verge up. The mucosa shows erythema, friability, and often frank superficial bleeding (Fig. 48.5). Slight edema usually causes a shiny appearance. Additionally, there may be granularity with a typical grayish discharge. In moderate ulcerative colitis, one can appreciate erosions and microulcerations, and in more severe attacks shallow ulcerations may develop (Figs 48.6 & 48.7). Only rarely do deeper ulcerations and luminal narrowing occur. "Cecal patch" inflammation represents a limited zone of colitis surrounding the appendiceal orifice in patients with left-sided colitis [27].

In patients with long-standing moderate to severe colitis the colonic mucosa will show signs of chronic inflammation and healing. The colon may contain pseudopolyps and even mucosal bridging and an attenuated or loss of vascular pattern. Once stricture formation is encountered, a high level of suspicion is warranted as this may be a sign of malignancy. In reality it may be

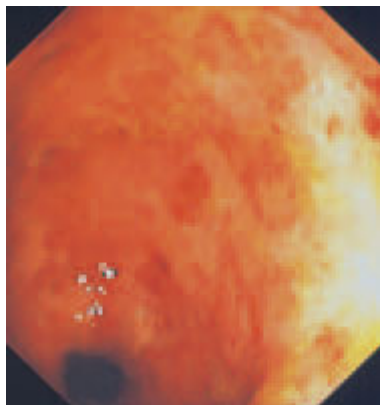


Fig. 48.6 Severe ulcerative colitis characterized by superficial ulceration.



Fig. 48.7 Spontaneous bleeding mucosa in severe active ulcerative colitis.

difficult to detect dysplastic lesions, especially in a scarred colon with many pseudopolyps. Therefore colonoscopies performed for prevention of colorectal cancer in patients with long-standing pancolitis should always include multiple biopsies from all different segments.

Differentiation between Crohn's disease, ulcerative colitis, and indeterminate colitis (Table 48.1)

In the majority of patients with chronic idiopathic colitis, the differential diagnosis between Crohn's disease

and ulcerative colitis will be quite clear. Pera and colleagues [28] prospectively examined 357 patients with 606 colonoscopies in order to determine the accuracy and "weight" of various endoscopic signs. Complete colonoscopy allowed a correct differentiation between Crohn's disease, ulcerative colitis, and indeterminate colitis in 89% of cases, with 4% errors and 7% indeterminate diagnoses. Errors were more frequent in the presence of severe colonic inflammation. The most distinctive endoscopic features in the differential diagnosis were discontinuous involvement, anal lesions, and cobblestoning of the mucosa for Crohn's disease and erosions, microulcers, and granularity for ulcerative colitis. Between 5 and 10% of patients showed abnormalities that were suggestive of both conditions. Most of the patients had an ulcerative colitis-like endoscopy with one or more features possibly suggesting Crohn's disease. These so-called "indeterminate features" included anal abnormalities (such as skin tags, an unusual fissure, or an abscess), rectal sparing, skip areas, and deeper ulcerations [28]. In these patients the term "indeterminate colitis" should be used as a reminder that the differential diagnosis is not completely clear.

Endoscopic assessment of extent and severity of IBD

Knowledge about the location of the intestinal inflammation affects management decisions, since certain medications can be used topically. The extent of the inflammation tends to be underestimated in both ulcerative colitis and Crohn's disease. The severity of the inflammatory lesions also has some prognostic value in a number of situations. For example, in ulcerative colitis deep ulcers are an indicator of a poor response to medical therapy. In Crohn's disease the severity of endoscopic lesions in the neoterminal ileum after an ileocolonic resection is an indicator of the ensuing clinical disease behavior [30].

The French GETAID (Groupe d'Etudes Thérapeutiques des Affections Inflammatoires du Tube Digestif) developed and validated a Crohn's disease endoscopic index of severity (CDEIS). The four mucosal lesions that were found to be of significant importance for establish-

Crohn's disease	Ulcerative colitis
Discontinuous involvement	Continuous involvement
Cobblestoning	Erosions/microulcers
Aphthous ulcers	Loss of vascular pattern
Deep, longitudinal, serpiginous ulcers	Rectal involvement
Rectal sparing or segmental inflammation	Ileocecal valve patulous and free of ulceration
Anal lesions	
Ileocecal valve stenotic and ulcerated	

Table 48.1 Differentiation between Crohn's disease and ulcerative colitis.

Table 48.2 Endoscopic indices for ulcerative colitis.

Powell-Tuck <i>et al.</i> [32]	0, no bleeding	1, bleeding on light touch	2, spontaneous bleeding	
Sutherland <i>et al.</i> [33]	0, normal	1, mild friability	2, moderate friability	3, exudation, spontaneous bleeding
Rutegard <i>et al.</i> [34]	0, normal	1, nonvisible vessels, friability	2, ulcers, single or scattered	3, confluent ulcers with pus
Schroeder <i>et al.</i> [35]	0, normal	1, disturbed vessels, friability, granularity	2, loss of vascular pattern, mucopus, spontaneous bleeding	3, ulcers, mucopus, spontaneous bleeding

ing a final formula for calculation of CDEIS were deep ulcerations, superficial ulcerations, nonulcerated stenosis, and ulcerated stenosis. The presence of the lesions is scored in each of five ileocolonic segments. For every segment, the proportion of surface which is ulcerated or affected by any other lesions is also scored. With this score interobserver agreement was excellent ($P < 0.001$) [31]. The same group then studied 142 patients with active colonic or ileocolonic Crohn's disease who all underwent a colonoscopy prior to treatment with prednisolone 1 mg/kg daily. Treatment was continued until clinical remission for a maximum of 7 weeks. Surprisingly, a significant correlation between Crohn's disease activity index (CDAI), biochemical markers, and CDEIS could not be established [8].

Conversely, in ulcerative colitis the endoscopic lesions represent an important parameter of disease activity and correlate better with clinical course of the disease. Although the endoscopic appearance does not give an exact estimate of the histologic changes in the colonic mucosa, endoscopic criteria are included in most clinical trials. Several endoscopic scoring systems have been developed. All scores distinguish three or four stages of mucosal alterations based on the disturbance or disappearance of the vascular pattern, presence of friability, and/or bleeding of the mucosa and presence of several types of ulcers and/or mucopus. An overview of several scores is given in Table 48.2 [32–35]. The extent of inflammation in ulcerative colitis often changes during the course of the disease. Niv and colleagues [36] reported change of extent in 77% of patients during a mean follow-up period of 17 months.

Endoscopic monitoring of therapeutic efficacy and its value in clinical trials

As mentioned above, the correlation between endoscopic severity and clinical activity is often poor in Crohn's disease but not in ulcerative colitis. GETAID demonstrated that only about one-quarter of patients in clinical remission under corticosteroid treatment also had endoscopic healing of their ulcerations. Persistence of lesions was not predictive of early relapse and adjustment of steroid treatment duration based on endoscopic

findings proved to be without benefit. It was concluded that endoscopic monitoring of "healing" is a waste of time and money [8,37,38], although it needs to be emphasized that this statement may only be applicable to treatment with corticosteroids. In general, the pattern of healing of endoscopic lesions under glucocorticoid therapy depends on the location of the lesions: esophageal lesions almost completely and rapidly disappear, whereas gastric lesions hardly show any change, even with symptomatic relief. Ileal lesions have the same tendency to persist, whereas colonic lesions can heal slowly after tapering of the steroids [39].

Data on mucosal healing with antiinflammatory agents other than glucocorticosteroids are scarce. Azathioprine was shown to induce significant healing in Crohn's ileocolitis, colitis, and severe postoperative recurrent ileitis [40,41]. Variable degrees of ileal and colonic healing have also been reported with methotrexate [42]. The most impressive and rapid healing of Crohn's disease lesions was observed after treatment with the monoclonal antibody against tumor necrosis factor, infliximab [43]. A group of European investigators demonstrated significant healing of colonic lesions only 4 weeks after intravenous administration of a single dose of this drug. All parts of the colon improved to the same extent. A significant correlation between clinical improvement (Δ CDAI) and endoscopic changes (Δ CDEIS) was demonstrated [44]. A few patients in this study developed fibrous strictures, which were dilated endoscopically. It remains to be studied if clinical remission with accompanying endoscopic healing should become a treatment objective in the future.

Perioperative endoscopy in Crohn's disease

Up to 70% of patients with Crohn's disease will undergo at least one surgical resection of inflamed bowel segments, usually in order to treat complications of the disease. Generally, the surgeon aims to be curative, i.e. to resect all macroscopic disease, although sometimes resections are limited to segments which are responsible for the symptoms, leaving active disease behind (segmental resection). More and more patients are treated

Table 48.3 Scoring system for recurrent lesions of Crohn's disease in the neoterminal ileum.

i_0	No lesions
i_1	Less than five aphthous lesions
i_2	More than five aphthous lesions with normal mucosa between the lesions, or skip areas of larger lesions, or lesions confined to the ileocolonic anastomosis
i_3	Diffuse aphthous ileitis with diffusely inflamed mucosa
i_4	Diffuse inflammation with already larger ulcers, nodules, and/or narrowing

with strictureplasties whereas bypass operations are no longer performed.

After surgery most patients will suffer recurrence of their disease. Risk factors for early symptomatic recurrence are perforating indications for surgery (abscess or fistula), ileocolonic anastomosis, and smoking. Ileocolonoscopy is a key method for planning treatment strategies in the preoperative as well as postoperative period.

In order to optimize the outcome of surgery it is critical to study the anatomic distribution of Crohn's involvement prior to surgery. This has become even more imperative with broader use of the laparoscopic surgical approach, since reliable evaluation of disease extent based on serosal inspection may sometimes be difficult. If the colon is spared at endoscopy, the surgeon performs an ileal resection with ileocecal or ileoascending anastomosis. If right colonic disease is visualized, the surgeon should extend the colonic resection guided by colonoscopic findings and suture the neoterminal ileum to uninvolved colon.

Systematic endoscopic studies following curative resection in Crohn's disease have allowed study of the evolution of Crohn's disease, from the earliest lesions to full-blown disease. Within weeks to months after resection with ileocolonic anastomosis, "new" lesions can be visualized in the neoterminal ileum [5]. Ileocolonoscopy studies after surgery also allow prediction of the clinical outcome of Crohn's disease after resection. The severity of recurrent lesions as visualized at endoscopy predicts the clinical evolution in the years following surgery [30]. The severity of recurrent lesions early after resection are assessed using an endoscopic scoring system (Table 48.3).

Patients displaying no or only mild lesions (score i_0 , i_1) do well over time and carry a low risk of rapid symptomatic relapse, whereas patients presenting with diffuse severe endoscopic recurrence (score i_3 , i_4) are at risk of progressive clinical disease. Patients with endoscopic lesions of intermediate severity also have an intermediate risk. This score has also been valuable for studies of drug prophylaxis of postoperative recurrence [45,46].

Patients with an ileostomy can also develop recurrent inflammation in the most distal ileal segments, but the risk is much lower than after an ileocolonic reanastomosis. Endoscopic examination of the bowel proximal to the stoma allows easy and precise evaluation of the abnormalities and collection of biopsies.

Endoscopic features of the ileoanal pouch and pouchitis

Restorative colectomy with ileal pouch–anal anastomosis (IPAA) has become an established surgical option for patients with severe ulcerative colitis [47]. The most common long-term complication besides intestinal obstruction is inflammation of the pouch, known as "pouchitis." Approximately 50% of patients with an IPAA can be expected to develop an episode of pouchitis [48]. This inflammation becomes chronic in as little as 5% of patients.

Although the inflammation remains limited to the pouch reservoir, in the majority of patients extension into the prepouch ileum can occur. The endoscopic features of pouchitis resemble those of ulcerative colitis: in an early stage erythema, fading of the vascular pattern, granularity, and friability appear. Later, punctiform mucosal hemorrhages, mucus secretion, adherent purulent material, and superficial ulcerations develop. Less frequently, large isolated ulcers with normal surrounding mucosa can be found as in Crohn's disease. Undiagnosed Crohn's disease is a rare but important differential diagnosis, particularly if large ulcers or fistulae (e.g. pouch–vaginal fistulae) are present. Occasionally, pseudomembranous lesions may be observed, which mandates stool sampling to exclude *Clostridium difficile* infection.

Several scores to assess the severity of pouchitis have been developed, the first of which was proposed by Moskowitz and colleagues [49] and applied very strict clinical and endoscopic criteria. Sandborn and colleagues [50] introduced the pouchitis disease activity index, combining clinical, endoscopic, and histologic findings, and is now most often used in clinical studies. This score evaluates the presence of edema, granularity, friability, faded vascular pattern, mucous exudate, and ulceration. Equal weight is attributed to all these parameters. A similar score, the pouchitis activity score, was proposed by the Heidelberg group and uses the same endoscopic criteria but differentiates between mild and severe lesions [51]. The treatment of pouchitis should aim not only at symptomatic improvement but also at complete healing and restoration of the pouch mucosa.

Pouchitis generally involves most of the pouch reservoir and should be differentiated from "cuffitis." This entity represents a recurrence of ulcerative colitis in the short cuff of the rectoanal transitional zone that has

been preserved in case of a double-stapled pouch anastomosis. It usually extends over a distance of 1 cm. The endoscopic feature is that of a distal ulcerative proctitis with a clear demarcation to ileal pouch mucosa. It is important to know that mucosal dysplasia can occur in this transitional zone, although the risk is very low [52].

Endoscopic treatment of Crohn's disease complications

Fibrotic strictures are commonly observed in Crohn's disease, even in quiescent disease or in bowel segments "healed" with immunomodulatory or biologic therapy. Strictures causing obstructive symptoms can occur anywhere in the gastrointestinal tract, but there is a clear predilection for the ileocecal valve, ileocolonic anastomosis, duodenum, sigmoid colon, and anal canal. Anal and distal colonic strictures can be treated with Savary dilators over a guidewire but for stenoses more proximal in the colon endoscopic balloon dilatation is the sole option. The efficacy and safety of through-the-scope balloon dilatation for Crohn's disease strictures has been reported in a number of studies [53–58]. Success rates in our series (defined as easy passage of a 13.6-mm colonoscope through the stenosis after dilation) was achieved in 90% of patients; 62% of patients avoided a surgical resection in the long term. A minority of patients need repeated dilatations. Complications of through-the-scope dilatation include perforation and bleeding. On average, a 10% complication rate has been reported in the literature. For this reason, patients should be carefully selected on the basis of X-ray studies. Anastomoses situated in a sharp angle from the colon, long stenoses, multiple stenoses, and stenoses more proximal in the terminal ileum usually do not qualify for endoscopic dilation procedures.

Anal or supra-anal dilation is usually performed with a thin endoscope and additional Savary dilation. The procedure can be reinforced by home autodilation of the stenosis. It is our opinion that balloon dilatation of the anus is not recommended because of the potential risk of sphincter damage.

Summary: indications for endoscopy in IBD (Table 48.4)

The endoscopic evaluation of patients with IBD is extremely valuable and has changed the management of these diseases. Ileocolonoscopy has replaced contrast enemas in the first evaluation of patients with suspected IBD. Nonetheless, these procedures are only justified when they are likely to influence therapeutic decisions. Ileocolonoscopy can establish an exact ("tissue") diagnosis, determine the severity and extent of inflammatory activity, "guide" the surgeon in the preoperative

Table 48.4 Indications and questionable indications for colonoscopy in Crohn's disease.

<i>Indications for (ileo)colonoscopy</i>	
Establishing the correct diagnosis of inflammatory bowel disease	
Differential diagnosis of Crohn's colitis vs. ulcerative colitis	
Infective/acute self-limited colitis	
Assessment of extent and grading of severity	
Preoperative delineation of the diseased areas	
Postoperative evaluation of recurrent Crohn's disease, diverted bowel segments	
Endoscopic balloon dilatation of (ileo)colonic strictures	
Investigation of radiographic abnormalities (strictures, mass lesions)	
<i>Questionable indications for colonoscopy</i>	
Severely active disease	
Monitoring of therapeutic efficacy	

setting, and examine the bowel proximal to stomas. Early endoscopic examination of the ileocolonic anastomosis after resection of the terminal ileum and part of the colon enables evaluation of the severity of recurrence of Crohn's disease, predicting clinical outcome.

Endoscopic examination of the upper gastrointestinal tract should be performed whenever upper gastrointestinal symptoms develop. It is important for the treatment to differentiate between intrinsic Crohn's lesions, peptic disease, or drug-associated lesions in the esophagus, stomach, or duodenum.

Endoscopic observations certainly have therapeutic consequences in pouchitis, in patients with Crohn's disease following surgical resection, and in severe attacks of ulcerative colitis. Complete mucosal healing should be a therapeutic goal in all patients with ulcerative colitis. Whether it should be a therapeutic goal in Crohn's disease as well remains to be established.

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Chapter 49

Infections and Other Noninflammatory-Bowel-Disease Colitides

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Introduction

This chapter covers a variety of infectious and noninfectious colitides which may share similar clinical presentations. For some conditions, endoscopic evaluation is necessary to establish the diagnosis and severity of disease, in others, endoscopy plays no role or may be contraindicated in certain circumstances. We discuss the clinical presentation of these disorders, the indications for and anticipated findings during colonoscopy, the value of biopsies and supplemental studies, and treatment alternatives.

Infectious diarrhea

In the USA, most episodes of acute diarrhea are due to mild, self-limited viral infections. There is no role for colonoscopy in the care and management of these patients. Because of the self-limited nature of most bacterial causes of diarrhea in the immunocompetent person, colonoscopy is rarely necessary. Clinical evaluation, blood tests, and microscopic examination and culture of stools may often yield a diagnosis [1].

Despite its limited role, endoscopic findings may help distinguish between infectious colitides and other etiologies. Histopathology from mucosal biopsies can distinguish acute self-limited colitis (ASLC) seen with enteric pathogens from the chronic colitis associated with idiopathic inflammatory bowel disease [2]. Findings of ASLC include mucosal edema (Fig. 49.1), inflammatory infiltrate in the lamina propria, and damage to the surface epithelial layer. In contrast to IBD, there is generally preserved mucosal and crypt architecture [3].

Salmonella

Salmonella species comprise a group of motile, gram-negative rods that cause food-borne infections. The three species of *Salmonella* responsible for most of these infections are: *S. typhi*, *S. cholera-suis*, and *S. enteritidis*. Most outbreaks are related to ingestion of contaminated poultry, meat, and dairy products. The organism commonly



Fig. 49.1 ASLC showing erythema and edema with tiny focal erosions.

invades the ileum, and to a lesser extent, the colon. Most cases involving the ileum and right colon result in uncomplicated gastroenteritis, but enterocolitis or enteric fever with diarrhea may occur [4].

Patients with enteric (typhoid) fever develop abdominal pain, bloating, and constipation followed by diarrhea. Colonoscopy is unnecessary to establish the diagnosis, but findings include nonspecific focal hemorrhage, friability, and ulcerations (Fig. 49.2). Diagnosis is made by stool culture, and therapy is not generally recommended because it will prolong organism excretion.

Nontyphoidal *Salmonella* cause self-limited gastroenteritis and enterocolitis characterized by sudden onset of vomiting, colicky abdominal pain, and watery diarrhea resembling pea soup. Colonic involvement is predominantly right-sided, patchy, with rectal sparing, but pancolitis can occur. Nonspecific endoscopic findings are



Fig. 49.2 *Salmonella* colitis showing diffuse erythema with loss of the normal vascular pattern, and granularity with edema. (Courtesy of David M. Martin MD, "Atlas of Gastrointestinal Endoscopy," www.EndoAtlas.com.)

seen: edema, friability, focal hemorrhage, and ulcerations with crypt abscesses on histopathology. Severe cases may develop pseudomembranes or deep cecal ulcerations associated with significant hemorrhage [5]. Treatment is indicated for severe symptoms, immunocompromised individuals, and the elderly. Chloramphenicol, ciprofloxacin, ampicillin, amoxicillin, and TMP-SMX are all effective [6].

Shigella

Shigella species are aerobic, gram-negative rods that cause bacillary dysentery. Human infection results from one of four species: *S. dysenteriae*, *S. flexneri*, *S. boydii*, and *S. sonnei*. Its highly infectious nature distinguishes it from other enteric pathogens; ingestion of fewer than 100 organisms may cause colitis [7]. Its clinical picture is uniquely biphasic in nature. After fecal–oral transmission, *Shigella* organisms reach high concentration in the small intestine, initially causing fever, abdominal cramping, and watery diarrhea in the first 48 h, mediated by enterotoxin production. With subsequent tissue invasion in the colonic mucosa, dysentery ensues with fever, small-volume bloody stools, tenesmus, and signs of systemic toxicity [8]. Extraintestinal manifestations include nonsuppurative arthritis, hemolytic uremic syndrome, and febrile seizures [4,9].

The spectrum of endoscopic findings is broad, ranging from mucosal edema and hyperemia with loss of

vascularity to severe pancolitis with confluent ulcerations and overlying exudate. Rectosigmoid involvement is most frequent, but confluent proximal or patchy involvement with aphthous ulcerations has also been described [1,10]. Severe cases may mimic ulcerative colitis, while the differential diagnosis includes Crohn's disease and other bacterial infections in milder cases. Histology of mucosal biopsies is consistent with ASLC, and diagnosis depends upon microscopic examination and culture of stool.

Although shigellosis is most commonly self-limited, antibiotic therapy shortens the duration of disease and fecal excretion of the organism [4]. Supportive care and treatment with fluoroquinolones are preferred, although ampicillin and TMP-SMX can be used [6].

Campylobacter

Campylobacter species are microaerophilic, gram-negative rods that require selective culture media for isolation. *C. jejuni*, the most common cause of bacterial diarrhea, is transmitted by the fecal–oral route or by contaminated food or water sources [11]. A relatively low inoculum of 400–800 organisms may cause infection, usually within 1 week after ingestion [12,13]. It is characterized by a prodrome of fever, myalgia, nausea, abdominal discomfort, and anorexia, followed by non-bloody watery diarrhea with jejunal involvement. More than half of patients progress to ileal and colonic involvement characterized by fever, bloody diarrhea, and abdominal pain. Symptoms are usually self-limited, 1–7 days in duration, but may last longer. Complications include mesenteric adenitis, appendicitis [14], and toxic megacolon [15].

Endoscopic evaluation typically reveals pronounced rectal involvement, although focal involvement of proximal areas of the colon may be seen [16,17]. Typically, the endoscopic features are similar to ulcerative colitis, but patchy erythema and friability with superficial ulcerations may mimic Crohn's disease or amebic colitis [18]. Histology shows ASLC without disruption of crypt architecture.

Because infection is usually self-limited, therapy is only recommended for severe or prolonged symptoms which last more than 1 week. Erythromycin, azithromycin, and fluoroquinolones are effective [6].

Yersinia

Yersinia species are gram-negative coccobacilli which cause enteric infection in humans by invasion with *Y. enterocolitica* or *Y. pseudotuberculosis*. Outbreaks commonly stem from ingestion of contaminated milk products, meat, or vegetables. Acute diarrheal syndromes resemble shigellosis. Acute presentations may mimic



Fig. 49.3 Ulcers in *Yersinia colitis* which resemble tuberculosis or Crohn's disease. (Courtesy of Hans Bjorknas MD.)

appendicitis, with fever, leukocytosis, and relatively minor diarrhea [4]. *Yersinia* should always be considered when the misdiagnosis of acute appendicitis reveals a normal appendix at the time of surgery. Chronic diarrhea, more common in children, may mimic Crohn's disease [4]. Extraintestinal manifestations include erythema nodosum [19], nonsuppurative arthritis [20], and autoimmune thyroiditis.

The pattern of involvement may mimic Crohn's disease. Colonoscopic features include aphthous ulcers with surrounding erythema, particularly in the right colon, although pancolitis less commonly occurs (Fig. 49.3) [21–23]. Terminal ileoscopy reveals ulcers, edema, and round or oval mucosal elevations [23]. Histopathology shows nonspecific ASLC, although the presence of granulomas may further confuse the diagnosis with idiopathic Crohn's disease. Diagnosis is made by stool culture with special cold-enrichment technique or by positive serum agglutinin titres.

Yersinia is sensitive to TMP-SMX, tetracycline, chloramphenicol, and ciprofloxacin. Most authors advocate treatment, particularly in patients with severe enteritis, mesenteric adenitis, and erythema nodosum [24,25].

Escherichia coli

Escherichia coli are aerobic, gram-negative rods which cause diarrheal syndromes, most commonly affecting the small bowel. Two types of *E. coli* cause colitis: enteroinvasive (EIEC) and enterohemorrhagic *E. coli* (EHEC). EIEC proctocolitis is a rare entity which resembles *Shigella* infection [26–28]. By contrast, noninvasive EHEC adheres to the colonic mucosa, causing hemorrhagic colitis via elaboration of Shiga-like toxins (SLT). The most common serotype, *E. coli* O157:H7, was first isolated in

1982 after a series of outbreaks linked to contaminated hamburger meat at a fast food restaurant chain [29]. Bloody diarrhea occurs within several days after ingestion, and fever is typically absent [30]. Complications include hemolytic uremic syndrome, which occurs in up to 10% of cases with diarrhea, and thrombotic thrombocytopenic purpura [31,32].

Endoscopy reveals friable, edematous mucosa with superficial ulcerations and fresh blood. The most severe changes occur in the ascending and transverse colon; this may mimic ischemic colitis in the elderly versus inflammatory bowel disease (IBD) in the pediatric population [1,17]. Histopathology may show changes of ASLC or may mimic ischemic colitis [17]. Diagnosis depends on thorough clinical evaluation and appropriate stool cultures. Special MacConkey sorbitol agar culture media is necessary. Detection of SLT in stool or serum antibody titers to SLT may confirm the diagnosis [1].

Treatment is generally supportive, as the disease is self-limited, usually resolving spontaneously over 5–10 days. The role of antibiotic therapy is yet undefined, as antibiotics may increase the risk of hemolytic uremic syndrome [29,33].

Mycobacterium tuberculosis

Gastrointestinal tuberculosis occurs by ingestion of organisms by swallowed pulmonary secretions, although less than 50% have concomitant pulmonary TB [34–36]. It typically presents with fever, leukocytosis, weight loss, abdominal pain, and right lower quadrant mass [37–39]. Complications include obstruction, hemorrhage, fistula or stricture formation, and perforation [40–42].

Although any part of the gastrointestinal tract from the stomach to the rectum may be affected, the ileum and cecum are most commonly involved [43]. Segmental colitis with skip areas [39,44–46] and, more rarely, pancolitis [39] may also be seen. Differential diagnosis includes Crohn's disease, *Y. enterocolitica*, cecal carcinoma, amebic colitis, and syphilis. Endoscopic appearance varies according to type of involvement. In the ulcerative form, focal erythema and edema with ulceration are seen. The ulcerohypertrophic form is characterized by segmental, thickened skip areas typically shorter than those seen in Crohn's disease [17,43]. Furthermore, the ulcers may have a rolled edge and lack the sharp definition usually associated with ulcers of Crohn's disease [17,41]. Transmural inflammation with stricture formation can occur. In the hypertrophic form, intestinal tuberculosis may present with colonic mass mimicking carcinoma [38]. The definitive diagnosis requires demonstration of acid-fast bacilli on mucosal biopsy or culture [47,48]. Positive tuberculin skin test or chest X-ray is supportive, but these studies are often negative [35,36].

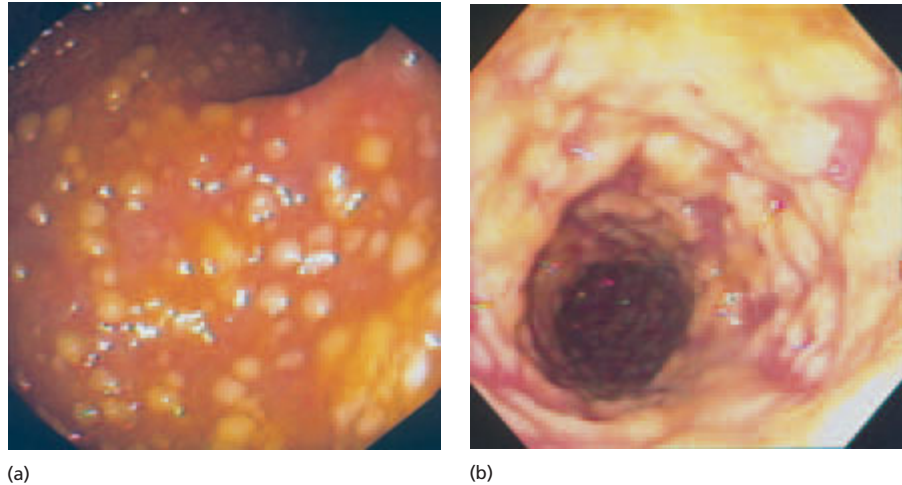


Fig. 49.4 (a,b) *Clostridium difficile* infection may cause a spectrum of mucosal abnormalities, but the characteristic pseudomembranes are unmistakable.

As with pulmonary TB, treatment is with combination antituberculous medications.

Clostridium

Clostridium difficile is a gram-positive, spore-forming anaerobic rod that causes pseudomembranous colitis (PMC) by production of two enterotoxins. It is the most common nosocomial infection in humans; its relationship with antibiotic exposure is clearly established, although sporadic infections also occur. Symptoms include profuse, foul-smelling, green or mucoid diarrhea, usually beginning within 1–3 weeks after antibiotic therapy. Frank bleeding is uncommon, and symptoms may be delayed up to 8 weeks after completion of antibiotics [41,49]. Tenesmus, nausea, fever, crampy abdominal pain, and leukocytosis may ensue. Toxic megacolon is the most significant major complication.

Proctosigmoidoscopy typically reveals the characteristic pseudomembranes consisting of multiple sharply demarcated raised yellow-white mucosal plaques (2–8 mm in size), although nonspecific mucosal changes of mild erythema, edema and ulcerations may be present (Fig. 49.4a,b). However, up to one-third of patients will have disease isolated to the right colon beyond the reach of flexible sigmoidoscopy [50,51]. Pseudomembranes may also be seen with other forms of infectious colitis or with colonic ischemia. Histopathology reveals the characteristic “volcano lesion.” Diagnosis is based on history of exposure to antibiotics and stool toxin assays. Stool culture cannot necessarily distinguish between asymptomatic carriers and those individuals with colitis [1].

The two most commonly used antibiotics are oral metronidazole or vancomycin, both with equal efficacy in mild disease. Metronidazole is typically preferred as first-line therapy due to the higher cost and antibiotic resistance associated with vancomycin use [41]. The majority of patients respond within 1–4 days of initiating

therapy. Unfortunately, of those responders, approximately 20% will relapse [52–54]. Relapses can be treated with high doses of vancomycin for several weeks. Rifampin may be added as an additional therapeutic agent. Intravenous metronidazole and/or vancomycin via nasogastric tube, rectal enemas, or cecostomy tube may be necessary in more severe cases, particularly in the clinical setting of toxic megacolon [74]. Colonoscopy is advocated by some authors for placement of a colonoscopic decompression tube to relieve dilation and to deliver vancomycin.

Histoplasmosis

Histoplasmosis rarely affects the colon, but when colitis does develop, the ileocecal area is most often involved, with mucosal hyperemia, friability, ulcerations, and pseudopolyps (Fig. 49.5) [78]. The rectum is frequently spared, but when involved, may contain discrete granular plaque-like lesions, which on biopsy usually demonstrate the organism.

Entamoeba histolytica

Entamoeba histolytica causes amebic colitis following ingestion of cysts from contaminated food or water sources via fecal–oral transmission. The cysts are resistant to digestion by gastric acid, passing intact into the small intestine to proliferate. The cysts liberate trophozoites which invade the colonic mucosa to cause disease. Symptomatic patients complain of mild to severe abdominal pain with frequent loose stools with occult or gross blood.

Colonoscopy, as opposed to flexible sigmoidoscopy, is typically necessary, as segmental involvement of the cecum and right colon is most common, followed by rectosigmoid and appendix. Endoscopic findings vary according to the stage and severity of the disease. The

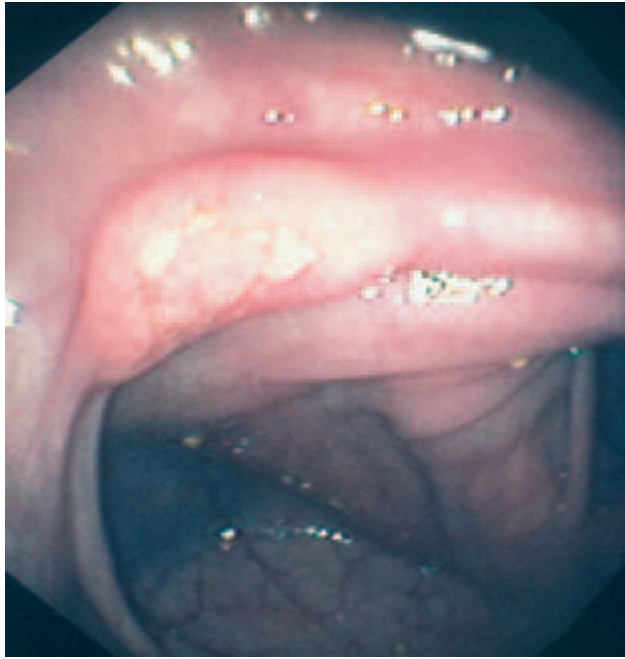
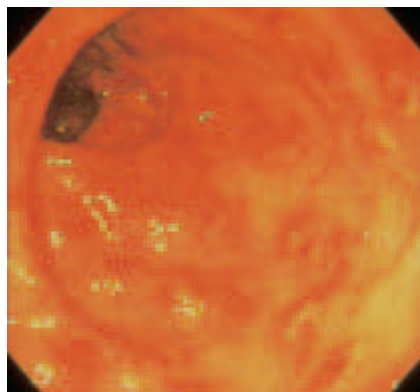
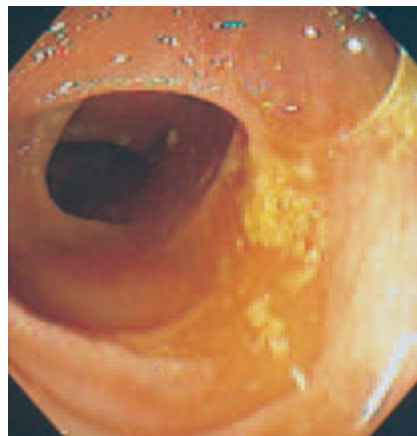


Fig. 49.5 Histoplasmosis with focal ulcerations and edema.

early lesion comprises a small area of necrosis or nodular elevation with an opening that leads to flask-shaped ulcers containing necrotic cells, amebas, mucus, and inflammatory debris. As the disease progresses, collar-button ulcers and erythematous halos may develop (Fig. 49.6a,b) [55]. As with Crohn's disease, the intervening mucosa is normal. Chronic mucosal destruction with reparative granulation tissue formation is responsible for the radiographic sign of "coning" of the cecum and for ameboma, a mass of granulation tissue which may mimic carcinoma in the cecum or ascending colon [56]. Biopsy of ulcers or exudate may show trophozoites (Fig. 49.7) and Charcot-Leyden crystals. Cysts and trophozoites may be seen on microscopic examination of stool. Serum antibody testing is diagnostic.



(a)



(b)

Fig. 49.6 (a) Punctate ulcerations in a diffuse pattern caused by invasive amebic trophozoites. (Courtesy of Christina Surawicz, MD.) (b) Advanced disease with deep and diffuse ulcerations adjacent to uninvolved mucosa.

The treatment of choice is metronidazole, followed by an intraluminal amebicide such as paromomycin. Immunosuppressive therapy for IBD should be avoided as this may induce severe invasive amebic colitis. Some experts advocate mandatory testing of serum antibodies to *E. histolytica*, prior to initiating immunosuppressive therapy for presumptive IBD.

Schistosoma

Intestinal schistosomiasis is caused by *S. mansoni* and *S. japonicum*. Infection is via a fresh water source, where cercariae penetrate human skin or are swallowed. Organisms enter the peripheral capillary bed, circulate in the bloodstream, and mature in the portal system. Adult worms migrate and produce eggs in the mesenteric venules, which are swept in the circulation to the liver and lungs, and are capable of invading through the wall of the intestine or bladder to pass through the feces or urine. Acute disease develops when eggs penetrate the viscera, causing symptoms of fever, malaise, weight loss, myalgia, abdominal pain, diarrhea, and dysentery. Eosinophilia is common. Other complications include portal hypertension, pulmonary hypertension with right heart failure, and nephrotic syndrome.

Endoscopic findings are related to egg deposition in the colonic wall, with resultant inflammatory and granulomatous reaction. Mucosal abnormalities are most often seen in the proximal colon. Features of early infection include mucosal edema, friability, with granularity and ulceration resembling ulcerative colitis. The classic endoscopic finding is a pseudopolyp with whitish surface exudate consisting of a large number of eggs and granulomatous reaction [57]. Dense fibrous tissue and strictures may develop. Histopathology demonstrates degenerating ova with surrounding acute or granulomatous inflammation [57]. Examination of fresh rectal biopsies with the crush technique will demonstrate the eggs in 80% of cases, but stool examination for

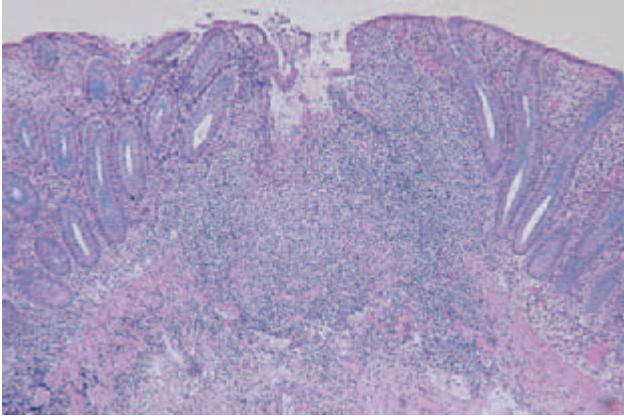


Fig. 49.7 Histology of amebic ulceration with underlying amebic trophozoites. (Courtesy of Christina Surawicz, MD.)

schistosomal ova is the preferred method of diagnosis [58].

Treatment with praziquantel is effective against all species of *Schistosoma*.

AIDS enteropathy

Cytomegalovirus

Cytomegalovirus (CMV) infection is seen primarily in patients who are immunocompromised by AIDS or immunosuppressive drugs. CMV is a double-stranded DNA virus which affects any portion of the gastrointestinal tract, most commonly the esophagus and colon. Infection is caused by reactivation of latent CMV in immunocompromised hosts, although the disease rarely occurs in immunocompetent individuals [59]. Patients with colonic involvement develop lower abdominal pain, fever, weight loss, and diarrhea. Bloody stools, tenesmus, and urgency are also seen.

Colonoscopy is useful to make the diagnosis [80]. Typical colonoscopic features include multiple discrete

ulcerations ranging from 5 mm to greater than 2 cm surrounded by otherwise normal mucosa (Fig. 49.8a,b). While the involvement may be anywhere in the colon, up to one-third of patients may have disease confined to the proximal colon [1]. Histopathology demonstrates viral inclusion bodies from deep biopsy specimens obtained from centers of ulcerations; immunohistochemical staining and culture of biopsy material may be confirmatory. Stool cultures and serum antibodies are not helpful.

In immunocompetent hosts, supportive therapy is warranted as infection is usually self-limited. The treatment of choice for CMV colitis is intravenous ganciclovir for immunocompromised patients.

Mycobacterium avium–*intracellulare* complex

Mycobacterium avium–*intracellulare* complex (MAC) infection of the gastrointestinal tract is seen primarily in patients with advanced AIDS. MAC comprises two distinct organisms, *M. avium* and *M. intracellulare*, which are found environmentally in water and soil. Although MAC may cause pulmonary disease similar to tuberculosis in immunocompetent individuals, GI tract involvement usually occurs in the setting of disseminated MAC infection with severe immunosuppression. Low CD4+ cell counts (usually < 50–100 cells/mm³) appear to be the greatest risk of disseminated MAC infection in patients with AIDS [81]. Small intestinal involvement is more frequent. Symptoms include fever, diarrhea, malabsorption and weight loss.

Colonoscopic findings may be normal or show erythema, edema, and erosions [1]. Large segments of colon showing a circumferential whitish hue may represent massive accumulation of lipid-filled macrophages packed with mycobacteria. Acid-fast bacilli should be evident from biopsy specimens, but culture results can distinguish this from *M. tuberculosis* [4]. Positive stool or blood cultures may obviate the need for endoscopic examination.

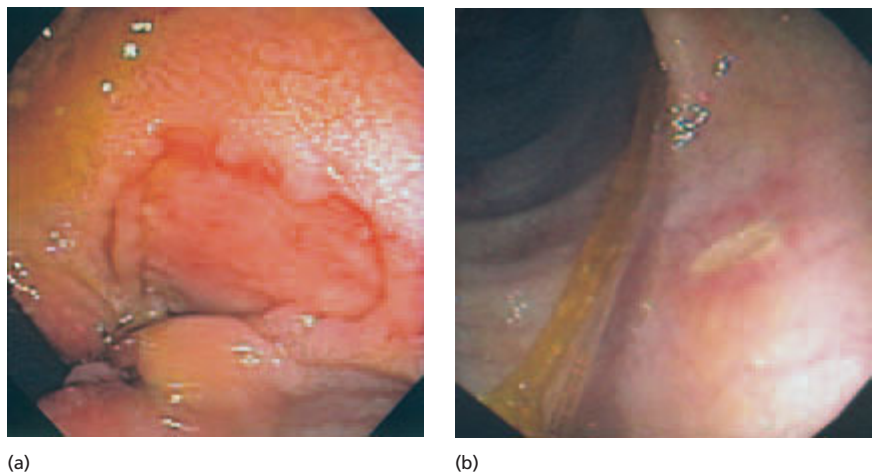


Fig. 49.8 Cytomegalovirus. (a) Shallow ulcer near anal canal in a retroversion view. (b) Isolated ulcer of descending colon.



Fig. 49.9 Nonspecific ulcerations can occur in immunosuppressed patients. This cecal ulcer was seen in a transplant patient.

Combination treatment is difficult, with poor response and high relapse rates. After treatment, chronic suppressive therapy for secondary prophylaxis is necessary.

Ulcerations

Nonspecific ulcers can occur in immunosuppressed patients (Fig. 49.9).

Cryptosporidiosis

This microscopic parasite, *Cryptosporidium parvum*, causes diarrheal disease in immunosuppressed patients, but can infect normal people as well. The parasite is protected by an outer shell that allows it to survive outside the body for long periods of time. During the past two decades, Cryptosporidiosis has become recognized as one of the most common causes of waterborne disease (drinking and recreational) in humans. There may be no specific colonoscopic findings, and biopsies are required to make the diagnosis if stool specimens fail to demonstrate the organism (Fig. 49.10).

Sexually transmitted diseases causing colitis

Proctitis caused by sexually transmitted organisms are usually associated with anorectal-receptive intercourse.

Treponema pallidum

Syphilis, usually transmitted via anorectal intercourse, is commonly known as “the great imitator.” While clinical symptoms of painful defecation, rectal bleeding,

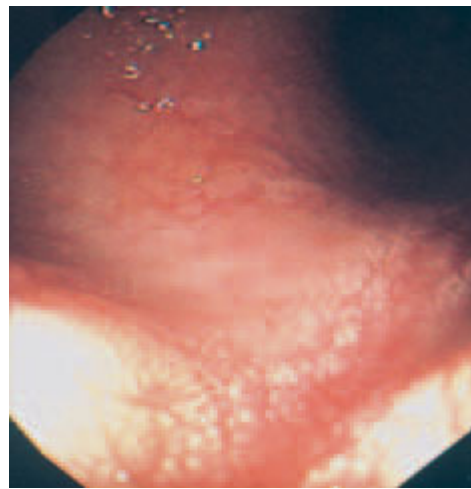


Fig. 49.10 Cryptosporidiosis may cause nonspecific mucosal abnormalities.

mucopus, and tenesmus may be present, many individuals are asymptomatic.

The initial lesion is a painless anal chancre, which progresses to anorectal ulcerations or diffuse confluent involvement of the rectum with mucopurulent discharge [1,60–62]. Dark-field examination of a biopsy or smear of an ulcer demonstrates the presence of spirochetes, and serology confirms the diagnosis. As with primary syphilis, therapy with high-dose benzathine penicillin is the treatment of choice.

Gonorrhea

Neisseria gonorrhoea is the most common cause of proctitis in the male homosexual population related to rectal intercourse. Many patients are asymptomatic, but mild anal pain and burning, bleeding, and mucoid discharge may be seen [63].

Endoscopic findings include edematous, hyperemic rectal mucosal with purulent discharge. Superficial erosions have also been noted (Fig. 49.9). Gram stain of the exudate reveals gram-negative diplococci; culture confirms the diagnosis.

Single-dose treatment options include oral cefixime, ciprofloxacin, and ofloxacin, or intramuscular ceftriaxone. As with gonococcal urethritis and cervicitis, patients should be treated for concomitant *Chlamydia* infection.

Chlamydia

Chlamydia trachomatis is transmitted most commonly via anal intercourse. Infections with lymphogranuloma venereum (LGV) types are most severe, and patients infected with non-LGV strains may be asymptomatic. Symptoms include anorectal pain, discharge, tenesmus,

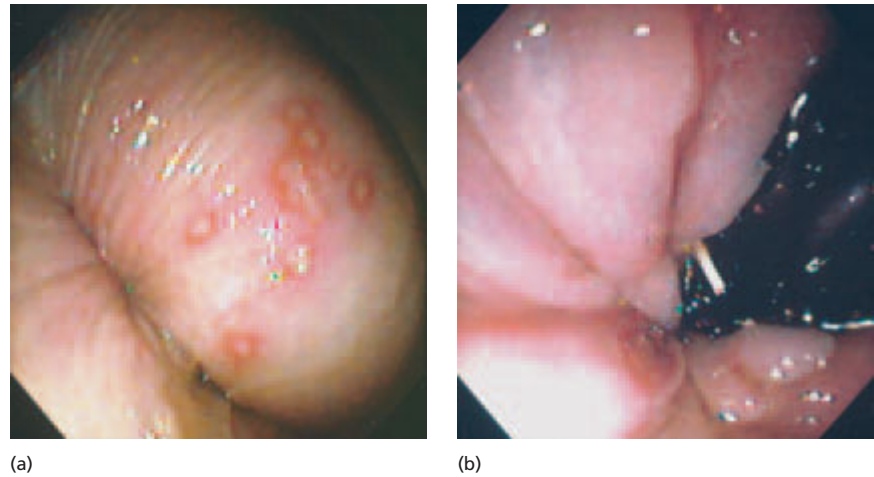


Fig. 49.11 Herpes simplex virus causes typical round ulcerated lesion on the skin (of the buttock) (a), but may also occur inside the rectum as seen in this retroversion view (b).

and bleeding. Fistulas, perirectal abscesses, rectal strictures, and inguinal lymphadenopathy have also been noted [41,64].

Sigmoidoscopic findings vary from nodular or cobblestone appearance to friable, edematous, erythematous mucosa. Histopathology from rectal biopsies shows granulomatous proctitis with crypt abscesses, granulomas, and giant cells [65]. Diagnosis is made by culture of rectal swab sample for *Chlamydia* or by immunofluorescent monoclonal antibody testing.

Treatment options include doxycycline, erythromycin, tetracycline, or single-dose azithromycin.

Herpes

Anorectal herpes simplex virus infection produces a painful proctitis. The combination of external perianal vesicles, rectal lesions, mucosal erythema, friability and ulceration in the distal 10 cm of the rectum is highly suggestive of herpetic proctitis, although similar findings can be seen in other forms of sexually transmitted proctitis, such as LGV, gonorrhea, and syphilis (Fig. 49.11a,b) [79].

Condyloma

Condyloma genital warts caused by the human papilloma virus usually affect the external genital area, but may be seen in the rectum as well (Fig. 49.12a,b).

Idiopathic diarrhea and miscellaneous

Collagenous colitis

Collagenous colitis causes chronic watery diarrhea predominantly in middle-aged women. Crampy abdominal pain and flatulence are often present in this condition, which is often mistakenly diagnosed as irritable

bowel syndrome. Nausea, weight loss, incontinence, and urgency have also been reported. Coexisting arthritis and celiac disease may suggest an autoimmune phenomenon, possibly triggered in some cases by nonsteroidal anti-inflammatory drug (NSAID) use [66].

The gross appearance of colorectal mucosa in collagenous colitis is usually normal. The hallmark of the disease is a characteristic thickened layer of subepithelial collagen (greater than 10 μm) with surface epithelial injury and prominent lymphocytic infiltration in the lamina propria. Because the involvement is patchy, accurate diagnosis requires biopsy samples throughout the colon [67].

Treatment includes avoidance of potential triggers such as NSAIDs. Symptomatic treatment employs the use of nonspecific antidiarrheals, cholestyramine, bulking agents, and antiinflammatory agents such as sulfasalazine and other 5-ASA compounds or oral and topical corticosteroids, including budesonide [75].

Lymphocytic colitis

Lymphocytic colitis is a nonspecific chronic diarrheal syndrome affecting middle-aged individuals. Its clinical picture resembles that of collagenous colitis. However in contrast to collagenous colitis, it affects females and males in equal distribution. While this condition is also felt to be immune mediated, there is no association with NSAID use [68].

Like collagenous colitis, the gross endoscopic appearance is normal. Biopsies from colonic mucosa reveal surface epithelial damage with plasmacytic-lymphocytic infiltrate in the lamina propria. However, the thickened subepithelial collagen band seen in collagenous colitis is absent.

Treatment is similar to that of collagenous colitis. Other therapeutic agents include bismuth subsalicylate and cholestyramine, but the role of immunosuppressants

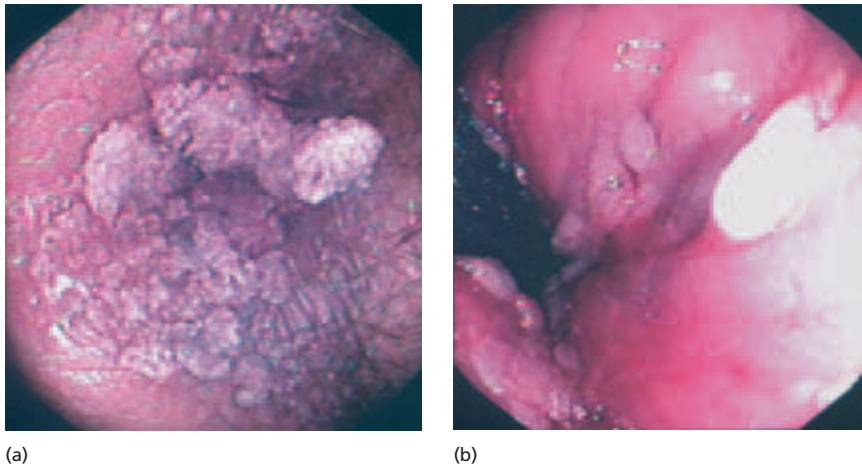


Fig. 49.12 Condyloma usually affects the skin in the genital area (a), but can appear as a verrucous papillary growth in the rectum (b).

such as azathiaprine, and its active metabolite 6-mercaptopurine (6-MP), or cyclosporin is not defined.

Ischemic colitis

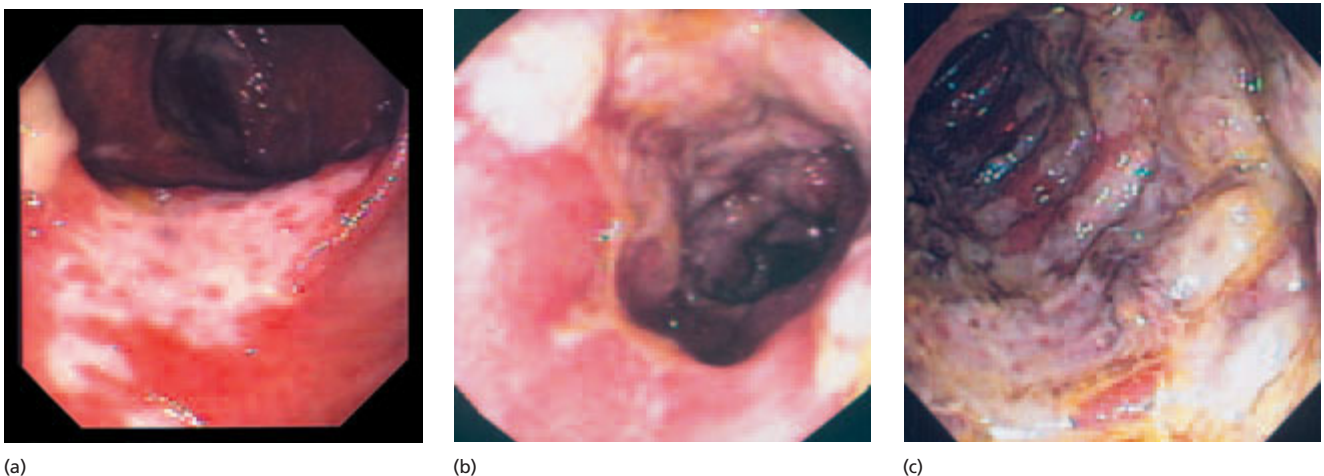
Colonic ischemia typically presents with sudden onset, crampy left lower quadrant abdominal pain, followed by passage of blood or bloody diarrhea within 24 h. Blood loss is usually not severe; hemodynamically significant bleeding argues against the diagnosis of colonic ischemia [1].

Endoscopy, which should be performed within 48 h of presentation, can differentiate ischemic colitis from other colitides, as well as assess the disease extent and severity of involvement. However, colonoscopy is con-

traindicated in patients with suspected gangrene or perforation. Endoscopic findings vary greatly depending upon severity of the ischemia and timing of endoscopy (Fig. 49.13a,b,c). Classically, segmental colitis with rectal sparing is seen, with sharp demarcation between involved and normal colon. While any part of the colon may be affected, the splenic flexure, descending and sigmoid colons are the most common sites of ischemic injury [69]. Initially, edema and purplish blebs of the mucosal and submucosal hemorrhage are seen. This correlates with thumbprinting seen on barium studies. As the hemorrhage is resorbed, friability, inflammation, necrosis, and ulceration can occur. In the acute stage, differential diagnosis includes IBD and infectious colitis (particularly *E. coli* O157:H7), therefore stool cultures for enteric pathogens are necessary. On biopsies, mucosal infarction, ghost cells, and hemosiderin-laden macrophages are pathognomonic for ischemia; vascular congestion with acute or chronic inflammation is more commonly seen.

Approximately 50% will resolve spontaneously with complete recovery. The other half follow three different

Fig. 49.13 Ischemic colitis. (a) Ulcerated mucosa with adjacent normal area. (Courtesy of David M. Martin MD, "Atlas of Gastrointestinal Endoscopy," www.EndoAtlas.com.) (b) Descending colon with diffuse ulcerations and spasm-induced narrowing. (c) Severe damage with loss of the mucosa over a wide area.



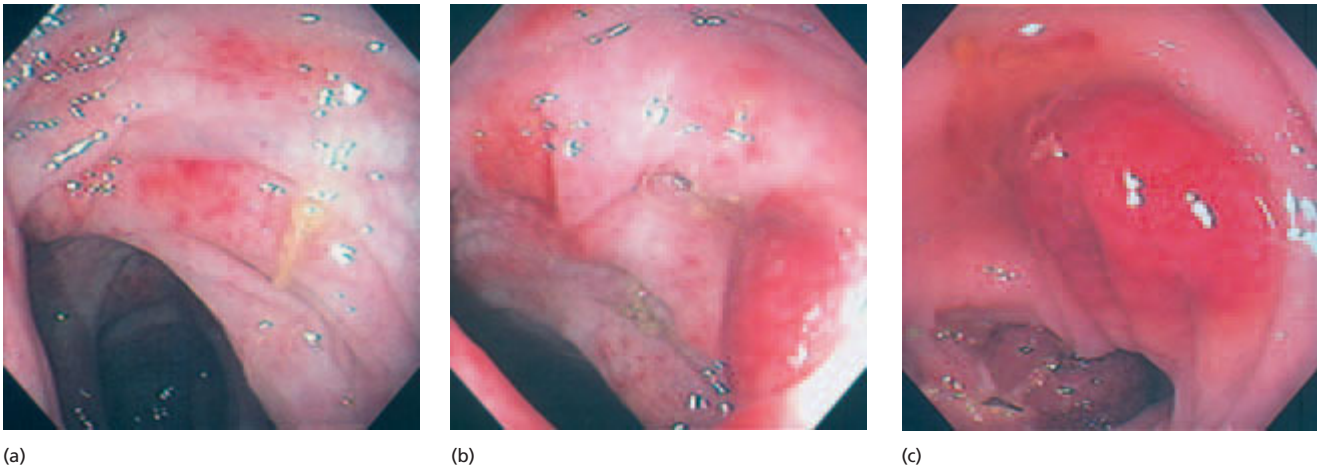


Fig. 49.14 Diverticular disease. (a) Petechial intramucosal hemorrhage may occur from muscular contractions associated with diverticular disease. (b,c) Occasionally, the intramucosal bleeding can be a focus for peristaltic activity, which causes more trauma and the development of large protuberant red folds which are polypoid in appearance.

courses: acute gangrene and perforation, chronic ischemic colitis mimicking IBD [70], and late colonic stricture. Treatment of reversible ischemia is supportive. Repeat colonoscopy or barium studies help determine the outcome of ischemic injury.

Diverticular disease

Acute diverticulitis results from microperforation in a single diverticulum [71]. Patients classically present with left lower quadrant abdominal pain and change in bowel habits. Fever, anorexia, nausea, and vomiting also occur. However, its clinical presentation may sometimes be confused with ischemic colitis, acute appendicitis, IBD, or colon carcinoma.

Colonoscopy is relatively contraindicated during an attack of acute diverticulitis due to risk of perforation from instrumentation or air insufflation [72]. However, when the diagnosis of diverticulitis is unclear, limited sigmoidoscopic examination with minimal air insufflation may be helpful to exclude alternate diagnoses, such as ischemic colitis and pseudomembranous colitis. Classic endoscopic findings include markedly edematous folds and luminal narrowing related to edema and spasm. Petechial-like reddening of intrahaustral folds of affected diverticular segment can also be seen (Fig. 49.14a,b,c) [17]. Fecoliths are frequently encountered, while sites of gastrointestinal hemorrhage are rarely seen. A variant, segmental colitis associated with diverticula, has also been described, with sparing of the remaining colon (Fig. 49.15) [73]. Biopsies from the broad segment of erythematous, friable mucosa are unlike



Fig. 49.15 Diverticular colitis with mucosal inflammation confined to the area of diverticulosis.

IBD in its hemorrhagic infiltration and lack of inflammatory cell response. Hemosiderin deposits may be present in the large reddened folds occasionally seen in diverticular disease.

Treatment includes broad-spectrum antibiotics with adequate gram-negative and anaerobic coverage. After the inflammation from acute uncomplicated diverticulitis resolves, elective colonoscopy is appropriate to exclude luminal malignancy, particularly if a history of weight loss or rectal bleeding raises the suspicion for carcinoma.

Diversion colitis

Diversion colitis occurs in segments of colon diverted from the fecal stream. The underlying cause is believed to be starvation of the colonic mucosa via deprivation of its major energy source, which is luminal short chain fatty acids [76]. Patients are often asymptomatic but may develop rectal bleeding, passage of mucus, tenesmus,

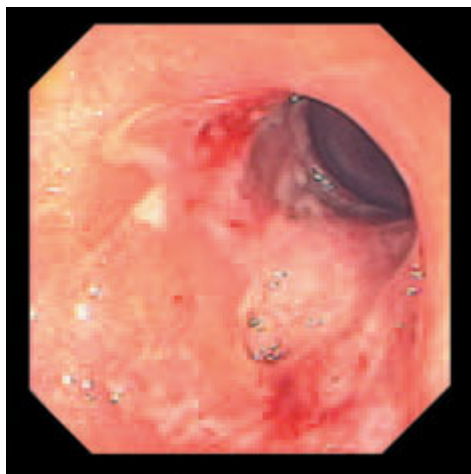


Fig. 49.16 NSAID ulceration of the colon. (Courtesy of David M. Martin MD, "Atlas of Gastrointestinal Endoscopy," www.EndoAtlas.com.)

stricture formation, or fever and abdominal pain. In patients diverted because of IBD, the principle difficulty is in distinguishing diversion colitis from IBD. In patients without IBD, the diagnosis is usually readily apparent based on endoscopic features and histology. The most common endoscopic appearance is diffuse erythema, granularity, loss of vascular pattern, friability, spontaneous bleeding, and small superficial ulcers. The histologic features overlap IBD, though diffuse lymphoid hyperplasia is typical. The treatment of choice is restoration of the fecal stream. The administration of short chain fatty acid enemas is effective but the preparations are foul smelling and often poorly tolerated.

Nonsteroidal antiinflammatory drug colopathy

A complete listing of drug-induced colitides is beyond the scope of this book. In clinical practice, by far the most common cause of drug-induced colonic injury is nonsteroidal anti-inflammatory drugs (NSAID) [77].

NSAID injury can be diffuse but the most common injury has been ulceration (Fig. 49.16) with or without stricture formation in the proximal colon. Isolated ulcers are often located on the ileocecal valve. Diaphragm-like strictures may develop in the right colon. A variety of NSAIDs have been associated with colopathy but diclofenac accounts for a disproportionate percentage of cases. The histologic features are typically non-specific, though occasionally there is a predominant eosinophilic infiltrate. Withdrawal of NSAIDs is the treatment of choice and healing generally occurs within several months.

Melanosis coli

Melanosis coli is a brown discoloration of the colonic mucosa (Fig. 49.17a) that occurs in persons chronically using anthraquinone laxatives, including senna, aloe, rhubarb, frangula, and cascara. The pigment consists of lipofuscin in the macrophages of the lamina propria. The condition is reversible and generally will resolve within a matter of months after laxative withdrawal. Adenomas do not take up the pigment and are easily recognized in a background of melanosis coli (Fig. 49.17b). The condition has no known adverse effects on colonic function.

Radiation colitis (see Chapter 51)

Radiotherapy may cause diffuse changes in the mucosa related to radiation therapy. The areas may bleed, but are not a true "colitis" and are the result of tissue damage and repair. The vascular abnormality is distinctive as a collection of friable angioectasias on the mucosal surface (Fig. 49.18).

Stercoral ulcers

Impacted stool can result in traumatic abrasion of the mucosa and cause ulcerations which may be quite

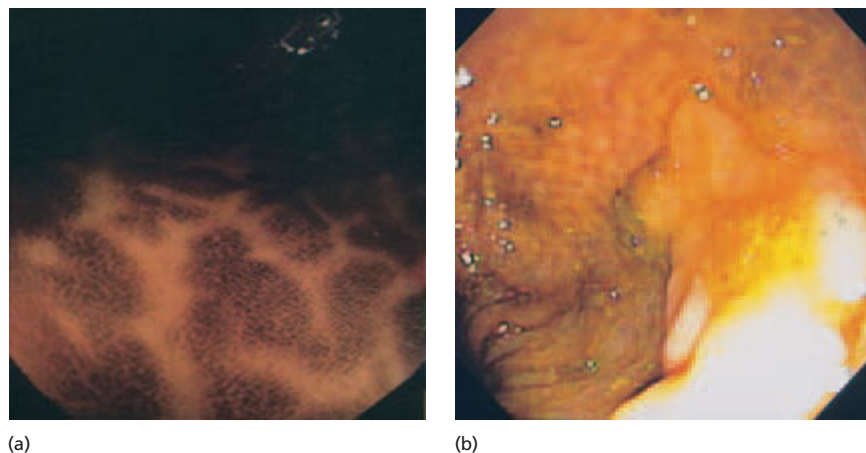


Fig. 49.17 (a) Dark pigmentation in melanosis coli. (b) Mild melanosis coli, but the adenoma is not pigmented.

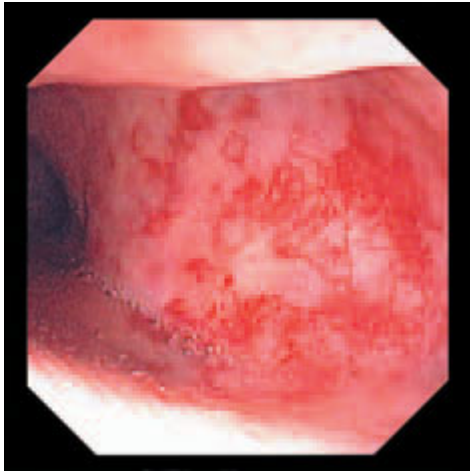


Fig. 49.18 Angioectasias of radiation proctopathy over the prostate gland. (Courtesy of David M. Martin MD, "Atlas of Gastrointestinal Endoscopy," www.EndoAtlas.com.)

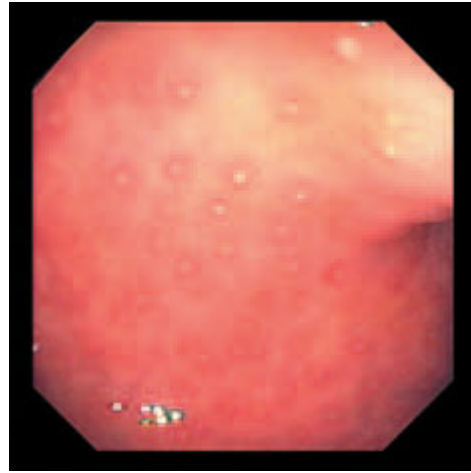


Fig. 49.20 Typical red-ring signs of a phospho-soda prep. as seen in the rectum. (Courtesy of David M. Martin MD, "Atlas of Gastrointestinal Endoscopy," www.EndoAtlas.com.)

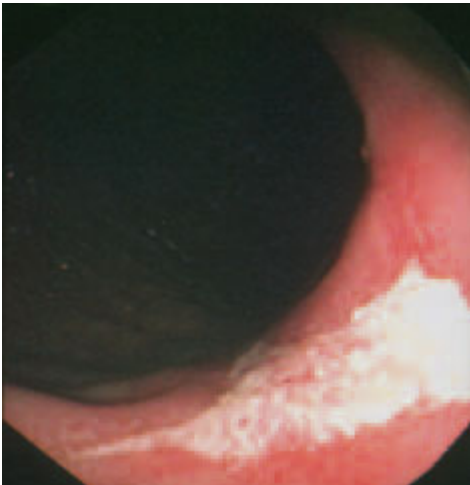


Fig. 49.19 Stercoral ulcer due to fecal impaction.

large. Therapy is dependent on prevention of impaction (Fig. 49.19).

Preparation artifacts

The preparation for colonoscopy can induce mucosal changes in the rectum which could be mistaken for IBD. They are not friable, and regress within days of the procedure (Fig. 49.20).

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Chapter 50

Acute Colonic Pseudo-obstruction

Hubert Nietsch and Michael B. Kimmey

Introduction

Sir William Heneage Ogilvie first described acute colonic pseudo-obstruction (ACPO) in 1948 in two patients with far-advanced intraabdominal malignancies [1]. He was the first to postulate an underlying imbalance between the sympathetic and parasympathic innervation of the colon as the cause of this disorder. Ogilvie's patients, however, developed subacute symptoms over the course of 2 months and thus represent an atypical presentation of what we now recognize as ACPO. The hallmark features of ACPO consist of acute colonic dilation in the absence of a mechanical etiology. This condition is increasingly recognized and is associated with substantial morbidity and mortality.

Epidemiology and predisposing factors

The exact incidence of ACPO in hospitalized patients is unknown. Vanek and Al-Salti [2] analyzed 400 cases of ACPO and found that it occurred most commonly in the sixth decade and was more common in men than women. More than 90% of patients had significant comorbid disease, thought to be contributing to the syndrome. About 50% of cases occurred in the post-operative state. The diverse underlying medical and surgical problems associated with ACPO are listed in Table 50.1.

Pathophysiology

The pathophysiology of ACPO is still not entirely understood but there is evidence of an imbalance between the sympathetic and parasympathic nervous system, which leads to a functional obstruction caused by atony of the distal colon followed by progressive dilation of the cecum and ascending colon [1,3].

Ogilvie favored the sympathetic deprivation theory, leading to unopposed parasympathic stimulation and thereby resulting in "excessive and probably incoordinated contraction" of the distal colon [1] mimicking obstruction. More recent theories postulate either an impairment of the sacral parasympathetic outflow [3–5] or excessive sympathetic stimulation [6,7]. The clinical

presentation of ACPO resembles Hirschsprung's disease, supporting the hypothesis of impaired parasympathetic function [5], which is also supported by the commonly observed transition point at the level of the splenic flexure. The parasympathetic innervation of the colon distal to the splenic flexure is via the pelvic splanchnic nerves whereas the more proximal colon is innervated by the vagus (Fig. 50.1).

The proponents of the sympathetic stimulation theory [6,7] argue that right-sided colonic motility is impaired

Table 50.1 Causes of acute colonic pseudo-obstruction [2,11,17,18,33,45–50].

<i>Neurologic</i>	<i>Neoplasia</i>
Parkinson's disease	Retroperitoneal
Alzheimer's disease	Metastatic cancer
Cerebrovascular accident	
Multiple sclerosis	<i>Post surgical</i>
Spinal cord disease	Cardiac surgery
Craniotomy	Cesarian section
	Gynecologic surgery
<i>Cardiovascular</i>	Pelvic surgery
Myocardial infarction	Organ transplantation
Congestive heart failure	Orthopedic surgery
Post cardiac arrest	
	<i>Post traumatic</i>
<i>Respiratory</i>	Pelvic trauma
Pneumonia	Spinal cord injury
Mechanical ventilation	Femoral fracture
Acute respiratory distress syndrome	
	<i>Drugs</i>
<i>Metabolic</i>	Narcotics
Hyponatremia	Tricyclic antidepressants
Hypocalcemia	Phenothiazines
Hypomagnesemia	Antiparkinson agents
Liver failure	Calcium channel blockers
Renal failure	Benzodiazepines
Hypothyroidism	Clonidine
	Vincristine
<i>Infective/inflammatory</i>	
Acute cholecystitis	
Pelvic abscess	
Spontaneous bacterial peritonitis	
Acute pancreatitis	
Sepsis	
Herpes zoster	
Appendicitis	

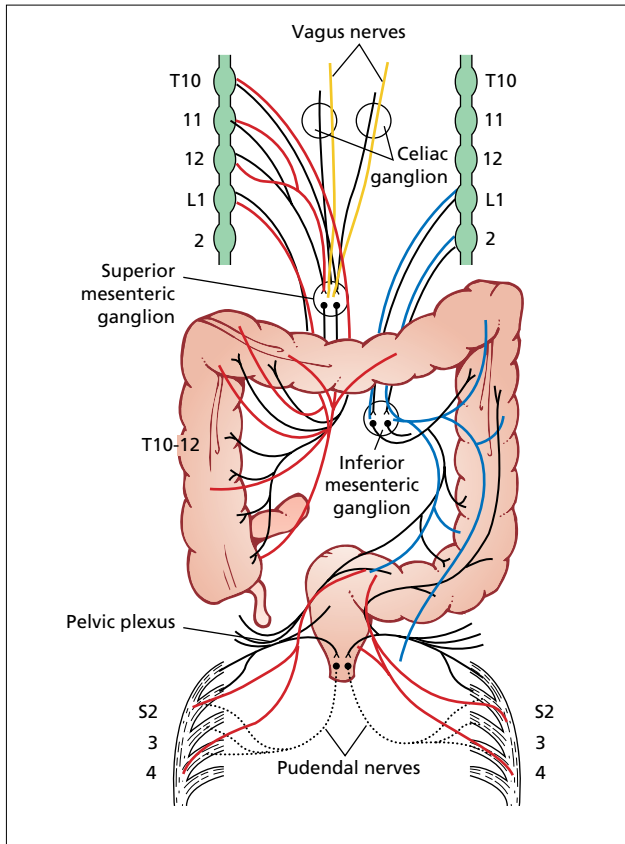


Fig. 50.1 Schematic diagram illustrating colonic innervation. Parasympathetic pathways (stimulatory/prokinetic): prevertebral ganglia and sacral nerves (red) and vagus (yellow). Sympathetic pathways (inhibitory): thoracic spinal cord to inferior mesenteric plexus and pelvic plexus (green).

by excessive sympathetic inhibition. This theory is supported by animal experiments performed in the 1920s and 1930s [8] showing increased colonic peristalsis after spinal anesthesia, which leads to a temporary paralysis of sympathetic input. This was the rationale for the induction of spinal anesthesia as a successful treatment of adynamic ileus in Europe in the 1920s.

Clinical presentation

ACPO is usually seen in middle-aged to elderly critically ill patients in the intensive care unit or postoperatively and is exacerbated by immobility and narcotic pain medications. Symptoms usually develop gradually over 3–7 days. Significant abdominal distension is seen in all patients, associated with pain (83%), vomiting (57%), constipation (51%), and fever (37%). The bowel sounds are variable and can be normal or hyperactive (40%), hypoactive (31%), high-pitched (17%), or absent (12%) [2]. If peritoneal signs are present, transmural ischemia or perforation should be suspected.

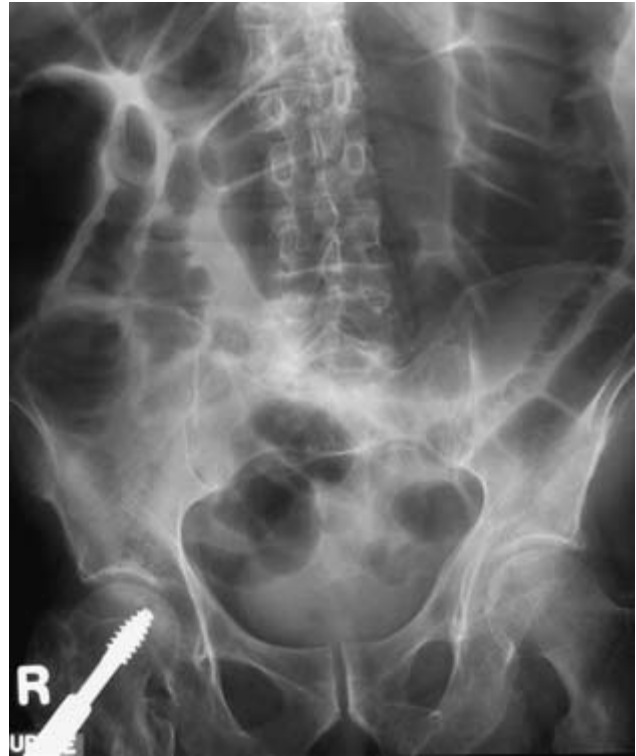


Fig. 50.2 Abdominal radiograph of patient with acute colonic pseudo-obstruction following internal fixation of a fractured femur.

Diagnosis

Abdominal examination shows significant distension in all patients, with variable degrees of tenderness. The presence or quality of bowel sounds is also variable. Peritoneal signs are suggestive of transmural ischemia or perforation and mandate surgical consultation.

The diagnosis is confirmed by plain abdominal radiographs, which typically show significant distension of the colon with predominance of the right side in the absence of mechanical obstruction (Fig. 50.2). A cut-off sign at the splenic flexure is frequently observed [5].

Initial studies suggested that a cecal diameter of greater than 12 cm increases the risk of perforation substantially [9]. The case series by Vanek and Al-Salti [2] reported no cecal perforation with a cecal diameter < 12 cm, 7% perforation risk with cecal diameters of 12–14 cm, and 23% perforation risk with a cecal diameter > 14 cm. However, more recent reports suggest that the duration of significant cecal dilation is more predictive of ischemia than the cecal diameter *per se* [10].

A water-soluble contrast enema should be cautiously performed to confirm the functional etiology, if a mechanical obstruction (absence of rectal air) cannot be entirely excluded by the initial radiographs. Barium should not be administered, because this could

complicate surgery if perforation is present and endoscopic decompression if this is required.

Complications

The dreaded complication of progressive colonic dilation is transmural ischemia followed by perforation. However, the frequency of this complication, which requires emergency colonic resection, has significantly decreased in recent case series. The risk of perforation was initially reported to be as high as 13% with a mortality of 43% [11]. A summary of more recent studies shows a perforation risk of 3% [12]. The surgical mortality may be as high as 40–50%, if perforation occurs [13].

Management

Supportive medical care

Initial management for the first 24–48 h is conservative, with close attention to correcting any fluid and electrolyte imbalances that may be present. The medication list should be carefully scrutinized and drugs that might delay intestinal transit, such as anticholinergics or opiates, should be discontinued if possible [14]. The abdominal examination needs to be followed carefully and daily abdominal radiographs obtained to monitor for progressive dilation and evidence of perforation. The introduction of a nasogastric tube for decompression is advisable for most patients, and in selected cases a rectal tube might also be of help. Mobilization of the patient with frequent turning might facilitate the passage of flatus. Success rates of supportive management are variable but can be as high as 96%, as reported in a cohort of cancer patients from Sloan-Kettering Cancer Center [15].

Pharmacotherapy

When colonic dilation persists or progresses despite conservative therapy, specific pharmacotherapy to stimulate the parasympathetic innervation of the colon should be attempted (Table 50.2). Catchpole [16] first proposed the combined use of a sympathetic blocker (guanethidine) followed by a cholinesterase inhibitor (neostigmine) to correct the sympathetic/parasympathetic imbalance. Subsequent small case series suggested that a majority of patients with ACPO could be effectively treated using neostigmine [17–19].

A double-blind, randomized, placebo-controlled clinical trial reported by Ponec and colleagues [20] conclusively showed a dramatic improvement of clinical status and colonic distension in the majority of patients treated with intravenous neostigmine, making endoscopic intervention unnecessary in most cases. In this study, patients were treated with 2 mg of neostigmine administered over a few minutes by slow intravenous push. Patients were monitored continuously by electrocardiography with atropine available at the bedside, as symptomatic bradycardia is the most significant adverse effect of this treatment. Of 11 patients who received neostigmine, 10 (91%) had prompt colonic decompression with a median time to response of only 4 min, whereas none of the patients receiving placebo (saline) had a clinical response. Seven patients in the placebo group and the one patient in the neostigmine group who failed initial response received open-label neostigmine 3 h after the initial infusion, with prompt colonic decompression noted in all patients. Only two patients developed recurrent symptoms requiring colonoscopic decompression [20].

Several studies have since confirmed the safety of neostigmine for the treatment of ACPO, reporting

Medication	Reference	Number of patients	Initial decompression (%)	Recurrence (%)
Erythromycin	Armstrong <i>et al.</i> [27]	2	100	0
	Bonacini <i>et al.</i> [28]	1	100	0
	Rovira <i>et al.</i> [29]	2	100	0
Cisapride	MacColl <i>et al.</i> [7]	1	100	0
	Pelkmans <i>et al.</i> [30]	2	0	0
	Mazloum <i>et al.</i> [31]	1	100	0
Neostigmine	Hutchinson & Griffiths [17]	11	72	0
	Stephenson <i>et al.</i> [18]	12	83	16
	Turegano-Fuentes <i>et al.</i> [19]	16	75	0
	Ponec <i>et al.</i> [20]	21	81	11
	Paran <i>et al.</i> [21]	11	82	0
	Trevisani <i>et al.</i> [22]	28	93	0
	Abeyta <i>et al.</i> [23]	8	87	0
	Van der Spoel <i>et al.</i> [24]	24	79	0

Table 50.2 Reports of pharmacotherapy of acute colonic pseudo-obstruction.

successful colonic decompression in 79–93% of cases. Several different neostigmine infusion protocols have been used, including 2-mg and 2.5-mg intravenous boluses and 2.5 mg administered over 60 min [21–24], all with similar success rates.

Recurrence of colonic distension following successful decompression using neostigmine occurs in up to 16% of patients. In these situations, neostigmine can be safely readministered, leading to colonic decompression in approximately two-thirds of cases [21,23].

The observed adverse effects of neostigmine, like other cholinesterase inhibitors, include excessive salivation (38%), vomiting (9%), abdominal pain (62%), bradycardia (9%), and bronchospasm. Patients must therefore be closely monitored during drug administration with continuous electrocardiography and atropine available at the bedside [20]. Symptomatic bradycardia responds to administration of atropine, but this also leads to a reversal of any benefit of neostigmine in relieving colonic dilation. The coadministration of glycopyrrolate, an antimuscarinic anticholinergic agent, seems to decrease the incidence of bradycardia without reducing neostigmine’s efficacy [25,26].

Suitable candidates for neostigmine administration are hence patients with ACPO who have no evidence of mechanical bowel obstruction, a resting heart rate greater than 60 beats per minute with a systolic blood pressure greater than 90 mmHg, and no active bronchospasm [14,20]. Neostigmine is contraindicated in patients on β-blockers and those who have significant acidosis or recent myocardial ischemia, because of the risk of inducing cardiac arrhythmias [18].

Anecdotal case reports with other prokinetic agents show variable success rates in the treatment of ACPO. Intravenous erythromycin, which acts as a motilin receptor agonist, showed some success in a total of five reported cases [27–29]. The efficacy of intravenous cisapride, no longer available in the USA, was highly variable in case reports of five patients [7,30,31].

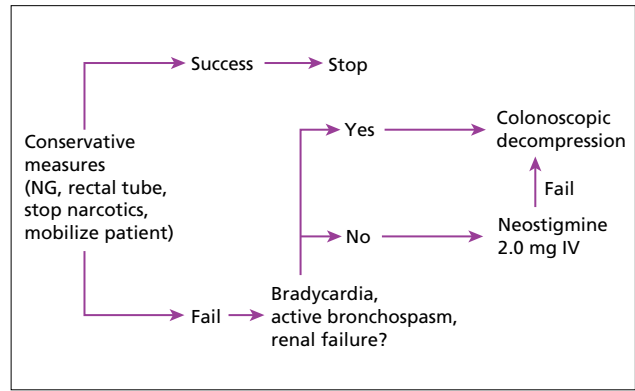


Fig. 50.3 Algorithm for management of acute colonic pseudo-obstruction.

The new 5-hydroxytryptamine 5-HT₄ receptor agonists (tegaserod, prucalopride) might be theoretically useful for stimulating colonic motility in the setting of ACPO, but no data are yet available with the use of these medications in ACPO [14].

Colonoscopic decompression

Pharmacologic treatment of ACPO has markedly reduced the need for urgent colonoscopic decompression. While previously considered to be the treatment of choice for progressive colonic dilation, it is now usually reserved for patients who have failed treatment with neostigmine (Fig. 50.3). No randomized comparative studies of colonoscopic decompression with neostigmine or other treatment modalities are available. A summary of 11 retrospective studies involving 264 patients shows a high initial success rate for colonoscopic decompression (64–100%), with an average recurrence rate of 23% (range 13–65%) (Table 50.3). Complications were reported in 3% [32,33]. The largest single-center series from the Mayo Clinic shows a similar experience in 50 patients, with an overall success rate of 88% complicated

Table 50.3 Reports of colonoscopic decompression of acute colonic pseudo-obstruction.

Reference	Number of patients	Initial success	Recurrence	Complications (death)	Surgery
Kukora & Dent [51]	6	5 (83%)	0	0	1 (17%)
Nivatvongs <i>et al.</i> [5]	22	19 (86%)	4 (21%)	0	4 (18%)
Strodel <i>et al.</i> [35]	44	32 (73%)	5 (13%)	5% (2%)	9 (20%)
Starling [52]	17	17 (100%)	3 (18%)	12%	0
Bode [55]	22	20 (91%)	4 (20%)	5% (5%)	3 (14%)
Nakhgevany [53]	10	9 (90%)	0	0	1 (10%)
Fausel & Goff [54]	12	11 (91%)	3 (25%)	0	2 (17%)
Nano <i>et al.</i> [47]	17	13 (76%)	6 (46%)	0	0
Gosche <i>et al.</i> [32]	19	17 (89%)	11 (65%)	5%	2 (11%)
Jetmore <i>et al.</i> [33]	45	29 (64%)	13 (29%)	0	5 (11%)
Geller <i>et al.</i> [34]	50	39 (78%)	9 (18%)	2% (2%)	1 (2%)
Total	264	83%	23%	3% (1%)	11%

by one procedure-related perforation. The overall hospital mortality is 30% [34].

Colonoscopic decompression is technically more challenging compared with routine colonoscopy since the colon is unprepared and the patients are often critically ill, necessitating performance of the procedure in an intensive care unit. Enemas are not very helpful in preparation for colonoscopy and should be done gently, if at all, due to the risk of perforation. Liquid stool must be suctioned and irrigated at the time of colonoscopy in most cases. Air insufflation should be kept to a minimum to prevent further cecal dilation, which could potentially precipitate perforation. It is important to reach the hepatic flexure in order to achieve significant decompression, although cecal intubation is not required [35]. Jetmore and colleagues [33] reported that colonic decompression was almost twice as successful if the ascending colon was reached (initial success 71% vs. 37%). If mucosal changes suggestive of acute ischemia are encountered, the procedure should be terminated and the patient referred for emergency colectomy. The overall decrease in cecal diameter following colonoscopic decompression

is generally quite modest, with an average reduction of only 2 cm [36].

Up to 40% of patients develop recurrence of colonic distension after initial successful colonoscopic decompression. This led to the introduction of decompression tubes, which are inserted at the time of the initial procedure. Harig and colleagues [37] performed a randomized trial in 20 patients comparing endoscopic decompression alone vs. additional insertion of a modified enteroclysis catheter and demonstrated a reduction in the recurrence of colonic dilation from 44% to 0%. Decompression tubes remained in place for an average of 3–4 days without any reported complications.

The two most commonly used decompression tubes are a modified enteroclysis catheter, with additional side holes at the tip or a 14F colon decompression kit (Wilson-Cook Medical, Winston-Salem, NC). A flexible guidewire is placed through the endoscope channel and the tip is directed into the cecum under fluoroscopy. The endoscope is then slowly withdrawn leaving the wire in place. Fluoroscopy is helpful in keeping the wire straight during complete withdrawal of the colonoscope. The decompression tube is then advanced under fluoroscopic guidance, using traction on the wire to keep it straight while the tube is advanced. The decompression tube is then taped to the patient's buttock and connected to low intermittent suction. It is advisable to flush the tube with water every 4 h to prevent clogging with stool.

Fig. 50.4 (a) Abdominal radiograph of patient with acute colonic pseudo-obstruction following bone marrow transplantation for leukemia. (b) Abdominal radiograph of same patient immediately following colonoscopy at which time a 14F decompression tube was placed.



The patient's clinical status should be followed carefully with daily abdominal radiographs (Fig. 50.4). The catheters are usually left *in situ* for 2–4 days, until colon decompression is complete and underlying reversible contributors to ACPO are reversed. Use of larger tubes up to 40F in diameter (Levacuator, Mallinckrodt Medical, St Louis, MO) has been described in case reports, with more rapid decompression and less tube clogging [38]. A minority of patients may not respond to these measures and if there is suspicion of acute ischemia or perforation the patient should be referred for immediate surgery.

Percutaneous cecostomy

In the absence of ischemia or perforation, percutaneous cecostomy (PCC) should be considered as a minimally invasive alternative to surgery in those critically ill patients where induction of general anesthesia poses a significant risk. Both transperitoneal and retroperitoneal approaches for PCC have been described [39–41]. The early work by VanSonnenberg and colleagues [42] showed the technical feasibility and safety of PCC tubes. The theoretically safer retroperitoneal approach did not lead to a lower risk of peritonitis than the anterior transperitoneal approach [42]. The technique was recently refined by using additional T-fasteners, which allow for better colonic apposition to the abdominal wall, thereby potentially reducing the risk of fecal soilage of the abdominal cavity [43]. No studies comparing the efficacy and safety of pharmacotherapy, endoscopic intervention, radiographically guided PCC, and surgery are available.

Surgery

Peritoneal signs or free air on abdominal radiography are clear indications for laparotomy and colectomy [2]. The definitive surgical management depends on the viability of the cecum and ascending colon at the time of exploration. Partial colectomy is indicated for transmural ischemia and perforation but carries a high mortality in these critically ill patients. Surgical decompression in the absence of perforation, through an open or laparoscopic cecostomy, is an alternative to colectomy if the local expertise is not available to perform computed tomography-guided PCC [44].

Prognosis

The overall mortality of ACPO remains approximately 30%, despite the recent advances in its management [2,34]. This reflects the severity of the underlying disease process leading to ACPO and is not directly related to the colonic complications. The impact of pharmacologic therapy on the outcome of patients with ACPO has not yet been fully assessed.

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Chapter 51

Radiation Proctopathy

Christopher J. Gostout

Introduction

Radiation proctopathy can be a disabling delayed outcome of radiation therapy directed at pelvic malignancies. Rectal outlet bleeding can be severe enough to result in anemia and transfusion dependency. Bleeding typically develops from 6 months to 1 year after completion of radiation therapy and is due to friable mucosal angiectasias. Although many approaches to controlling bleeding from chronic radiation proctopathy have been attempted, ranging from topical enema formulations to surgical diversion of the rectum, endoscopic coagulation therapy is effective and the easiest to use successful therapy. This chapter discusses the issues surrounding the development of chronic bleeding due to radiation proctopathy and focuses on endoscopic methods of treatment.

Radiation proctopathy (a better term than “radiation proctitis”) is a frustrating problem for patients and managing physicians. Radiation therapy (external beam and intracavitary) is a common modality of treatment for pelvic malignancies, especially with supervoltage techniques and computerization for modeling dosimetry. Malignancies of the uterus, prostate, cervix, bladder, and rectum as well as lymphomas are treated with pelvic radiation. The rapidly dividing mucosa of the gastrointestinal tract is vulnerable to radiation, with the entire colon, rectum, and pelvic small bowel susceptible to injury. Although the rectal mucosa is more resistant to the damaging effects of radiation compared with the rest of the colon and small bowel, because of its proximity to the uterine cervix and prostate, the rectum is the most common gastrointestinal organ to be affected by pelvic radiation (> 90%) [1]. In addition to the close anatomic relation of the rectum to the pelvic organs, the rectum is in a fixed position within the pelvic field of radiation. Fixed organs are generally more likely to be damaged by radiation compared with mobile organs such as the small bowel, where peristalsis causes different portions of the intestine to move in and out of the field of radiation.

Acute radiation injury is common and typically occurs during radiation [2]. The findings within the rectum are consistent, with a proctitis with mucosal edema, ulceration,

erythema, and spontaneous bleeding. Histologic findings include mucosal cell loss, acute inflammation, eosinophilic crypt abscesses, and endothelial swelling of arterioles. Most patients recover but some progress to a chronic stage. Radiation proctopathy is diagnosed when there are rectal mucosal changes and clinical symptoms that develop 3–6 months after completion of therapy [3,4]. The frequency of this late complication varies from 5 to 20% in different series [4,5].

The clinical features of radiation proctopathy include diarrhea, tenesmus, rectal pain, rectal bleeding (low grade or severe), stricture, and fistulae into adjacent organs [6]. Rectal bleeding can be daily or episodic, with multiple passages of blood and clot. Incontinence of blood is a common complaint.

The endoscopic findings of radiation proctopathy include mucosal pallor, friability, spontaneous oozing, angiectasia, and rarely ulceration (Fig. 51.1) [7]. The angiectasias are the hallmark findings distinctive for this disorder. These endoscopic features begin at the dentate line and typically occupy the distal rectum (Fig. 51.2). An occasional patient may have sigmoid involvement, typically women whose radiation has been directed higher in the pelvis, which has implications regarding treatment strategy and outcomes (Fig. 51.3) [8]. The histology of this late sequela includes fibrosis within the lamina propria and endarteritis of the arterioles [2].

Treatment approaches for radiation proctopathy

Rectal bleeding is the most vexing problem for which endoscopic treatment is sought. A variety of treatment regimens have been attempted without objective data to support efficacy. Steroids (oral and by retention enema), sulfasalazine, 5-aminosalicylic acid preparations (oral and enema), sucralfate enemas, sodium pentosan-polysulfate PPS (synthetic sulfated polysaccharides), hyperbaric oxygen, short-chain fatty acids, nutritional therapy, and even angiographic embolization (despite the ischemic origins postulated and even observed) are among the various treatments attempted for radiation proctopathy [3,9–13]. Sucralfate enemas have been

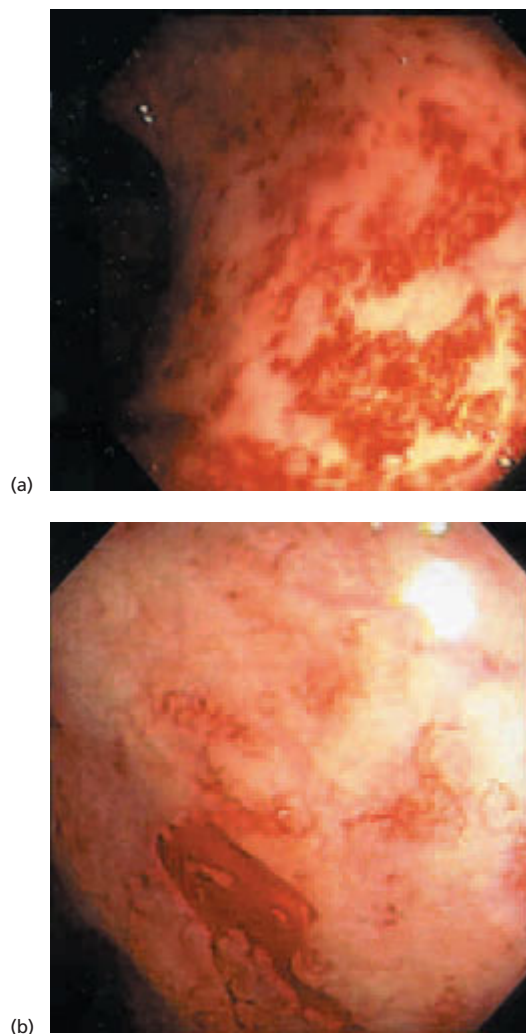


Fig. 51.1 Angiectasias of radiation proctopathy can vary in presentation within the distal rectum: (a) dense vascular lesions with coalescence; (b) scattered infrequent lesions.

shown to offer benefit in a small randomized and short follow-up trial compared with oral sulfasalazine and steroid enemas [9].

Surgery is reserved for intractable cases as a last resort and also for obstruction, perforations, and fistulae [6]. Surgical treatment is approached individually and has consisted of diverting colostomy and resection with potential coloanal pull-through anastomosis [14]. The morbidity of surgery is significant and complications as high as 79% have been reported [15].

Endoscopic therapy has become the favored intervention for control of bleeding. Laser phototherapy was first described by Leuchter and colleagues in 1982 [16] and since then confirmed by different experiences to be a useful method to treat the friable angiectasias. The rationale of endoscopic therapy has been to eradicate the many angiectatic lesions using either direct coagu-

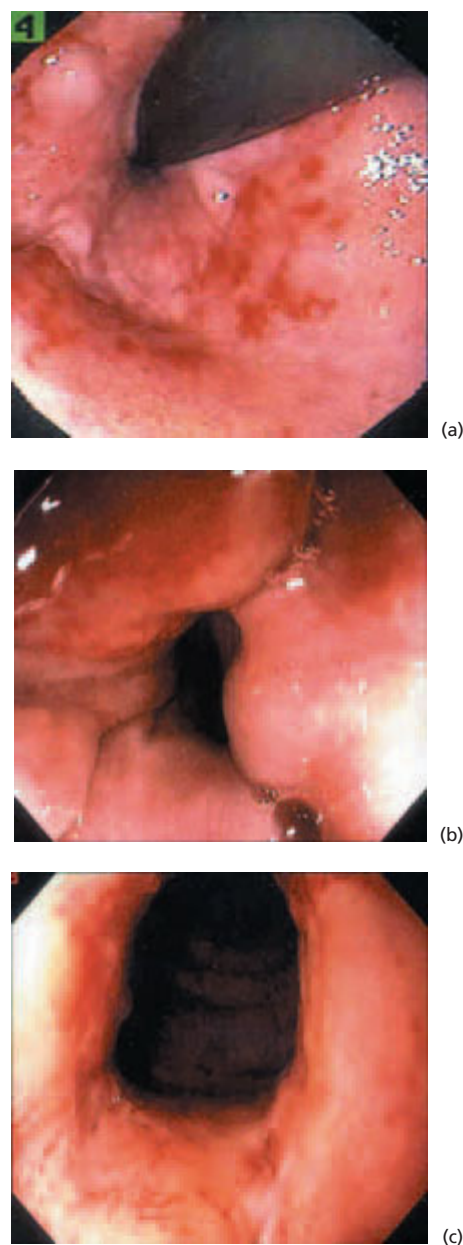


Fig. 51.2 Angiectasias typically extend down to the dentate line and can be approached from (a) retroflexed or (b,c) straight viewing positions.

lation or panmucosal injury (e.g. topical formalin). Both general methods are intended to eventually induce scarification of the mucosa to prohibit the reformation of angiectasias. The Nd:YAG and argon laser have been the most commonly used early reported methods followed by bipolar electrocoagulation and argon plasma coagulation [8,17–29]. Dilute formalin can be instilled into the rectum via an enema or directly applied during proctoscopy or flexible sigmoidoscopy [30–36]. On follow-up after endoscopic therapy, the number of angi-



Fig. 51.3 Segmental involvement of the distal sigmoid above and separate from the distal rectal lesions.

Table 51.1 Criteria for selection of ideal patients for endoscopic coagulation.

Chronic hematochezia
Transfusion-dependent anemia for 6 months or longer
Bleeding refractory to medical management
No active nonrectal bleeding source
No tumor recurrence
No postradiation fistulae, ulceration, or strictures

Table 51.2 Assessment of the efficacy of treatment for chronic radiation proctopathy.

Decrease in rectal bleeding
Patient satisfaction (quality-of-life improvement)
Increase in hemoglobin level
Reduction in transfusion requirements
Reduction in hospital admissions
Improvement in endoscopic appearance

ectatic lesions are noticeably diminished or completely eradicated and mucosal friability may also disappear.

Criteria for selection of ideal patients for endoscopic coagulation have been described and are shown in Table 51.1. Assessment of the efficacy of endoscopic therapy can be based on the criteria listed in Table 51.2. However, "patient satisfaction" has not been directly assessed by quality-of-life measures.

Endoscopic therapy

Endoscopic therapy can be carried out in the outpatient setting. It is important to perform an initial complete

colonoscopy to assess the extent of involvement (rectum and/or sigmoid) and to seek other causes of bleeding. A formal bowel preparation is needed when electrocoagulation (bipolar or argon plasma coagulation) is to be used in order to eliminate the risk of gaseous explosion.

In the patient with bleeding from radiation proctopathy, the angiectasias within the distal rectum are extremely friable, with bleeding induced by the slightest contact of any instrument or device. This degree of friability generated the interest in noncontact therapy with laser photocoagulation as an alternative to the traditional thermal contact methods of endoscopic treatment. Because of its portability, safety, and excellent results, the argon plasma coagulator has become an alternative noncontact method to the laser.

There are three critical aspects of endoscopic therapy that are applicable to all the treatment methods and worthy of emphasis prior to the discussion of each treatment approach. Consideration of these key points will improve the outcome of the experience for both the endoscopist and the patient.

1 *Endoscope selection* has not been formally studied. The use of a gastroscope has intuitive advantages, chiefly the small caliber of the insertion tube. This minimizes unwanted contact-induced bleeding due to straight and retroflexed tip positions, permitting greater atraumatic maneuverability within the rectum. The narrow radius of the retroflexed tip also enhances access to the lesions at and immediately above the dentate line.

2 *During thermal therapy, use the least amount of coagulating energy* (Fig. 51.4). This will avoid creating deep, slowly resolving, and invariably problematic thermal ulcers (Fig. 51.5). Such ulceration can cause bleeding that may exceed the bleeding experienced prior to endoscopic therapy. Bleeding is from the margins of these ulcers and is not amenable to any endoscopic intervention. The ulcers are usually associated with troublesome rectal and perineal pain. There is no treatment for the symptomatic thermal ulcer other than time to allow healing. Overtreatment should be avoided when coagulated areas bleed lest deep thermal injury result. Often bleeding will stop by washing and waiting for reactive edema to appear. Nothing further should be done if the treated site appears to be adequately coagulated with a uniform white coagulum. Minimization of excessive thermal energy will eliminate the development of strictures as well.

3 *The goal is to treat all the angiectasias in each session.* Changing the patient's position from the more common left lateral decubitus may allow access to lesions obscured by pooled materials. Cleansing accumulating blood and clot continuously will avoid obscuring the treatment site and also prevent inadvertent coagulation of adherent blood mistaken for vascular lesions, as only vascular lesions should be coagulated. More widespread

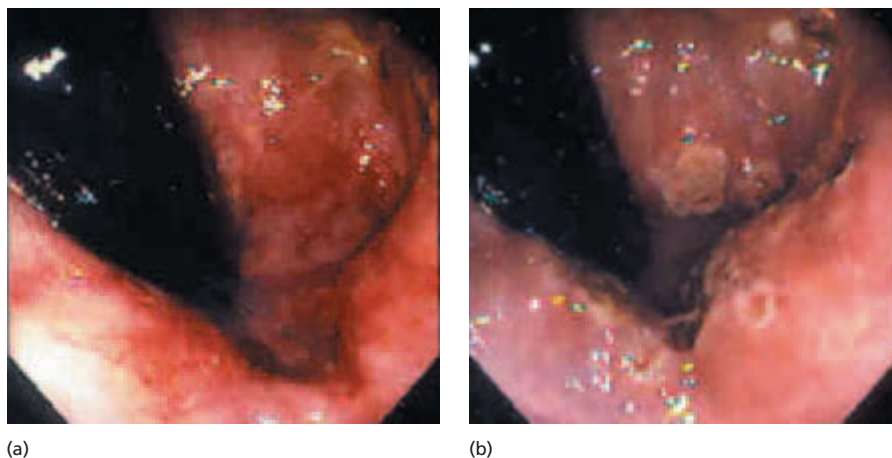


Fig. 51.4 (a) Before and (b) after argon plasma coagulation. Note that a white coagulum ablates the angiectasia. Charring and cavitating the mucosa should be avoided.



Fig. 51.5 Thermal ulceration complicating argon plasma coagulation. This ulceration is typically deep, accompanied by anal pain, and gives rise to refractory bleeding. Some may heal in time.

coagulation of surrounding mucosa will increase the risk for stricture and ulceration. Angiectasias must be treated down to the dentate line. Failure to do so is a common reason for “refractory bleeding.”

Once bleeding has been controlled, patients may direct their attention to nonbleeding symptoms, which include frequent stooling, tenesmus and, particularly, urgency.

Laser therapy

The Nd:YAG laser with a wavelength of 1.06 nm has a depth of penetration of up to 5 mm compared with 2 mm for the argon and KTP (potassium titanyl phosphate) 532 nm lasers. The monochromatic light energy from these lasers is absorbed more efficiently by the darker ectatic blood vessels as opposed to the surrounding non-vascular mucosa [8]. Argon laser energy is preferentially

absorbed by red-colored or pigmented tissues as is the light energy of the KTP device [37].

With the Nd:YAG laser, the lowest power setting should be used with a maximum pulse duration of 0.5 s. A starting power of 40 W per pulse can be used, with further reductions by 5 W if there is cavitation or charring at any treatment site. The tip is maintained at a distance of 1 cm or less from the mucosal surface. All visible lesions are coagulated in a proximal to distal sequence. Dependent portions are treated first to avoid pooling of blood and suboptimal access to the vascular lesions. Tangential distal lesions, if difficult to approach by the noncontact method, can be conveniently treated by contact coagulation using a heater probe (Olympus America, Mellville, NY) or bipolar electrocautery probe. Angiectasias clustered at and just above the dentate line present the greatest challenge to noncontact laser photocoagulation. They are best approached from a retroflexed position. Frequent decompression of the colon to prevent gaseous distension is necessary for patient comfort. As mentioned above, all visible lesions should be treated in each treatment session. The argon laser can be used at a power setting of 3–8 W with similar short pulse durations.

After the initial endoscopic coagulation session, the patient should be given a sufficient amount of time to allow the coagulated areas to heal. The treatment sites will ulcerate and can bleed. This usually occurs several days to a week following the treatment and after an initial period of absent bleeding. It is important to inform patients of this sequence and encourage patience. A practical interval for follow-up that will allow healing of treatment sites, cessation of treatment-induced bleeding, and an accurate assessment of residual lesions is 3 months. If at any point the patient notices resolution of bleeding or a marked reduction of bleeding to trivial and episodic amounts, with cessation of transfusion needs and anemia, then supplemental treatment can be avoided.

Results of laser treatment

The largest series of 47 patients reported a decrease of daily rectal bleeding from 87% of patients to 11% ($P < 0.001$) [8]. The median duration of rectal bleeding before treatment was 11 months despite previous medical treatment (98%) or bypass colostomy (6%). The median hemoglobin level increased from 9.7 to 11.7 g/dL ($P < 0.001$). Transfusion dependence decreased from 57% of patients to 9% after laser treatment ($P < 0.01$). In another series of eight patients using Nd:YAG laser therapy, there was a decrease in the average transfusion requirements and hospital admissions throughout the entire follow-up period subsequent to the first laser treatment [17]. In a series of 14 patients treated by argon laser photocoagulation, no recurrence of bleeding was reported in 50% of patients and only minor infrequent bleeding in the remaining patient group during follow-up [18].

Transmural necrosis and fibrosis with perforation or stricture formation are more common with Nd:YAG laser due to its inherently deeper penetration. Complication rates of 5–15% have been reported with the more widely used Nd:YAG laser for a variety of indications in the rectum, colon, and small bowel [18]. The Mayo laser group [8] experienced a 6% complication rate with no deaths; 4% of patients ultimately required surgery for control of bleeding. Nonfatal complications involved hypotension with subendocardial infarction, a seizure, and a rectovaginal fistula. Fistula was the only complication directly attributed to the laser treatment and was managed with rectosigmoid resection and an end-sigmoid colostomy. Of 47 patients, 39 (83%) were followed for longer than 6 months and of these 36 who responded to treatment continued to be in remission.

Long-term remission is the usual outcome, although female gender and sigmoid involvement were associated with poor outcome in the Mayo series. Gynecologic cancers requiring expanded radiation along with female pelvic anatomy may cause more proximal lesions in the sigmoid. The multiple bends of the sigmoid colon and the usually extensive number of vascular lesions overwhelm attempts at any coagulation modality. In patients with known sigmoid involvement, it is feasible to first concentrate therapy exclusively within the rectum since continued clinically significant bleeding from the sigmoid colon can then be managed by surgical resection. No immediate or later complications have been reported after argon laser therapy.

Preliminary results with photodynamic therapy performed by the Mayo laser group on patients with refractory bleeding limited to the rectum have been very encouraging. In theory, presensitizing the vascular lesions with a parenteral injection of a photosensitizing agent, such as hematoporphyrin derivative, before

inducing selective autodestruction after exposure to a preselected wavelength of laser light has great appeal. It is possible that this alternative form of laser therapy, although costly, may offer a less invasive and even better outcome in the more difficult patients, including those with involvement proximal to the rectum.

Argon plasma coagulation

Argon plasma coagulation (APC) has replaced laser coagulation therapy for radiation proctopathy for many practices. The device is portable and therefore available for use in any procedure room, provided that measures are taken to eliminate or dramatically reduce the electrical interference the device can produce in the endoscopic video imaging system. The advantages of this modality include noncontact coagulation and shallow depth of injury. As a result, treated areas of radiation proctopathy heal more quickly compared with the Nd:YAG laser and the endpoint of therapy can be reached sooner. The recommended settings include a power range within 30–45 W and a gas flow rate of 0.9 L/min. Care should be taken to avoid unnecessary contact between the APC probe and the rectal mucosal surface in order to maintain a shallow coagulation injury from the monopolar coagulating energy. Higher power or, more importantly, prolonged coagulation of a focal area will result in deep injury and a subsequent thermal ulcer. Ulcers in radiated mucosa are slow to heal and will frustrate care. The end-firing probe is more desirable than the side-firing probe, which often results in contact therapy. Those lesions at and just above the dentate line can be treated with the endoscope in a retroverted position, unlike laser therapy. This is possible because of the advantageous electrical plasma arcing toward the mucosa with the probe tip in any position relative to the intended area of treatment. As with laser therapy, treatment is interrupted regularly to decompress the colon.

Results of argon plasma coagulation

There are a number of experiences in the literature, most retrospective, that have reported on the number of treatment sessions observed until clinical improvement, as measured by direct endoscopic observation and use of bleeding scores, units of blood transfused, hemoglobin change, and complications. One of the earliest and largest experiences with APC reported dramatic improvement in bleeding scores and an increase in hemoglobin of 1.9 g/dL in anemic patients with no serious complications [20]. Overall success in controlling bleeding has ranged from 70 to 95%, with complete cessation of bleeding ranging from 47 to 80% [23–29]. Power settings in these reports have ranged from 40 to 50 W. Success in control of bleeding has occurred with

one to four treatment sessions, with control of bleeding reported as long as 36 months after completed therapy [27]. Complications have included pneumoperitoneum, refractory ulceration, and rectal stenosis. Recurrence of lesions have been infrequently reported after long periods of remission.

Bipolar and heater probe coagulation

Although less preferable because of contact-induced bleeding and tissue adherence to the tip of the coagulating probe, bipolar and heater probe coagulation can be performed with successful results [21,22]. The Gold probe (Boston Scientific Corporation, Microvasive Endoscopy, MA) is advantageous compared with the original multipolar probe because of the larger coagulating surface and less tissue adherence. These probes work well in coagulating vascular lesions in the very distal rectum, at and just above the dentate line, with the endoscope in a retroflexed position. Treating these extremely distal lesions adequately often makes a major difference to long-term outcome. The power settings are 12–16 W with a continuous pulse mode for the bipolar probe, and 10–15 J for the heater probe. There have been no complications other than anal pain during coagulation near the dentate line [22]. Of note, patients treated by these contact thermal modalities appeared to require more frequent treatment sessions compared with the laser and argon plasma devices.

Topical formalin

Initially used to control bleeding from the bladder in radiation-induced hemorrhagic cystitis, formalin treatment for radiation proctopathy was first reported by Rubinstein and colleagues in 1986 [30]. A dilute (4%) formaldehyde solution is used, which has been demonstrated in animal models to be free of toxic adverse effects [38]. Reported experiences have directly instilled formalin in up to 50-mL aliquots, exposing the rectal mucosa for a limited time, from 30 s to 15 min, followed by rinsing [30,31,33–36]. Alternative methods have

involved painting the mucosa with a formalin-soaked swab via an anoscope or rigid proctoscope or applying gauze-soaked pads for up to 45 min [32]. Comparison studies are underway (Mayo Clinic Developmental Endoscopy Unit) to prospectively compare formalin with argon plasma coagulation.

Unlike coagulation therapy, the endoscopic observations during and immediately after treatment are minimal. There is usually a diminution in the amount of friability and bleeding during the treatment and sometimes a blanching of the vascular lesions. Formalin can bind to proteins and, by doing so, causes cellular necrosis. Eventually, considerable edema develops that can reduce the rectal lumen by greater than 50%, although it is asymptomatic. Animal studies have shown no change in rectal compliance [38]. Over a span of days, superficial mucosal ulceration develops that resembles a proctitis. Formalin should not be used in patients who have any preexisting ulceration, since the superimposed chemical injury involving the ulcers induces considerable pain.

Results of formalin therapy

Success in the control of bleeding has ranged from 71 to 100%, with the majority of patients experiencing control after one treatment session [30–36]. Follow-up has been reported after 4–64 months [34]. Most surgical experiences have involved treatment under general anesthesia, although in our experience the procedure can be performed readily with or without conscious sedation. Described complications include lower abdominal cramps during treatment, anal and perineal pain after treatment, self-limited fissures, severe chemical colitis, and a rectovaginal fistula [30–36]. Anal pain after treatment has been reported in up to 25% of patients [30–36].

Summary (Table 51.3)

At present, there is little evidence to support the benefits of medical therapy. The scant but encouraging experience with sucralfate enemas suggests that an initial trial

Problem	Treatment
Minimal bleeding (infrequent, scant), no anemia	Sucralfate enemas (topical formalin)
Refractory bleeding (daily), clots and incontinence, ± anemia	Endoscopic coagulation (topical formalin)
Refractory bleeding, failed coagulation (formalin), sigmoid involvement, anemia	Photodynamic therapy
Refractory bleeding, failed photodynamic therapy, sigmoid involvement, complications, anemia	Surgery

Table 51.3 Treatment recommendations for radiation proctopathy.

should be considered for those patients who experience nuisance rectal outlet bleeding, unassociated with anemia [39]. For patients who are anemic due to bleeding, endoscopic coagulation therapy is the first line of treatment. Argon plasma coagulation has performed so well that it can be endorsed as the preferred coagulation treatment method. Since the argon plasma coagulator and the laser are not universally available, meticulous contact coagulation with shallow injury devices such as the heater probe or any of the bipolar electrocautery probes can be used. Careful use of these devices may require a few extra treatment sessions compared with the noncontact therapies. Patients who remain refractory to endoscopic therapy, especially those with segmental involvement of the colon proximal to the rectum, are candidates for surgical extirpation of the involved segment or bypass surgery to facilitate management of the frequent loss of blood. Photodynamic therapy may offer an excellent alternative to surgery for the refractory patient when there is more extensive involvement. Additional prospective experience with topical formalin, including the identification of an ideal endoscopic method of application, may bring this modality into the mainstream and has the potential to change this treatment schema.

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Chapter 52

Benign and Malignant Colorectal Strictures

Todd H. Baron

Introduction

A variety of conditions may lead to the formation of benign and malignant strictures of the colon and rectum (Table 52.1). Colonoscopy facilitates the clinical and histologic study of stenotic areas in the large bowel. Therapeutic interventions through the colonoscope may be performed as an adjunct or alternative to surgery in selected patients with symptoms related to colorectal strictures. This chapter reviews the use of colonoscopy in the management of benign and malignant strictures of the colon and rectum.

Colonoscopy in the diagnosis of colorectal strictures

Colonoscopy allows direct visualization and inspection of colorectal strictures. The endoscopic appearance of the stricture may, in most instances, provide the correct diagnosis. For example, endoscopic features of a malignant stricture include an obvious mass, ulceration,

and bleeding, whereas benign strictures usually appear smooth and symmetrical, although the visual appearance is not always accurate. The combination of endoscopic, clinical (prior cancer or surgery), and radiologic features on computed tomography (CT) (presence or absence of mass or inflammatory changes) allows a fairly accurate diagnosis of benign or malignant disease to be made.

During endoscopic evaluation or treatment of an obstructive colonic stricture the endoscopist must be careful not to overinsufflate air, since the segment between the stricture and a competent ileocecal valve can become overdistended resulting in a proximal pneumatic colon rupture, even though the instrument did not pass beyond the stricture. This is the "closed loop phenomenon," which must be considered whenever a narrow colon stricture is inspected [1]. Tissue sampling during colonoscopy allows for a positive diagnosis of malignancy to be made in a high percentage of patients. Direct forceps biopsy is the standard method of tissue acquisition. Sampling of the entire portion of the stricture may produce a higher yield than sampling of only the distal portion, but can be technically difficult because a severely narrowed lumen may prevent passage of the endoscope. It may be necessary to dilate a suspected malignant stricture to allow passage of the endoscope through the stricture so that complete endoscopic evaluation with tissue sampling is possible (Fig. 52.1). Even if the endoscope can be insinuated into the stricture, it is unusual to be able to angulate the scope tip within the narrowed segment to permit adequate tissue sampling of the walls. Another alternative to stricture dilation is the use of smaller-diameter endoscopes such as a pediatric or upper endoscope. Although not routinely used, brush cytology sampling may increase the diagnostic yield of malignancy over biopsy alone [2].

Colorectal strictures occurring in the setting of established chronic ulcerative colitis should be assumed to be malignant in nature. Predictors of a malignant stricture in the setting of ulcerative colitis include long duration of disease (> 10 years), proximal location, and symptomatic large-bowel obstruction [3]. Colorectal strictures in documented Crohn's colitis may also be

Table 52.1 Etiology of colorectal strictures.

Benign

Diverticular disease
Anastomosis (including ileocolonic)
Inflammatory bowel disease
Radiation
Ischemia
Nonsteroidal antiinflammatory drugs
Infectious
Severe acute pancreatitis
Endometriosis

Malignant

Primary colorectal cancer
Recurrent colorectal cancer
Intracolonic metastases
Lymphoma
Extrinsic compression
 Ovarian cancer
 Prostate cancer
 Drop metastases
 Nodal metastases

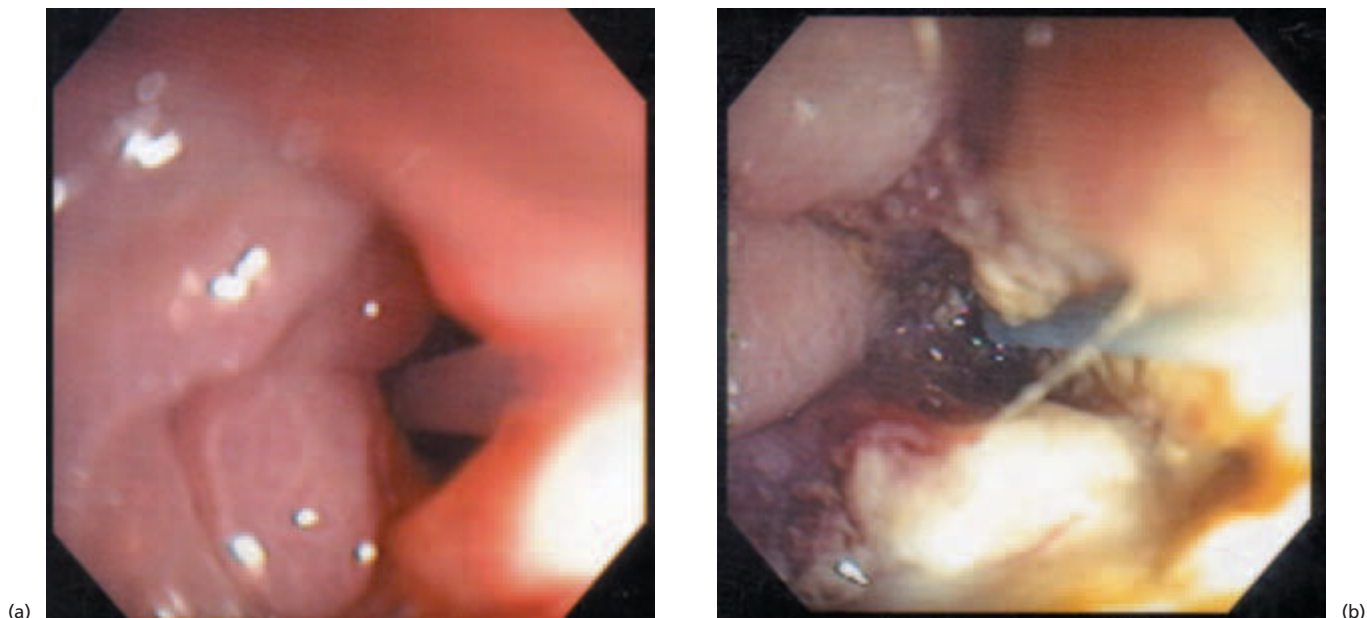


Fig. 52.1 Submucosal recurrence of colorectal cancer: (a) on initial inspection the stricture appears benign; (b) after stricture dilation and further passage of the endoscope, obvious features of malignancy are seen.

malignant; duration of disease more than 10 years, short strictures, and involvement of more than one-third of the large bowel appear to be associated with malignancy [4].

Most symptomatic benign colorectal strictures are fibrotic in nature. However, patients with inflammatory bowel disease or diverticular disease may have a component of luminal compromise as a result of chronic fibrotic changes that become symptomatically obstructive when acute inflammatory changes are superimposed on the underlying pathology. Once the acute inflammatory component resolves, usually with medical therapy, obstructive symptoms tend to resolve. Balloon dilation of a stricture in the setting of acute inflammatory changes is likely not to be as effective as when the obstruction is fibrotic.

In the setting of immunosuppression, infections such as cytomegalovirus may produce colonic strictures, some of which resemble primary colorectal malignancy [5]. Therefore, in immunosuppressed patients, biopsies should be obtained and processed appropriately for the detection of infectious agents.

Severe acute pancreatitis may result in acute and/or chronic inflammatory changes of the colon, with fixation and obstruction [6]. It is important for the endoscopist to recognize this well-described but underappreciated entity, since dilation is not appropriate for the treatment of these strictures.

Endoscopic therapy of colorectal strictures

Benign disease

Dilation

Most of the data concerning the endoscopic dilation of symptomatic benign strictures comes from experience with anastomotic strictures. Dilation may be achieved using balloon dilators or rigid (bougie) over-the-wire dilators, with or without electrosurgical devices. The data for each disease process are discussed separately.

Anastomotic strictures

Colonic anastomotic strictures occur in up to 22% of patients following bowel resection and anastomosis [7]. Factors promoting development of anastomotic strictures include ischemia, anastomotic dehiscence, preoperative or postoperative radiation therapy, or cancer recurrence (when resection is for malignant disease). The success rate of endoscopic dilation depends on several factors. Pucciarelli and colleagues [8] analyzed the outcome following dilation of anastomotic strictures. Factors associated with a successful response to dilation were high anastomosis (> 8 cm from the anal verge), no adjuvant radiation therapy, minimal or no dehiscence, no neoplastic recurrence, simple stricture morphology, and short stenosis (< 1 cm). These authors found when radiation therapy, local neoplastic recurrence, and large dehiscence were present, there was nearly a 100% probability of dilation failure. When these three factors were absent, the probability of dilation failure was 5%. An

important anatomic concept is that some anastomotic strictures are membranous and more responsive to endoscopic therapy, while others are transmural and concentric and less responsive to endoscopic therapy.

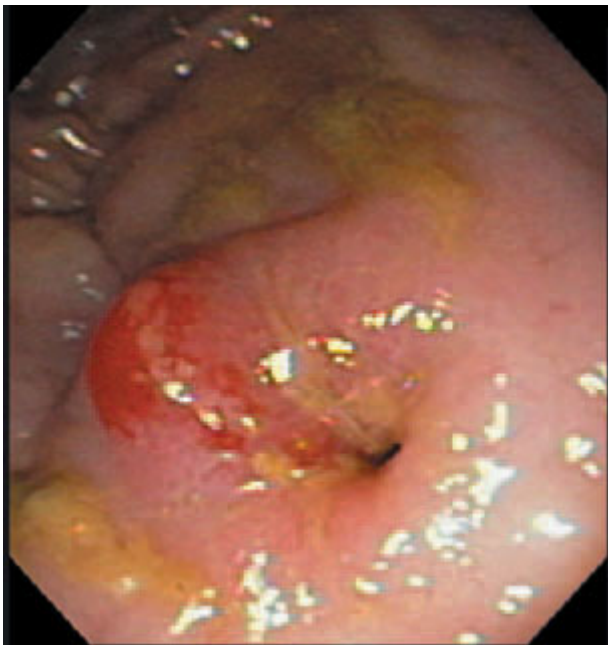
The first endoscopic therapy in which balloon dilation was performed for a postoperative colonic stricture was described in 1984. Since then, there have been numerous reports using through-the-scope (TTS) hydrostatic balloon dilators for dilation of anastomotic strictures. Kozarek [9] published the results of a survey of 3000 endoscopists who were queried about their use of hydrostatic dilation of benign strictures. Of 64 patients who underwent colonic stricture dilation, 44 had anastomotic strictures. Immediate objective and symptomatic relief was reported in 83% and 73% of patients respectively, while objective and symptomatic relief at more than 3 months were persistent in 73% and 86%. Additionally, the size of the balloon is an important parameter for success. Of all patients undergoing colonic stricture dilation, immediate symptomatic improvement following balloon dilation was less than 50% when balloons with a diameter under 40 French (13 mm) were used, while a success rate of greater than 90% was achieved with balloon dilators having a diameter of at least 51 French (17 mm). Achalasia-dilating balloons with a diameter of 30–40 mm have been used to dilate rectal anastomotic colonic strictures [10], with good long-term results in 16 of 18 (94%) patients. Overall, the

success rates following balloon dilation of anastomotic strictures range from 70 to 90% [7].

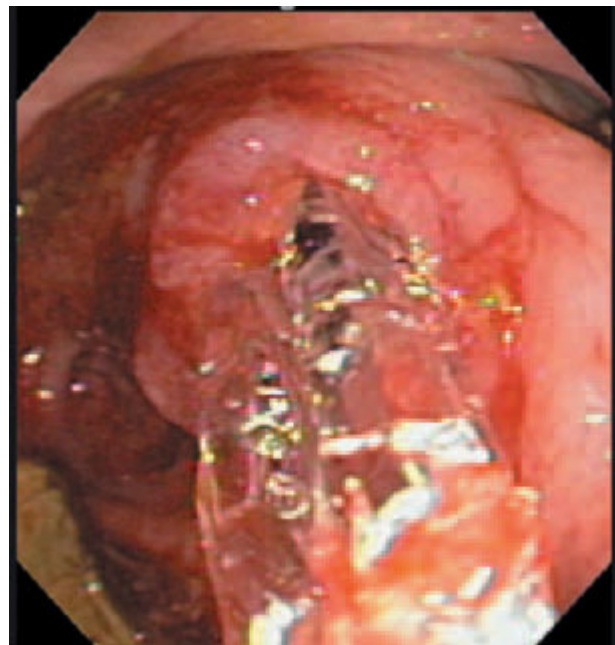
Over-the-wire plastic dilators (Savary–Gilliard) are also used to treat anastomotic strictures in the left colon, particularly those close to the anus. Werre and colleagues [11] described this technique in 15 patients. After endoscopic placement of a guidewire across the stricture, 10–19 mm dilators were passed through the narrow segment under fluoroscopic guidance. Ten patients had a complete response after three or less sessions, whereas five patients underwent four or more procedures without a complete response, suggesting that if patients do not respond to dilation within a few sessions, they are not likely to respond. There are no prospective trials comparing balloon dilation to Savary dilators. In a retrospective comparative study, balloon dilation was found to produce a better response after a single session than bougie dilation (77% vs. 52% respectively) [12]. Both methods of dilation may lead to complications of perforation and bleeding. There are no specific guidelines on diameters of dilators and number of dilations per session, as there are for esophageal dilation. Although there are no supportive data, it is assumed that more aggressive dilation may be performed in the rectum as opposed to more proximal disease. Additionally, there are no data to support injection of corticosteroids into anastomotic strictures to improve the long-term outcome following dilation.

In summary, the response rate following dilation of anastomotic strictures is variable and dependent upon several factors. With proper patient selection, balloon or rigid dilation is the initial nonoperative treatment of choice (Fig. 52.2).

Fig. 52.2 Anastomotic stricture: (a) smooth membranous-type anastomotic rectal stricture; (b) hydrostatic through-the-scope balloon dilation using a 20-mm balloon (the membranous nature is more obvious during dilation).



(a)



(b)

Electroincision

The use of an endoscopic electroincision technique has been described as a method to treat benign anastomotic colorectal stenoses. Brandimarte and Tursi [13] described 39 patients with central membranous anastomotic “strictures” defined by barium enema and endoscopy. A needle-knife electrocautery device, as used for endoscopic retrograde cholangiopancreatography (ERCP) precutting techniques, was used to incise the stricture radially in six directions. No other therapy (such as balloon dilation) was performed. Patients were followed clinically and endoscopically for a mean of 25 months without recurrence of stricture or symptoms. The use of this electroincision technique to augment balloon dilation therapy has also been proposed as a treatment for refractory strictures. In a series of 35 patients, Truong and colleagues [14] performed electroincision, cutting radially in four directions followed by balloon dilation. Two-thirds of the patients required one treatment. A good response was obtained in all patients following one to three sessions. Recently, the incision technique has been described using Nd:YAG laser with excellent results in 9 of 10 patients [15].

Because of the potential complications, electroincision should be performed only by experienced endoscopists in selected patients with membranous-type strictures.

Inflammatory bowel disease

Most of the data regarding endoscopic dilation of colonic strictures occurring in the setting of inflammatory bowel disease is derived from the treatment of recurrent Crohn’s disease with stricturing at the site of colocolonic or ileocolonic anastomoses. Nearly all of these reports have used TTS balloons [16]. Couckuyt and colleagues [17] prospectively evaluated the outcome of 55 patients with clinically symptomatic ileocolonic strictures following endoscopic TTS balloon dilation with balloons ranging in diameter from 18 to 25 mm. Long-term success was achieved in 62% of patients, although perforation occurred in six patients (11%). In another study where the maximum balloon diameter was 18 mm, similar results were achieved with no perforations [18]. The addition of corticosteroid injections may improve the outcome following endoscopic therapy [19,20]. One case of successful wire-guided bougienage dilation of an ileocolonic anastomotic stricture after failed TTS balloon dilation has been reported [21].

There are only a few reports of successful balloon dilation of colonic Crohn’s strictures in the absence of previous surgery [20,22,23], with the goal being an 18-mm dilator, achieved over several sessions. In one series of 10 Crohn’s patients under-going endoscopic therapy, six had colonic strictures not involving the ileum, five

of which were not postoperative [20]. Endoscopic “dilation” was performed using needle-knife electroincision followed by injection of triamcinolone. Unfortunately, the details of follow-up are unavailable and this approach cannot be recommended.

In summary, endoscopic dilation for the treatment of ileocolonic and colonic strictures in the setting of inflammatory bowel disease is a reasonable nonsurgical alternative, although up to one-third of patients will eventually require surgery. The ideal dilation strategy and the need for adjuvant corticosteroid injection are unknown.

Nonsteroidal antiinflammatory drug-induced strictures

One of the adverse effects of nonsteroidal antiinflammatory drugs (NSAIDs) is the development of colonic strictures. These strictures are usually symmetrical, 2–4 mm thick, may be multiple, and may occur in the right colon. There have been only a few reports of endoscopic therapy, but it appears that large-diameter TTS balloon dilation (15–20 mm) is safe and effective for treating NSAID-induced strictures [24–26].

Miscellaneous strictures

There are few or no data on the use of endoscopic dilation for the other benign strictures outlined in Table 52.1. In the report by Kozarek [9], 5 of 44 patients undergoing colonic dilation had diverticular strictures. All five patients had objective relief at more than 3 months following balloon dilation.

Self-expandable metal stents

Self-expandable metal stents (SEMS) are approved by the Food and Drug Administration (FDA) only for the treatment of malignant colorectal obstruction. However, there are reports of their use in benign obstructive colorectal diseases. The main safety concern with the use of metal stents for benign disease is the long-term consequences of implantation. When a stent is used as a bridge to surgery to relieve acute colonic obstruction and allow a one-stage operation (see preoperative decompression of malignant strictures later in this chapter), long-term safety is not a concern since the device is removed at the time of operation. However for the long-term nonoperative management of benign strictures, there are few data on their safety and they should be used only as the last option for patients with poor operative risk. There is a high rate of spontaneous migration of SEMS from benign strictures, which usually occurs in the first month after insertion. Although not designed for endoscopic removal, SEMS are potentially removable and it is strongly recommended that in benign

disease a cautious attempt should be made to remove them within 4–8 weeks of implantation before they are completely imbedded in the tissue. Whether SEMS spontaneously migrate or are removed, a lasting benefit from stent dilation may be seen.

Anastomotic strictures

In patients with anastomotic strictures unresponsive to endoscopic dilation, there are case reports of temporary expandable metal stent placement to dilate the stricture. In one case the stent migrated distally 6 days after insertion [27]. Endoscopically, the colonic lumen remained widely patent at last follow-up 12 months later. In another case, the stent was endoscopically removed 3 months after insertion and no further treatment was required over an 18-month follow-up [28].

Inflammatory bowel disease

There is one report where SEMS were placed in two patients for the treatment of refractory Crohn's strictures as an alternative to surgical strictureplasty [29]. One patient had a symptomatic descending colonic stricture and one patient had small-bowel obstruction due to an ileocolonic stricture. The SEMS spontaneously migrated in less than 1 month and 5 months respectively. In a subsequent report on the follow-up of these patients, both remained without stricture recurrence at 3 years and 4.5 years respectively [30].

Diverticular disease

In a series of patients who underwent endoscopic SEMS placement for treatment of colonic obstruction [31], three patients had diverticular disease as the cause of acute obstruction. SEMS were placed successfully in all three patients, with resolution of obstruction and subsequent one-stage operative resection with primary anastomosis. Another group has described this scenario as well [32]. The use of SEMS for long-term nonoperative management of fibrous diverticular strictures has not been reported.

Radiation-induced strictures

There are two case reports of SEMS placement for treatment of colonic obstruction from chronic radiation-induced colonic strictures. In the initial report [33], a stent was placed in a patient with complete rectosigmoid obstruction. The stent spontaneously migrated distally from the stricture 19 days after placement. There was clinical and radiographic resolution of the stricture at follow-up of 43 weeks. In the other case, the stent remained in place for 4 months until the patient died

from underlying medical illness unrelated to the stent [34].

Malignant disease

Colonic obstruction secondary to malignancy is the number one cause for emergency large-bowel surgery, accounting for as much as 85% of such procedures. There are two clinical scenarios for endoscopic treatment of malignant colorectal strictures: preoperative decompression and palliation. Additionally, there are two major endoscopic modalities for decompressing the obstructed colon: laser therapy and SEMS. Each of the two endoscopic treatment options and clinical scenarios are discussed separately.

General comments

Laser

Laser therapy of primary colorectal neoplasms has been performed for over 15 years. Laser therapy is most useful for treating patients who have intrinsic lesions in the distal colon that are bulky, polypoid, and exophytic (Fig. 52.3). One drawback is the inability to treat intrinsic scirrhous lesions and extrinsically compressive lesions. Laser therapy, however, has an advantage over SEMS in the ability to control bleeding from primary colorectal cancer. Since laser therapy has become largely supplanted by other modalities, its overall use is declining. Whether newer endoscopic tumor-ablative modalities, such as argon beam plasma coagulation (delivered at

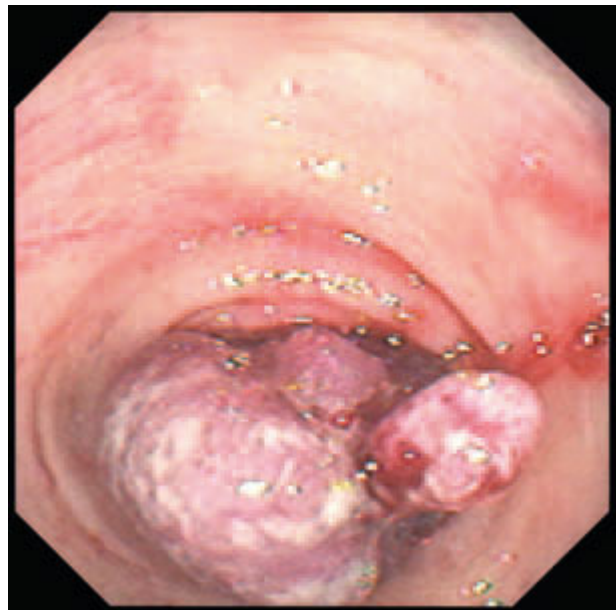


Fig. 52.3 Polypoid primary rectal cancer is an ideal lesion for laser therapy.

high settings), can produce results similar to laser therapy remains to be seen.

Self-expandable metal stents

SEMS are composed of a variety of metal alloys with varying shapes and sizes depending on the individual manufacturer and organ of placement. The radial expansile forces and degree of shortening differ between stent types [35]. Tissue reactions to SEMS *in vivo* are known based on animal data as well as autopsy and surgical findings in humans [36]. Once deployed, the tissue response to SEMS seems to be consistent throughout the gastrointestinal tract. The stent material becomes incorporated into both the tumor and surrounding tissue by pressure necrosis. In the areas uninvolved by tumor above and below the stenosis, the stent imbeds deep into the wall of the organ. This reaction anchors the stent and helps to prevent stent migration. With the use of fully covered stents this integration does not always occur and there is a higher rate of stent migration. At the present time, SEMS specifically designed for use within the colon are uncovered. Covered esophageal stents have been used in the colon to combat problems with tumor ingrowth and to close fistulae [37].

SEMS may produce imaging artifacts on both CT and magnetic resonance imaging (MRI) localized to the area around the stent that may prevent accurate interpretation. Most SEMS materials appear safe for MRI, although factors such as stent shape, orientation to the magnetic field, and type of alloy composition influence signal intensity *in vitro*. Therefore, information concerning magnetic reactivity should be obtained before MRI is performed in a patient who has undergone colorectal stent placement [38,39].

Preoperative decompression

The traditional management of patients with either subtotal or complete malignant colonic obstruction of the left colon involves creation of a diverting colostomy. In some series, 30% of patients with primary colorectal carcinoma presented with large-bowel obstruction [40]. These patients cannot undergo a one-stage operative resection of the lesion and primary colonic reanastomosis because stool in the uncleaned colon proximal to the obstruction leads to breakdown of the colonic anastomosis. The standard two-stage operative procedure consists of the initial surgery with diverting colostomy and resection of the primary tumor; reanastomosis of the colon is performed as a second-stage operation. Patients presenting with complete colonic obstruction tend to be acutely ill with more advanced disease compared with patients without obstruction. The goal of preoperative endoscopic decompression is to allow clinical stabiliza-

tion of the patient and subsequent colonic preparation so that a one-stage operation can be performed and a colostomy avoided. After successful endoscopic colonic decompression, the patient's comorbid medical illnesses and extent of malignancy can be addressed. Additionally, preoperative decompression allows preoperative chemoradiation therapy to be administered. If the patient is a poor candidate for surgical resection because of underlying illnesses, such as severe coronary artery disease, or has unresectable or widely metastatic disease discovered by imaging studies, laser therapy and/or SEMS can serve as the palliative approach.

Laser therapy

Although most series have described laser therapy as a palliative modality, it has the potential to serve as a bridge to surgery. Arrigoni and colleagues [41] used endoscopic modalities to recanalize the lumen of patients with acute large-bowel obstruction due to colorectal cancer. Using a combination of TTS balloon (18 mm) or Savary dilation (12–18 mm), snare debulking, and Nd:YAG laser therapy, emergency colostomy was avoided in 16 of 17 patients by successful restoration of the colonic lumen and relief of bowel obstruction. No complications occurred as a result of endoscopic therapy. Although no patients in this series ultimately underwent surgical resection, the data demonstrate the ability to decompress the acutely obstructed colon with this approach.

Self-expandable metal stents

The use of SEMS as a bridge to surgery is becoming more widely accepted. Metal stents have luminal diameters of 20–30 mm and remain in place until surgery when they are removed en bloc with the tumor [31]. Segmental colonic resection after successful stent placement and decompression has until recently been performed by open surgery but a recent series of laparoscopic stent and tumor resection [42] has been reported.

There are several small series describing successful preoperative placement of colonic SEMS with subsequent one-stage resections [31]. A recent large multicenter series of patients with primary colon carcinoma evaluated the effectiveness of preoperative placement of 20- and 22-mm diameter SEMS [43]. Successful stent placement, with clinical resolution of large-bowel obstruction within 96 h, was achieved in 66 of 71 (93%) patients; 65 patients underwent elective single-stage surgery with a primary colonic anastomosis at a mean of 8.6 days following stent placement. One severe complication, intestinal perforation, occurred. Although the stents were inserted by interventional radiologists, the data can be extrapolated to endoscopic placement.

Two studies have compared the outcome of patients undergoing endoscopic placement of SEMS for relief of acute large-bowel obstruction followed by elective resection to those patients undergoing surgical intervention without stent placement [44,45]. A retrospective study [44] reported 13 consecutive patients with colorectal carcinoma who received SEMS compared with a similar group that had traditional surgical management at the same institution. Stent placement and subsequent clinical resolution of large-bowel obstruction was achieved in 12 of 13 patients; in three the stents remained for palliation. A single-stage operation was performed in eight of the nine remaining patients in the stent group. Only 2 of 13 patients treated with colonic SEMS required colostomy compared with 10 of 13 patients in the traditional surgical group. When cost data were analyzed, a cost saving of 28.8% was seen in the SEMS group because of a decrease in total hospital days, days spent in the intensive care unit, and fewer surgical procedures. A more recent prospective study demonstrated similar findings [45] in 72 patients with primary colorectal cancer and obstruction; SEMS were used when personnel were available to place them. If not available, traditional surgery was performed. A primary anastomosis with avoidance of colostomy was achieved significantly more often (85% vs. 41%) in the SEMS group. Despite these promising results, there are no prospective randomized studies of SEMS vs. surgery for preoperative decompression. It remains to be seen whether long-term results such as tumor recurrence rates are altered by the use of preoperative colonic stent placement.

Preoperative radiation therapy prolongs survival after rectal cancer [46]. Stent placement for obstructing primary rectal cancer can allow the necessary time to provide this treatment. In one reported case, a full course of chemoradiation therapy was completed following which the tumor and stent were resected. No adverse pathologic effects were seen in the resected specimen [47].

Palliation of malignant colonic obstruction

Laser therapy

Laser therapy is useful for palliation of both colonic obstruction and bleeding from primary colorectal cancer. In patients with obstruction, it appears that laser therapy is most effective in treating small tumors. With tumors smaller than 3 cm in diameter there can be a high probability of symptomatic improvement from obstructive symptoms [48]. Patients with large tumors require several sessions to maintain an adequate lumen. The response rate in large tumors is not 100% and patients with extensive disease may not be improved with laser therapy.

Two large series of laser therapy for palliation of colorectal cancer have been published. The largest study [49] included 272 patients undergoing palliative therapy for rectosigmoid cancers, with a high immediate success rate (85%) and low major complication rate (2%) for palliation of obstructive symptoms. Another study [50] evaluated the long-term outcome of laser palliation of rectal cancer in 219 patients. Long-term follow-up was obtained until death (mean 6.7 months). Results were analyzed based upon the predominant symptom of obstruction, bleeding or other symptoms (soiling, tenesmus, and diarrhea). Significantly more patients in the obstruction group (25%) eventually required palliative colostomy. Patients with obstruction required significantly more treatment sessions compared with the other groups. Palliation of bleeding was achieved in 83% of patients. Major complications of perforation (4.1%), fistula (3.2%), bleeding (4.1%), and abscess formation (1.7%) were seen. This study demonstrates that the outcome of laser therapy depends on whether the modality is used to treat obstruction or bleeding.

Overall, successful palliation is achieved in 80–90% of patients using laser. An average of approximately three procedures is required to achieve sufficient and lasting relief of obstructive symptoms. Serious complications (bleeding, perforation, severe pain) occur in up to 10–15% of patients [51–53].

Self-expandable metal stents

Patients with colorectal carcinoma and colonic obstruction who have extensive local or metastatic disease are poor operative candidates for surgical resection, as are patients with obstruction secondary to noncolonic pelvic malignancies (e.g. bladder or ovarian carcinoma) or metastatic diseases (e.g. breast carcinoma). These patients are candidates for colonic SEMS placement for palliation [54–56]. Several other series have demonstrated successful palliation of obstruction with avoidance of colostomy in 85–100% of patients. In some series, the stents effectively palliated obstruction for more than 1 year [57–59].

The largest series of endoscopic stent placement for palliation of obstructive primary rectal and rectosigmoid obstruction was published by Spinelli and Mancini [60]. Stents were successfully placed in 36 of 37 patients. Three early migrations occurred. Of the remaining 33 patients, 28 had good long-term resolution of obstruction without need for further treatment.

Nearly all the published series have used uncovered stents. One study found an unacceptably high rate of migration using fully covered stents [61]. However, in a recent study using partially covered stents for palliation of malignant left-sided obstruction, only two stent migrations occurred in 16 patients [62]. At

a mean follow-up of 21 weeks, no stent occlusion was seen.

Although randomized comparative trials of stent placement vs. colostomy are lacking, SEMs is an option for avoiding permanent colostomy in terminally ill patients with colonic obstruction. Following uncomplicated colorectal stent placement, patients may resume oral food intake after clinical decompression. After palliative colorectal stent placement, patients are advised to consume a low-residue diet and use stool softeners or laxatives to avoid stent occlusion from stool impaction.

Complications of colon SEMs placement may occur during the procedure, early after placement (early complications), or late after insertion. Early complications include perforation, migration, bleeding, stent malposition, and stent occlusion by stool impaction. Free perforation during SEMs insertion may be a devastating complication, since fecal material is spilled into the abdominal cavity. This may be more difficult to manage surgically compared with proceeding directly to a diverting colostomy. Additionally, the patient will become more acutely ill, producing a potentially worse surgical outcome. Improper deployment of the stent or proximal stent migration after successful placement results in a stent floating freely within the lumen above the stricture. This is usually of no consequence, assuming an additional stent(s) is properly placed to relieve the obstruction (personal experience). Stents placed very distally in the rectum may produce tenesmus, rectal pain, and fecal incontinence; patients should be advised of this possibility prior to stent placement. In general, stent placement more than 2 cm proximal to the anal canal does not interfere with anal function. Late complications include distal stent migration, bleeding, and perforation [63]. Stent migration may be completely asymptomatic or result in rectal bleeding or tenesmus. Removal of distally migrated stents from the rectum is not technically difficult and is best performed using a rat-toothed forceps. Stent occlusion from tumor overgrowth, ingrowth, or stool impaction requires endoscopic intervention. Obstruction by tumor ingrowth or overgrowth can be managed with placement of additional stents through the original stent(s). It is unknown whether previous radiation increases the risk of stent-related complications.

Some patients with widely advanced malignancies and colonic obstruction may not improve following successful stent placement because of other unidentified sites of malignant gastrointestinal obstruction or diffuse peritoneal carcinomatosis with small-bowel encasement.

Palliation of malignant fistulae

Patients with malignancy within the pelvis may suffer from fistulae to surrounding structures such as the

vagina or bladder. In this setting, covered esophageal stents have been used to close such fistulae and produce excellent palliation [37,64].

Materials for and techniques of endoscopic insertion of colonic SEMs

The duration of the procedure is highly variable and depends on the degree of difficulty encountered traversing or accessing the stricture. At least one full hour of time should be allotted once sedation is administered. The stent chosen should be at least 3–4 cm longer than the obstruction to allow an adequate margin of stent on either side of the obstruction.

Stent types

Although any type of SEMs may be used within the colon, including esophageal, tracheobronchial, and biliary stents, dedicated colonic SEMs are commercially available. Three different self-expandable colonic stents are approved by the FDA in the USA for treatment of malignant obstruction [65]. One of these stents has a longer and smaller predeployment delivery system (10 French) that allows passage of stents directly through the working channel of a therapeutic colonoscope, and these stents can be placed as proximal as the ascending colon.

Distal lesions producing colonic obstruction are within the reach of a standard flexible sigmoidoscope or upper endoscope. For lesions proximal to the descending colon, it is usually necessary to use a colonoscope. If a stent is chosen that will pass through the working channel of the endoscope, a therapeutic channel (≥ 4.2 mm diameter) is required.

Other materials that should be readily available include biliary catheters and guidewires. Hydrophilic biliary guidewires (Terumo, Tokyo, Japan) are especially useful in order to “cannulate” or traverse obstructive lesions. A stiff 0.035 inch guidewire is needed for stability during stent placement once the lesion has been traversed. Water-soluble radiographic contrast may also be needed to define stricture length as well as to demonstrate the lumen for correct passage of catheters. If marking of the tumor margins is desired, injection needles for placement of radiopaque contrast are needed.

Patient preparation and positioning

Patients with complete obstruction have usually evacuated any stool below the lesion and bowel preparation is not necessary. In those patients who have subtotal obstruction in the distal colon, one or two cleansing enemas are usually adequate; with a more proximal lesion and subtotal obstruction, a cautious colonoscopy bowel

preparation should be given. Prophylactic antibiotics should be considered in patients with complete obstruction and a markedly dilated colon because insufflation of air during the procedure may promote microperforation and bacteremia.

The patient should initially be placed in the left lateral decubitus position. Rotating the patient into the supine position allows for a better anatomic view under fluoroscopy, if used. Standard intravenous conscious sedation is usually administered, but is not absolutely necessary for distal lesions.

Description of procedure

Placement of SEMS in the rectum and distal sigmoid without the use of TTS stents uses similar techniques as for esophageal stent placement. Deployment of TTS stents, which are usually necessary for treating more proximal obstruction, is more analogous to ERCP with placement of a metal biliary stent. These two approaches to SEMS placement are discussed separately. It is imperative to have nursing assistants competent in complex therapeutic endoscopic procedures and SEMS placement to assist with these procedures.

Nonfluoroscopic-guided stent placement

Non-TTS stent placement

For distal left-sided lesions, the area may be accessed entirely under endoscopic guidance [60]. If the endoscope cannot be passed through the lesion, the stricture

is cautiously dilated with a 15-mm TTS balloon. A 10-mm endoscope is then passed through the stricture to allow placement of a Savary guidewire as high as possible above the lesion. As the endoscope is withdrawn, the stenosis is measured and the position/orientation of the lumen assessed. After the undeployed stent is passed across the stricture, the endoscope is reinserted to verify and monitor the exact position of the distal end of the stent. Alternatively, in patients with intrinsic lesions, laser therapy may be used to recanalize the lumen to allow passage of the endoscope and guidewire [65]. Both of these methods permit stent placement without the use of fluoroscopy.

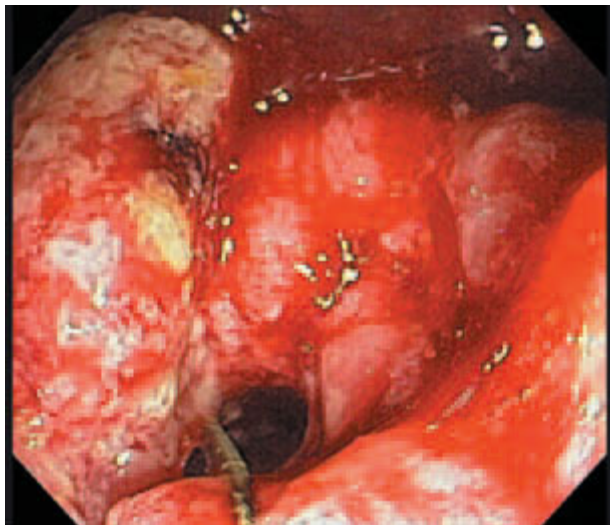
TTS stent placement

If the endoscope passes easily through the lesion, a stiff 0.035 inch guidewire with a floppy tip is placed through the endoscope channel and passed proximally at least 20 cm beyond the point of obstruction (Fig. 52.4a). Once the stent passes through the endoscope channel, the endoscope is withdrawn below the distal margin of the stricture and the stent is deployed under direct endoscopic guidance (Fig. 52.4b).

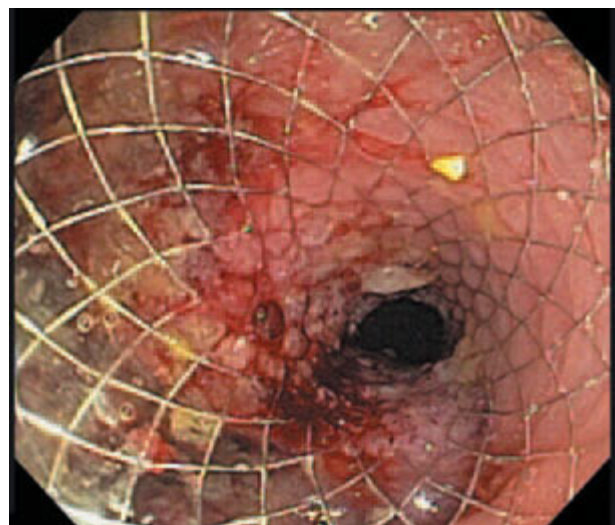
Endoscopic/fluoroscopic stent placement

If the endoscope cannot be passed easily through the lesion, a hydrophilic biliary guidewire preloaded through a standard biliary catheter is used to “cannulate” or traverse the stricture, as is done during ERCP (Fig. 52.5a). Once the wire has passed through the stricture, recognized fluoroscopically by the anatomically correct position of the wire passing into an air-filled dilated proximal bowel, the catheter is advanced over the guidewire through the lesion. After removal of the guidewire, water-soluble radiographic contrast is injected

Fig. 52.4 Endoscopic view of through-the-scope placement of self-expandable metal stent for palliation of malignant colonic obstruction: (a) a guidewire has been advanced across the lesion; (b) immediately after deployment of stent.



(a)



(b)

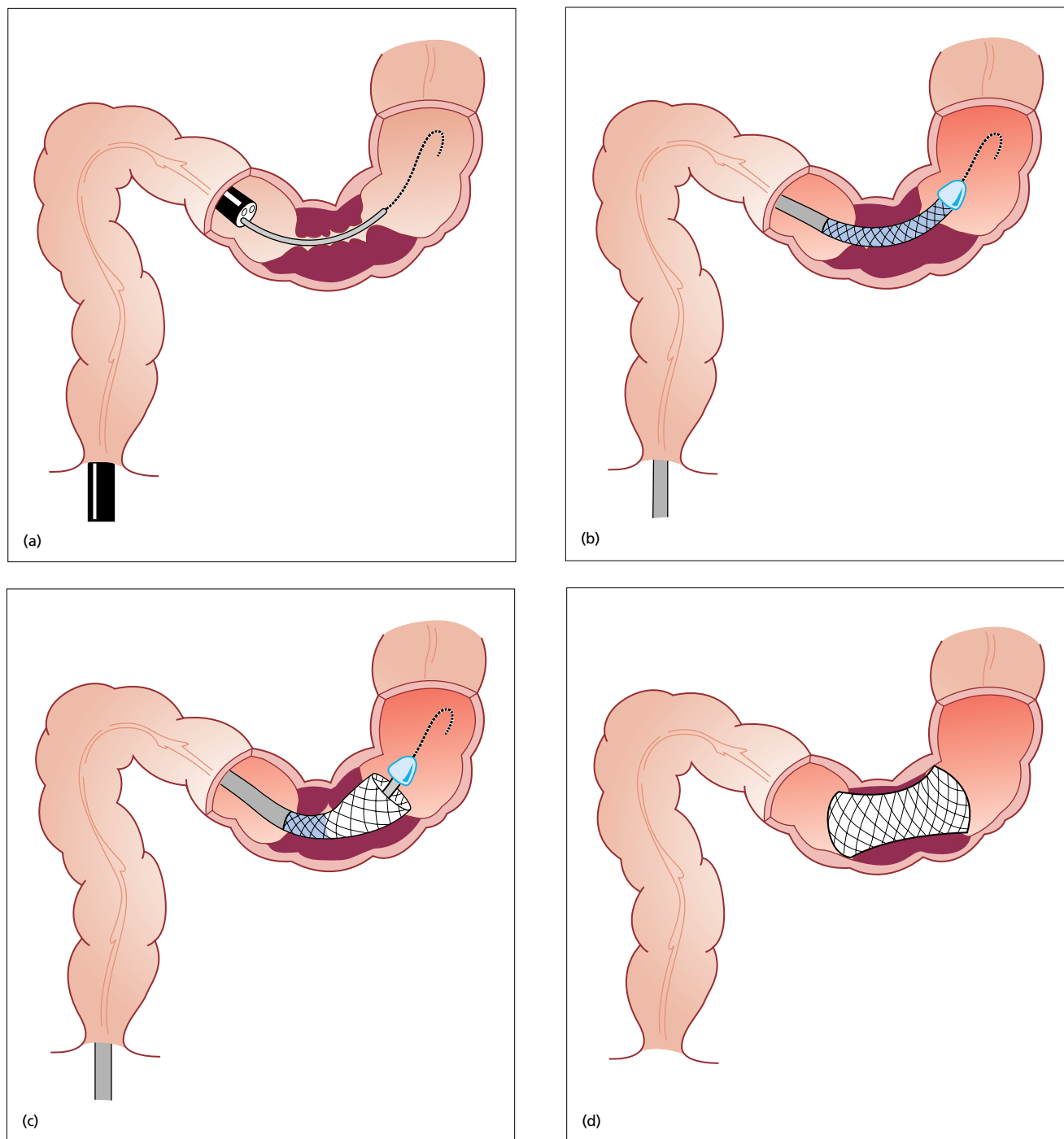


Fig. 52.5 Endoscopic placement of a through-the-scope stent using fluoroscopic guidance: (a) endoscope is advanced to the site of the lesion and a guidewire and catheter are advanced through the area of obstruction; (b) guidewire is replaced by a stiff guidewire and the delivery system is introduced;

(c) stent is initially deployed at the proximal portion of the lesion under both endoscopic and fluoroscopic guidance; (d) stent is fully expanded and symmetric in diameter throughout its length.

to confirm both proper position and luminal patency. At this point, the stiff 0.035 inch guidewire is placed through the catheter and the procedure proceeds as described above (Fig. 52.5b–d).

Once the stent is fully deployed, the ends of the stent should be carefully inspected fluoroscopically. If either end is not flared or fully expanded, the endoscopist should be suspicious that the stent chosen may have

been too short to cover the entire length of the stricture. At this point contrast can be injected into the stent to assess complete patency. If needed, a second (rarely third) overlapping stent may be required to adequately treat the stricture.

Limitations and success rate

The technical success rate for placement of colonic SEMS in experienced centers is close to 100%. Using endoscopic techniques stents may be placed into the right colon [66], whereas with radiologic guidance alone stent placement is limited to the left colon. Limitations of successful placement include inability to pass a guidewire through the stricture and anatomic difficulties such as a severely angulated and "fixed" sigmoid, which prevents advancing the endoscope to the site of the lesion.

Avoidance of complications

Two important tips are helpful in avoiding intra-procedural perforation. The first is limiting the amount of air insufflation during the examination, especially in patients with a dilated cecum. The second is avoiding aggressive dilation before or after stent insertion [65].

Summary

Colonoscopy plays a major role in the evaluation and treatment of patients with benign and malignant colorectal strictures. Tissue sampling allows the diagnosis of malignancy. Successful treatment of benign strictures is achieved using colonoscopically directed dilation. Endoscopic placement of expandable metal stents into the colon is useful for both preoperative and palliative relief of malignant colonic obstruction.

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Chapter 53

Pediatric Colonoscopy

Marvin E. Ament and George Gershman

Introduction

Since its introduction almost 40 years ago, colonoscopy has become a routine procedure, not only for adults, but also for pediatric patients with rectal bleeding, chronic diarrhea, change in stool caliber, and chronic lower abdominal pain. It is safely used in all groups of children, including newborns.

Although the instruments are similar, pediatric colonoscopy is different from colonoscopy in adults in many aspects, such as preparation, sedation, technique, and spectrum of therapeutic manipulations.

Indications for colonoscopy

Indications for diagnostic and therapeutic colonoscopy are listed in Table 53.1. Although colon cancer is not one of the usual indications for colonoscopy in children, colonoscopy and biopsy are performed for surveillance for detection of malignancy in patients with longstanding inflammatory bowel disease.

Patients who have undergone small intestinal transplantation may need to undergo ileoscopy and or colonoscopy to obtain specimens from transplanted bowel to look for rejection and evidence of lymphoproliferative disease.

When diagnostic colonoscopy is not indicated

Colonoscopy is not indicated in patients with:

- acute self-limited diarrhea;
- gastrointestinal bleeding with a demonstrated upper gastrointestinal source;
- stable recognized irritable bowel syndrome;
- chronic nonspecific abdominal pain;
- constipation with or without impaction;
- inflammatory bowel disease that is responding to treatment.

Diagnostic colonoscopy is absolutely contraindicated (Table 53.2) in anyone with fulminant colitis, toxic megacolon, and suspected perforated viscus. Recent intestinal resection represents a possible contraindication to the examination. However patients with acute severe colitis in which cultures are negative for bacterial pathogens

Table 53.1 Indications for colonoscopy.

Lower gastrointestinal bleeding
Hematochezia
Fecal occult blood
Inflammatory bowel disease
Diagnosis
Management
Extent and severity
Unclear response to treatment
Surveillance for colorectal cancer in chronic inflammatory bowel disease
Unexplained chronic diarrhea
Evaluation of anatomic abnormalities seen on barium enema
Family history of a familial polyposis syndrome
Cancer surveillance
Ulcerative colitis
Polyposis syndrome
Adenomatous or mixed polyp
Abdominal pain and chronic diarrhea in patients with HIV and other types of immunodeficiency disorders
Clinical signs of posttransplantation lymphoproliferative disorder
Intraoperatively
Identification of lesions that cannot be detected on palpation and/or inspection
Therapeutic colonoscopy
Polypectomy
Treatment of bleeding, angiodysplasia
Removal of foreign body
Decompression of toxic megacolon or colonic volvulus
Balloon dilation of stenotic lesions

Table 53.2 Contraindications to colonoscopy.

Absolute contraindications	Possible contraindications
Peritonitis	Severe colitis
Bowel perforation	Intestinal obstruction
Fulminant colitis	Recent surgical anastomoses
Toxic megacolon	Inability to visualize mucosa
	Poor bowel preparation
	Associated abnormalities
	Coagulopathy (no biopsies)
	Severe underlying medical problems

and parasites, such as *Entamoeba histolytica* and *Trichurus trichura*, should have an examination of the rectum and distal sigmoid colon to help establish whether they have a specific type of colitis. In such cases, limiting the area

viewed as indicated does not pose an undue risk. There are times when direct visualization of the mucosa gives a specific diagnosis, such as when pseudomembranes are seen or punched-out ulcers can be visualized.

Physicians should not consider doing colonoscopy in patients who have chronic or recurrent abdominal pain without other signs and symptoms, such as weight loss, failure to grow, loss of appetite, perianal disease, and positive indicators for inflammatory bowel disease, such as an elevated sedimentation rate, increased C reactive protein, and positive screening panel for inflammatory bowel disease.

Preparation of the patient for colonoscopy

Explanation to the patient

Preparing infants and children for colonoscopy can be difficult. Children who are less than school age may not understand why they are asked to have a restrictive diet and a simple explanation of why the test is being done is all that should be provided. The physician should try to use words that children will understand in order to clarify why they are going to be tested. Physicians and parents need to simply tell children they are going to have a test to look at where their "poop" comes from and it has to be clean inside to take a good look.

In school-age children and in adolescents fuller explanations may be provided depending on the level of sophistication of the child. It is useful to show the children and parents diagrams of the rectum and colon and distal small bowel to make them aware of what is going to be examined. Providing such knowledge ahead of time may make the child or adolescent more amenable to the procedure and more cooperative in preparing for the examination. It may be helpful to show pictures of the instruments used and simple diagrams of what may be normally seen.

Children at any age should be told that they will be given an intravenous infusion through which they will receive medications to make them sleep and to minimize any pain or discomfort.

Because most colonoscopists use medication to alter memory such as Valium or Versed, children should be told they will have little memory of their procedure other than going to sleep and that they will have little or no pain during the procedure.

Most children will be reassured by having the information that they will have devices attached to their fingers and arms, which measure their blood pressure or how hard their heart pumps, how fast their heart is beating, and the rate or speed at which they are breathing. Older individuals can be told that devices will be used to

tell how much oxygen is in their blood. Apprehension will be diminished by informing children of all ages that when they awake from their sleep their parent or parents will be nearby.

Most children, but not all, will accept the preprocedure explanation well and this will serve to alleviate much of their anxiety.

Bowel preparation

The most difficult preprocedure activity is to prepare the bowel so it can be adequately visualized. A number of different regimens are available that are based either on washout of the bowel (lavage) or cathartics. Both methods are subject to failure because they usually rely upon the cooperation of the infant or child, and even the best efforts of the medical staff may be frustrated in getting the infant or child adequately cleaned out.

In infants, the best technique usually involves clear liquids and milk of magnesia. Milk of magnesia 1.0 ml/kg of body weight is given two nights before the procedure and mid-day the day before the procedure.

Magnesium citrate may also be used in children above 1 year of age. This may be divided in two doses and given 24 and 12 h before the colonoscopy. It is best given cold and over ice, or mixed with lemon/lime-type soft drinks. Some individuals become nauseated with this and other cathartics. It is often better accepted to divide the dose of magnesium citrate in four fractions taken over a 4-h period of time.

The night before the colonoscopy, we often prescribe a glycerin suppository to enhance evacuation.

The above preparation regimen is probably the most benign of the various methods available and is the one with which the infant or child is most likely to cooperate.

In the lavage method the patient is allowed to eat and drink up until the afternoon before the procedure. The patient then fasts for 4 h. We prefer a flavored lavage solution which contains a nonabsorbable agent such as sorbitol or mannitol. Doses of 5–10 mL/kg up to 250 mL are given by mouth every 10 min, and continued until the rectal effluent is clear.

A large volume-balanced electrolyte lavage solution may also be administered. The dosage may be split so that half is given the day prior to the examination, and the rest on the day of the procedure. Some adolescents and teenagers will accomplish taking this solution readily. In the younger age child, however, success is less assured. Hospitalization for 24–48 h may be necessary before the procedure to cleanse the colon in uncooperative patients, where the placement of a nasogastric tube into the stomach may be the only way to guarantee administration of the solution. A randomized study of 2 doses of sodium phosphate versus a large (4 L) polyethylene-glycol preparation was performed in pediatric patients.

Compliance was easy or tolerable in 80% of the phosphosoda group but in only 33% of those who took the electrolyte prep. The bowel was well prepared in almost all of the former, but in only 40% of the group who were given the large-volume prep. Asymptomatic hyperphosphatemia was noted in the patients who took sodium phosphate.

If the child vomits in response to the lavage, the rate of infusion may have to be curtailed. Continuous nasogastric tube infusion of the large-volume electrolyte solution over a period of 12 h is very effective if children vomit the solution when it is given rapidly. During the infusion, metoclopramide 0.1 mg/kg is given to a maximum of 10 mg 20 min prior to lavage and every 4 h to enhance gastric emptying.

Overdistention of the stomach or slow gastric emptying should be suspected if stool is not passed within the first 4 h after starting the lavage technique. The rate of infusion of the balanced electrolyte lavage solution is usually between 100 and 200 mL per hour up to a full volume of 4 L. We typically give an infusion into a peripheral vein to provide maintenance fluids and electrolytes.

Enemas should not be used if the colonoscopist is looking for evidence of inflammatory bowel disease in the rectum and sigmoid colon, since enemas often cause erythema of the colonic mucosa and petechiae, giving a false-positive macroscopic image.

Equipment

Pediatric colonoscopes less than 11 mm in outer diameter are commercially available. They have a 3.2-mm biopsy channel, which allows the use of all accessories, such as standard biopsy forceps, snares, needles, and thermal probes. Colonoscopes with adjustable stiffness are more suitable for children over 4 years of age.

Colonoscopes specifically designed for infants and toddlers do not exist. Instead, pediatric upper gastrointestinal endoscopes can be used. Although it is more difficult to telescope the sigmoid colon with these instruments, higher flexibility and smaller diameter prevent excessive stretching of the bowel, especially in infants.

Sedation

The risks and benefits of colonoscopy are reviewed with the family usually at the time that the procedure is scheduled. At that time questions and answers about the procedure may be discussed. On the day of the procedure informed consent is again obtained. The child and one, or both, parents or grandparents, may be brought to the preendoscopy area, where an intravenous infusion is started. In order to minimize the discomfort of the intravenous needle, Emla cream may be applied to three or

four potential intravenous sites 45 min before an angio-cath is placed into a peripheral vein.

Full and continuous monitoring is necessary during the procedure. Sedation is begun after baseline vital signs are obtained. The most commonly used sedation for colonoscopy includes use of tranquilizers for relief of anxiety and narcotics for sedation-analgesia.

The narcotic of choice is fentanyl, which is rapid acting with a short half-life and minimal side effects. It rarely causes nausea and vomiting and does not lower the seizure threshold. Doses typically are 4 µg/kg given in 1 µg/kg boluses every 2–3 min. This regimen is continued until a state of sleepiness is reached or the patient, when asked to count to 10, cannot complete it.

Midazolam (Versed) is the most commonly used tranquilizer in children because of its speed of action and effectiveness. Doses range from 0.15 to 0.30 mg/kg given in divided doses. Midazolam is administered and each dose is flushed in with normal saline.

A 2-min time interval subsequent to each dose of medication is allowed before the patient is either questioned or (if old enough) asked to count from 1 to 10 and then backwards from 10 to 1.

If after giving a total dose of 4 µg/kg of fentanyl and 0.3 mg/kg of midazolam the patient is still awake, not sleepy, and can count coherently, promethazine may be given. The dosage used is 1 mg/kg up to 25 mg. Additional sedation with midazolam or fentanyl may be needed during the procedure.

If this routine is not successful in sedating the patient, anesthesia may be necessary. Agents such as ketamine and propofol may be necessary but they are best and most safely administered by an anesthesiologist. Many pediatric gastroenterologists do not use sedation-analgesia, and perform all cases under propofol anesthesia by the anesthetist.

Following sedation the patient is placed in the left lateral decubitus position. The parents are asked to leave the room once the patient is sedated. We do not make it a practice to allow parents to stay for the procedure.

Technique of colonoscopy

Complete colonoscopy can be performed successfully in the majority of children. Many factors can influence and complicate the procedure, e.g. redundant large intestine, improper preparation, previous surgeries, etc. It is important to understand the general principles of pediatric colonoscopy. Four guidelines are useful to perform a colonoscopy in children safely and effectively:

- 1 The intubated colon adopts configuration and shape according to manipulations and movements with the colonoscope, and the pattern of these changes are predictable, as well as the direction in which the colonoscope tip should be moved.

Table 53.3 Steps to ensure complete and successful colonoscopy in children.

Good bowel preparation to allow for optimal visualization
Superior sedation and patient monitoring (responds to calling name but resumes sleeping when not aroused)
Continuous patient monitoring with pulse oximeter
Check videocolonoscope for function before starting procedure
Proceed gently
Keep the colonoscope as straight as possible, try to keep lumen in view
Inflate with as little air as possible
Palpate for loops, have nursing assistant check for them, reduce them when they develop

2 Rotation, twisting, withdrawal, and simultaneous to and fro movements of the shaft will prevent formation of big loops, mesenteric stretching, and avoid related abdominal pain and discomfort.

3 Excessive insufflation leads to overdistention and diminishes ability to telescope the bowel.

4 During the procedure, the patient's comfort is provided by appropriate anesthesia, as well as optimal technique of colonoscopy. Excessive pushing forward creates more problems than benefits for the endoscopist.

The principles of pediatric colonoscopy are similar to those in adults (see Chapters 29 and 30), but because of the child's small stature, angulations may be more acute. In the child, it is often possible to palpate a loop of the scope in the abdomen, a clue that instrument withdrawal and straightening are needed. Meticulous attention to technique is required in children because the colon wall is thin, and, in the presence of anesthesia using propofol, there may not be any noticeable feedback from the patient that would provide a clue as to pain or discomfort from an overstretched mesentery or overdistended bowel (Table 53.3).

The principals of doing an effective colonoscopy are to minimize pain and discomfort. It is critical to try and keep the lumen of the bowel in sight knowing where the tip of the colonoscope is and trying to keep the colonoscope straight with avoidance of loops.

The mucosal pattern of the colon is best evaluated as the instrument is slowly withdrawn. However, we think it is important to carefully look at the mucosa while advancing forward, since trauma can sometimes occur to the mucosa with the passage of the instrument, and if abnormalities are not identified beforehand, one is always left wondering whether what one sees is due to colonoscopy, versus the underlying pathology.

Risks and complications of colonoscopy

The potential risks and complications of colonoscopy include bleeding, perforation, infection, and difficulties with sedation (such as paradoxical reaction to the agent

used). A higher dose of analgesic medication may be required for colonoscopy as compared with upper intestinal endoscopy, because procedures involving the colon may produce more intensive pain and/or require a longer procedure time. The higher doses of medication require careful monitoring because there may be a limited margin between inadequate sedation and oversedation.

Bowel perforation and hemorrhage related to pediatric colonoscopy are serious but rare complications of colonoscopy. During diagnostic colonoscopy the estimated frequency of colonic perforation, most commonly in the sigmoid, is in the range of 0.2–0.8%. This is an extremely low risk of perforation. The frequency is higher with therapeutic colonoscopy procedures such as polypectomy but is still comparatively rare, ranging from 0.5% to 3%. Mortality is extremely low and should be substantially less than 0.2%.

Prophylactic antibiotics are administered to children following the ASGE guidelines outlined in Chapter 19.

Indications for colonoscopy

Rectal bleeding

Careful history and physical examination may suggest the correct diagnosis, such as recent exposure to antibiotics (antibiotic-associated colitis), perianal streptococcal cellulitis, or an anal fissure. Allergy to cows' milk or soy protein may cause rectal bleeding in the absence of any other symptoms. Every child with hematochezia does not require colonoscopy. Eliciting a history of straining at defecation suggests an ano-rectal traumatic source (and predicts a large colon on examination). Perianal fistulas, skin tags, and hemorrhoids are indicative of Crohn's disease in children less than 18. Fissures are caused by passage of large bulky stools, with bright red blood on the outside of stool or mixed with the fecal stream if unformed.

Stool studies on every patient who has rectal bleeding should include a smear for polymorphonuclear leukocytes. Bacterial culture is indicated if leukocytes are present (*Shigella*, *Salmonella*, *Campylobacter*, *Escherichia coli*, and *Yersinia enterocolitica*). If antibiotics have been taken in the past 3 months, *Clostridium difficile* toxin titers (A and B) should be requested. The parasitology lab should look for *Entamoeba histolytica* and *Trichuris trichura*. The presence of eosinophils and Charcot-Leyden granules indicates allergic colitis.

In the pediatric patient with persistent or recurrent hematochezia and no identifiable cause, colonoscopy or flexible sigmoidoscopy is the procedure of choice to search for mucosal changes or other lesions associated with bleeding. Twenty-five per cent of patients at colonoscopy who have colitis will have unclassified

microscopic changes. Nodular lymphoid hyperplasia of the colon typically seen in early infancy is characterized by umbilicated lesions in the rectum, sigmoid, and/or colon.

The importance of colonoscopy in patients with inflammatory bowel disease is to define the extent of the inflammation, to obtain tissue samples that may establish the specific diagnosis, and as an aid in planning therapy.

Clostridium difficile may show characteristic pseudomembranes; however, this is not pathognomic for this bacteria and it may also be seen following shigellosis. Allergic colitis that is more typically seen in young infants may be nonspecific. Polyps, foreign bodies, and internal trauma from abuse may all be identified at colonoscopy. Lesions such as angiectasias or rectal varices may also be visualized. Cathartic abuse may also be recognized by the typical tigroid stripes seen in the mucosa.

Pain accompanying rectal bleeding may be caused by anal fissures, but intermittent cramping pain and the passage of "currant jelly-like" stool should raise the suspicion of intussusception, although dark or red blood may be seen. Vasculitis of the Henoch-Schönlein type typically presents with skin lesions, but the patient may have only abdominal pain and rectal bleeding. Endoscopic biopsy may be diagnostic when taken from areas of bleeding or from ulcerations.

Therapeutic colonoscopy

Juvenile or inflammatory polyps are not uncommon in children. They are most common in the age group 4–6 years, but may be present as early as age 1. They are uncommon after age 18. Although autoamputation may occur in these cases, many will not spontaneously disappear. This is the reason why when patients present with rectal bleeding and polyps are suspected, colonoscopy is indicated to remove the polyp with snare and cautery. The bleeding is usually painless, but the only symptoms may be anemia from more proximal polyps although most polyps are in the left colon.

Hereditary polyposis syndromes are often confirmed by following the patient colonoscopically and by doing polypectomy (see Chapter 14).

Chronic diarrhea

Nonbloody diarrhea is an uncommon indication for colonoscopy unless it is chronic and the stool cultures and ova/parasites have been nondiagnostic. Approximately 5% of patients who have colitis will not have polymorphonuclear leukocytes present in their stool. Microscopic colitis has been described in children presenting with chronic diarrhea, abdominal pain, loss of appetite, and weight loss. Multiple biopsies should be taken from the small bowel and colon in the patient

with chronic diarrhea even if no abnormality is visible to gross visual inspection.

Cancer surveillance

Children with either persistent or recurrent painless rectal bleeding should be colonoscoped. Development of adenocarcinoma of the colon in children is extremely rare but does occur even in children who never had ulcerative colitis. It typically presents with intermittent rectal bleeding and no diarrhea or with a progressive change in stool caliber.

The determining factor in the development of cancer in ulcerative colitis seems to be related to three factors: the severity of the original attack, the extent of mucosal involvement, and the duration of colitis. The cancer risk for patients with universal colitis involving the entire colon is not dependent on the age of onset, so children are at risk who have the disease for about 8 years, and even young persons with universal colitis should begin surveillance colonoscopy after 8 years of disease. Children of patients with inherited polyposis syndromes should have a surveillance colonoscopy to identify the presence of polyps, and this is recommended to begin at 11 years of age.

Summary

Colonoscopy in children is different from colonoscopy in adults. The preparation must be more carefully explained to the parents or guardians, and compliance can often be a problem. The equipment is the same as that used in adults, but a gastroscope can be quite useful for negotiating acute angulations. The technique of the examination is similar, but the bowel wall is quite thin and may not withstand the formation of large loops. The pathology in children as well as indications for colonoscopy are also different from that found in adults, with rectal bleeding being the commonest indication, and neoplastic disease being the least likely pathology finding. With adequate sedation, careful monitoring and meticulous attention to technique, colonoscopy in children can be a safe and rewarding procedure.

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Chapter 54

The Future of Colonoscopy

Paul Swain

Introduction

Colonoscopy clearly has a future, which will expand even if the technology stands still. There is a vast amount of colonoscopy to be done if recommendations for colon cancer screening in everyone over the age of 50 are to be put into practice. There is something awful about colonoscopy; it hurts, patients dread the procedure. Sometimes it is extremely difficult to do. Colonoscopists become inured to how terrible it sometimes is and simply say sorry as they push the colonoscope further into a patient already in pain. My three wishes for the future of colonoscopy are:

- 1 that it should become painless;
- 2 that sedation and analgesia should no longer be necessary;
- 3 it should become much quicker and easier.

There has been very little change in the nature of colonoscopy in the last 20 years. Despite some innovation, no substantial change altering the physical nature of colonoscopy has ever been tested in humans. The advent of video colonoscopes, better application of stiffening including variable-stiffness colonoscopes, magnifying images, and colonoscope magnetic localization systems have not altered the fundamental difficulty posed by colonoscopy. The most important limitation of colonoscopy is the tendency to form loops during advancement through the colon. The loops are associated with increasing loss of transmission of force to the tip and consequent failure of advancement.

It is possible that colonoscopy might be overtaken by other technologies, such as computed tomographic or magnetic resonance colography or virtual colonoscopy [1]. Screening for colon cancer might become unnecessary if fecal stool testing for genetic abnormalities or some form of screening blood test was found to be very specific. Some of these might reduce the anticipated volume of colonoscopy. Since magnetic resonance and computed tomography cannot produce color images and cannot identify flat or very small abnormalities, these technologies seem unlikely to replace colonoscopy. These preliminary screening procedures might usefully increase the ratio of therapeutic to diagnostic colonoscopies if they can selectively identify which patients do

not have polyps and therefore do not require colonoscopy. If an external imaging method such as magnetic resonance colography could be found to image the colon reliably without preparation, then the balance might tip substantially against diagnostic flexible colonoscopy.

The main purpose of this chapter is to outline a variety of devices of varying practicality that have been described which might allow the examination of the large bowel by other means. Some of these methods have been suggested for application at colonoscopy. These methods include tip propulsion by a variety of methods, robotics, wireless endoscopy, free capsule endoscopy, specialized overtube use, and "toposcopy".

Aids for advancing a colonoscope

A variety of devices have been described that can be used in conjunction with an endoscope to facilitate its advance. These include overtubes, internal stiffening devices (spines), and guide threads or wires.

Overtubes and spines

A problem of enteroscopy is that as the endoscope proceeds further and becomes more convoluted, so less and less of the force applied by the clinician is transmitted to the front portion of the endoscope. It has been suggested that this problem might be eased by using an overtube, which can be slid over the endoscope to support it along its shaft so that the forces applied are restrained by the overtube without stretching the bowel into loops. Overtubes have also been specifically developed to limit looping on the greater curve of the stomach. Similarly, there has been some interest in redesigning special overtubes for colonoscopy. These have been tried in the past but largely abandoned. The overtube can itself be an endoscope, as in the mother-and-baby system used for ileoscopy.

Effective overtubes are more difficult to design and construct than might be expected. The features that are helpful include a low coefficient of friction, a close fit between the endoscope and the tube, and increased stiffness in the sigmoid. The ideal overtube would be floppy while it was being pushed into place over the endoscope

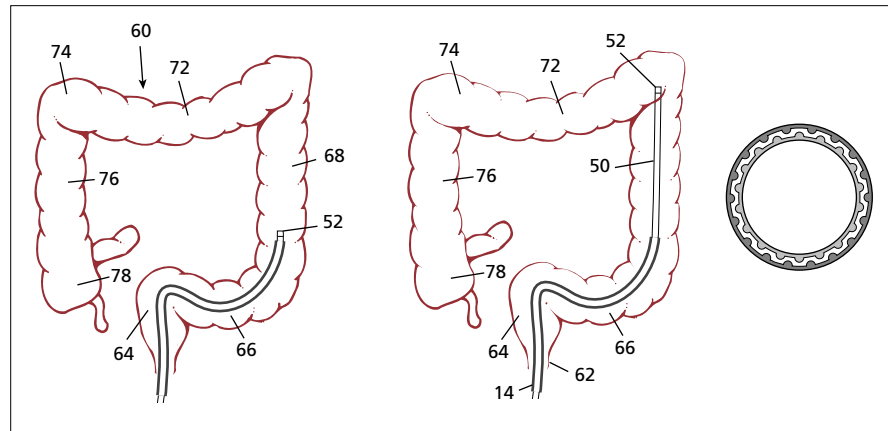


Fig. 54.1 Cross section of variable-stiffness overtube. (From Bauerfiend & Bauerfiend [2].)

and then become rigid so as to provide the best possible support. Bauerfiend and Bauerfiend [2] have proposed an overtube with a hollow wall (Fig. 54.1) so that when the air is sucked out of the annular gap the inner and outer walls are squeezed together making it (moderately) rigid.

An internal spine can be used instead of an overtube to alter the stiffness of the endoscope. One such device that has been used at enteroscopy is the stiffener made by Wilson Cook (Winston Salem, USA) that utilizes the tendency of a wound wire coil to become stiffer when it is compressed by tightening wires that run through the inside of the coil. This device can be passed through the biopsy channel of the colonoscope to increase its stiffness and may allow the tip of the endoscope to move further forward when the scope is advanced at the anus. This internal stiffener becomes fixed within the channel of the endoscope and they move as one. Olympus (Japan) have included a variable-stiffness mechanism in a new colonoscope design. Some clinical studies [3,4] but not all [5] using this mechanism suggest that it may speed up colonoscopy.

The effectiveness of an internal spine might be enhanced if the colonoscope could be slid over the spine so that the spine served to guide it around curves. Sturges and colleagues [6] have proposed a "slide motion" scheme, where a flexible spine is slid forward a few centimeters out of the tip of the endoscope and is then made rigid, and the endoscope is advanced over the spine until the tip of the endoscope is adjacent to the tip of the spine. At this point the spine is once again made flexible and the cycle is repeated with the spine being slid forward again. To make a spine that can be rapidly switched between flexibility and rigidity, these authors propose that the spine consist of a series of close-fitting balls and sockets that can be pulled into each other and locked when a wire that runs along the axis of the spine is tightened. They suggest that the tightness of the wire is controlled by passing an electric current through it so that its temperature and hence its length can be varied.

This spine would be too large to fit through the biopsy channel of an existing endoscope and they envisage an "endoscope conduit," i.e. a covering tube for the spine.

Mother-and-baby colonoscopy systems

A mother-and-baby ileoscopy system has been described by Jakobs and colleagues [7]. A specialized mother colonoscope with a large channel was used to allow a baby flexible endoscope of 3.1 mm outer diameter with up and down deflection and a 1.2-mm channel to be used to intubate the ileum in 10 patients over a distance of 5–60 mm. This might be classified as an endoscope constrained within a stiff overtube.

Thread-guided pull endoscopy ("rope-way" colonoscopy and enteroscopy)

Other endoscopic techniques have been used to evaluate the entire small intestine without surgery. A thread-guided method of enteroscopy is the oldest method to totally intubate the small intestine via the colon [8,9]. This technique involves having a patient swallow a guide thread, allowing it to pass through the whole gut until it emerges from the rectum. The thread is then exchanged for a somewhat stiffer Teflon tube over which an endoscope can be passed. In theory and in limited clinical practice with this method, a complete endoscopic examination can be obtained by a combination of pushing on the endoscope and pulling on the guide tube. The instruments are fully therapeutic, including cauterization and polypectomy. Because the examination is painful due to tightening of the guide tube, general anesthesia is usually required. This technique has been used with long flexible video endoscopes [10].

Friction reduction

Methods for reducing friction, including the use of silicone spray, vegetable oil spray, and even the use of

a vibrating endoscope, have been suggested or used. Toposcopic self-everting catheters that unroll against the bowel wall have been suggested for following the lumen at endoscopy with a minimum of friction.

Lubricating the endoscope

Friction can be reduced by using lubricants. Most endoscopists are familiar with the use of water-based lubricants such as KY jelly and use them to facilitate the introduction of gastroscopes or colonoscopes. Silicone spray was used for several years in endoscopy units but because of anxieties about possible toxicity, particularly if inhaled, there has been a trend away from using silicone toward using vegetable cooking oils or fats. Lubrication is particularly helpful if using enteroscopes in conjunction with overtubes. The overtube should be sprayed internally and externally from both ends and the endoscope should be sprayed as well. Routine lubrication of the shaft of the enteroscope is probably also helpful.

Vibrating the shaft of the endoscope

Friction might be reduced by vibrating the endoscope. Hibino and colleagues [11] have described an intricate endoscope that contains components to make it vibrate. This device can be made to vibrate “in the vertically (upward/downward) or horizontally (rightward/leftward) directions, in the form of swing motion in which the distal end draws a circle, or in the form of movement (advance/retreat) motion.”

Everting toposcopic endoscopy

In 1978, Masuda [12] proposed that a flexible fiberscope could be fed through a conduit by attaching it to the end of an everted tube (i.e. a tube whose end has been turned inward and pulled back through itself). When the tube is filled with liquid at pressure it will unroll itself and pull the endoscope forward and, since the tube is rolling against the conduit wall, there is no sliding friction between it and the wall. This technique has been used to pull catheters through vessels [13,14] and to carry an endoscope for fallopscopy [15].

Novel propulsion systems

The problems inherent in pushing a colonoscope have led to many proposals for methods providing propulsion at the tip so that endoscopes can pull themselves rapidly through the gastrointestinal tract. Most of these methods are similar to the various ways that animals move and it is convenient to group them together under the heading of the relevant creature.

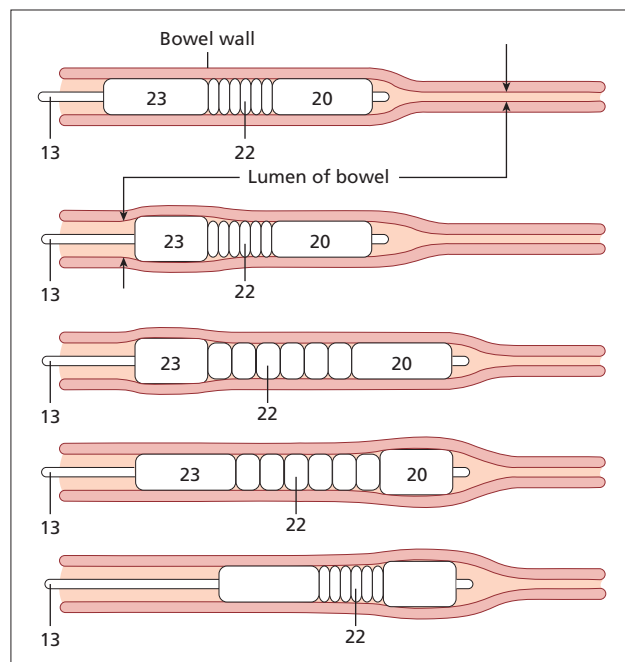


Fig. 54.2 “Earthworm.” (From Frazer [16].)

Balloons to grip the wall: earthworm

Earthworms move by alternately extending and distending sections of their body to produce peristaltic waves that drive them through the soil. The most common approach to propelling endoscopes has been to imitate the motion of an earthworm by attaching inflatable segments to the endoscope. As embodied in Frazer’s 1979 patent [16] (Fig. 54.2), there are two radially expandable bladders separated by an axially expandable bellows, with only the forward bladder attached to the endoscope. The sequence of operation is as follows:

- 1 the rear bladder is expanded to anchor it against the colon wall;
- 2 the bellows are then expanded to push the front bladder (and hence the endoscope) forward;
- 3 the front bladder is inflated so that it is locked in place against the colon wall;
- 4 the rear bladder is deflated;
- 5 the bellows are contracted to draw the rear bladder forward ready to start the next cycle.

Variations on the worm theme can be found in several other patents [17–21]. The device of Liddy and colleagues [20] was the first worm method to be tested with humans. They used an overtube (labeled 42 in the patent drawing reproduced in Fig. 54.3) to open or close the gap between the fore and aft balloons. It was tested in three patients with familial polyposis and apparently advanced well until, in every case, one or other latex balloon burst [22].

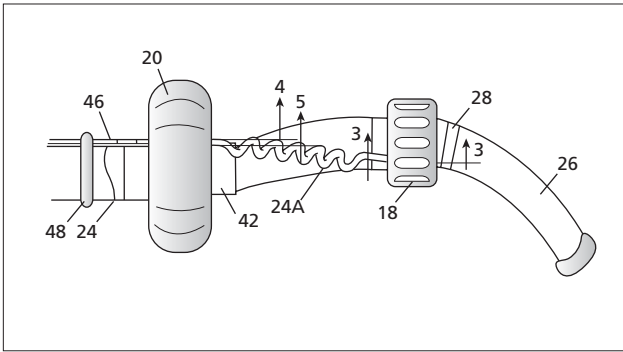


Fig. 54.3 "Earthworm." (From Liddy *et al.* [20].)

The methods described so far simulate an earthworm with only three sections: fore and aft sections that expand radially and a central section that moves axially. However, it is possible to make a more realistic worm with many sections. Such a worm is described by Grundfest and colleagues (Fig. 54.4) in a patent and an Internet article [21,23]. They use several segments so that waves of distension and extension can move along its body, simulating a real worm. The distension is provided by rubber balloons that can be inflated to grip the bowel wall while small pistons provide extension. It has been tested *in vivo* in the small intestines of an adult pig, which "strongly resemble those of a human juvenile in size and mechanical properties" [23]. They report that results were encouraging and that substantial traction was possible but conclude: "Although this machine could indeed move through a portion of the small intestine, it was clear that further development is required to support extensive *in vivo* experiments."

Walter and colleagues [24] described a double balloon or inchworm colonoscope. To shorten and lengthen the

colonoscope a push-and-pull flexible rod is used as a drive mechanism. A pneumatic cylinder is used to push the core in and out of the outer sheath.

Yamamoto and colleagues [25] have described a double-balloon method, mainly for enteroscopy but also for use in the colon. This uses an 8-mm endoscope 200 cm in length with a balloon that can be inflated at its tip and an overtube with a balloon at its tip. The endoscope can be advanced and the balloon inflated to grip the intestine. The endoscope is then gently withdrawn, straightening the bowel. The overtube is advanced and the balloon on its tip is inflated. By repeating this cycle the bowel is pulled back and pleated over the overtube as the endoscope is advanced. The device requires two operators. It features pressure monitoring of the balloons in a control box. The whole procedure is performed under X-ray screening and an enteroscopy may take more than 2 h to perform. This is the first double-balloon system to have been used clinically in patients. It represents a substantial advance in the technique of push enteroscopy since it allows therapeutic enteroscopes much further into the small intestine than hitherto. The biopsy channel is only 2.2 mm in size, which somewhat limits therapy, although biopsy, cautery, polypectomy, and injection are possible. Experience in the colon with this device is extremely limited.

There has been interest in applying recent "high-tech" developments in micromachining and shape memory alloys to the manufacture of more sophisticated worms. Guber [26] at the Karlsruhe Institut für Mikrostrukturtechnik has proposed using minute valves and balloons to produce a worm to crawl through blood vessels, while Carrozza and colleagues [27,28] have proposed a "teleoperated" worm that has tiny robot arms to manipulate a video camera and take biopsy samples

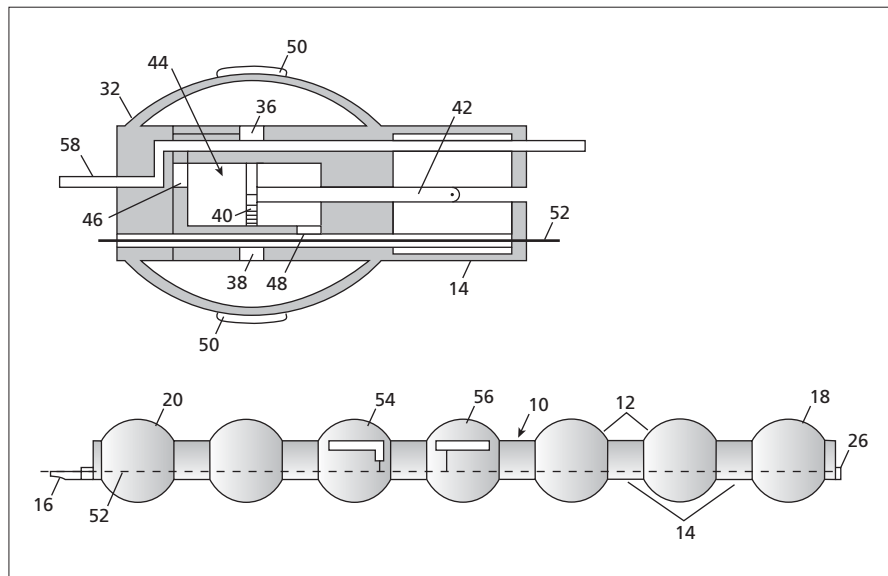


Fig. 54.4 Schematic diagram of the worm and a close-up of one section. (From Grundfest *et al.* [21].)

where required. They report that *in vivo* tests have been made and that “the principle is suitable for propelling the microrobot in the colon efficiently without significant damage to the colon wall.”

The issue of damage to the bowel wall is relevant since any earthworm system obtains its grip by inflating a balloon that presses outward against the walls, and it has been known for many years that relatively small pressures can burst the colon and presumably the small bowel. In 1931, Burt [29] inflated the colons from a series of 18 cadavers and found that the pressure required to tear the serosa ranged from 43 kPa (325 mmHg) to only 5.4 kPa (41 mmHg), with a mean value of 18 kPa (137 mmHg). Balloon inflation has caused perforation of the small bowel during Sonde-type enteroscopy [30].

Suction crawler: limpet or starfish

Suction can be used to grip the walls of the colon, which may have some advantages over using balloons because these tend to slip and may perforate the colon if over-inflated. Carrozza and colleagues [31] have used a pair of suction heads separated by a bellows to move through lengths of excised porcine colon. The device looks very similar to the worm illustrated in Fig. 54.3, with the front and back bladders being replaced by suction heads that use an array of small suction holes to hold the wall; the sequence of operation is the same as for the earthworm. The authors report that the “prototype was able to navigate into the colon, both in the forward and backward directions, efficiently, consistently and at sufficient speed.” This group have more recently reported further development of a suction crawling device, adding Velcro-like burrs to the suction heads [32]. Farhadi [33] filed a patent on a somewhat similar idea using suction. An internal tube is extended when a spring is unlocked and released. Suction is applied to the colon wall and a mechanism is applied that compresses the spring and locks it. By this mechanism, the endoscope tip is dragged forward.

We have built a prototype system designed to fit onto an existing small-diameter endoscope. In this system the tissue is gripped by the fore and aft suction heads, which are moved apart or together by a Bowden cable (a Bowden cable is a “bicycle brake cable,” i.e. an inner wire transmits force by sliding through an outer sleeve that is flexible but of fixed length). The sequence of operation is as follows. The endoscope, with the front suction head extended, is inserted into the bowel and pushed in the conventional way. When progress becomes difficult, the suction in the front head is activated and once the tissue is gripped the head is retracted so that it pulls the tissues over the tip of the endoscope. The tissue is then gripped by the rear head and released by the front head, which is slid forward ready to repeat the cycle [34].

Experience with excised porcine colon arranged into tortuous curves showed that it was straightforward to advance through sigmoid bends that were difficult to traverse with a conventional instrument. We found that gripping the wall with suction caused no visible damage.

Vijayan and colleagues [35] designed a hybrid balloon and suction device. This also used an extensor module sandwiched between two clasper modules. The clasper is a closed toroidal or doughnut-shaped balloon with six passive vacuum cups embedded onto a surface to give it a better grip. The air under the vacuum cups is squeezed out as the balloon expands against the bowel wall, generating positive adhesion. The extensor module can then extend axially or change the direction of the robot colonoscope’s tip.

Serpentine robot: snake

Earthworms move by extension and distension; in contrast, many snakes rely on serpentine motion where “the body literally swims along in a series of curves which gain a grip from exerting pressure against sticks, exposed roots, grass blades, pebbles or slight irregularities in the ground” [36]. Robot snakes exist and at least one group of authors has considered using them for endoscopy [6]. These authors rejected snake robots because they become “computationally and mechanically burdensome as the number of degrees of freedom increases” and because it is difficult to miniaturize them sufficiently to be of use in endoscopy.

The mechanical aspects of this problem have been tackled by Ikuta and colleagues [37], who made an “active endoscope” that is in effect a five-segment snake. It uses shape memory alloy tendons arranged about a spine so that each section can bend in three dimensions. The authors show a series of pictures of it progressing along a rubber model of a section of bowel. In fact they do not operate it as an intelligent snake but rather use a joystick to manually control the two tip segments; tip-bending instructions are then passed back along the line as the endoscope is pushed forward so that subsequent sections follow the actions of the tip.

The computational aspects of making a snake have been addressed by Shan and Koren [38]. They made a simple snake that can move across a floor (i.e. in two dimensions) and is clever enough to move toward a planned position despite encountering obstacles.

Many legs: millipede

This is not an apt animal analogy but the principle is that the endoscope has many legs or rings around it that can be made to move back and forth and so march the endoscope forward.

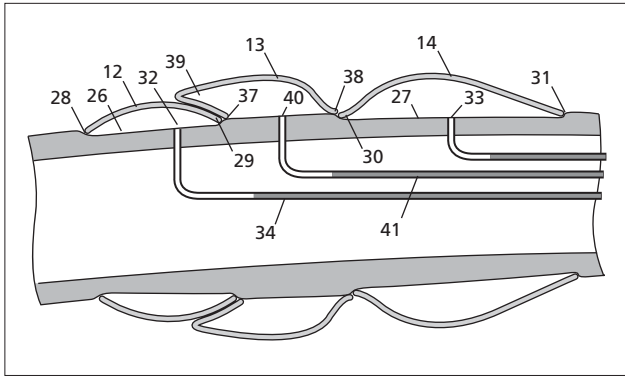


Fig. 54.5 Walking system. (From Utsugi [39].)

Figure 54.5 is from Utsugi’s patent [39] and shows the three inflatable cuffs that form one section of the millipede. The middle (“propellant”) cuff is the leg that is pushed backward and forward by the cuffs either side of it. The sequence of operation is that the “propellant” cuffs are inflated so that they press against the walls of the colon with enough force not to slip. Next, the “drive” cuffs are inflated, thereby pushing the propellant cuffs backward so that the sheath, and hence the endoscope, moves forward. The “return” cuffs are now inflated so that they first lift the wall of the gut off the propellant cuffs and then push those cuffs back onto the drive cuffs, which are simultaneously deflated. The cycle is now complete and one step has been taken.

Eleven years later, Krauter [40] described a somewhat similar but simpler method in his patent graphically titled “Walking borescope.” In 1994, Krauter’s colleague at Welch Allyn, Allred [41], produced an ingenious

design that used washers as feet. In this design (Fig. 54.6), the endoscope is surrounded by groups of five washers. All the groups are connected together and move in unison, but within each group every individual washer can be moved independently. Each of the five washers performs a cycle in which it moves slowly backward and then rapidly forward. If all five washers did this together, then the endoscope would simply rock back and forth; however, the washers are all out of phase so that at any one time four are moving slowly backward and only one is moving rapidly forward. As any driver can attest, the frictional force resisting skidding is independent of the speed of the skid, so in this case the forward propulsion from the four slow washers outweighs the reverse thrust from the one fast washer and the endoscope slowly advances.

Few legs: lizard and ant

Treat and Trimmer [42] present a four-legged device whose legs can extend as well as pivot at their proximal ends so that the quadruped can literally walk along the gut. It can be seen in Fig. 54.7 that the animal analogy is striking and that the creature has a single eye that transmits a video image through its tail to the endoscopist.

The article by Goh and colleagues [43] shows a picture of a robot called Attila that looks like a giant ant and was designed for lunar exploration. The authors speculate that it might be possible to miniaturize this 2-kg robot and allow it to roam the gastrointestinal tract, but they do not review any of the problems that might arise and only conclude that “the technology to do this is still not available.”

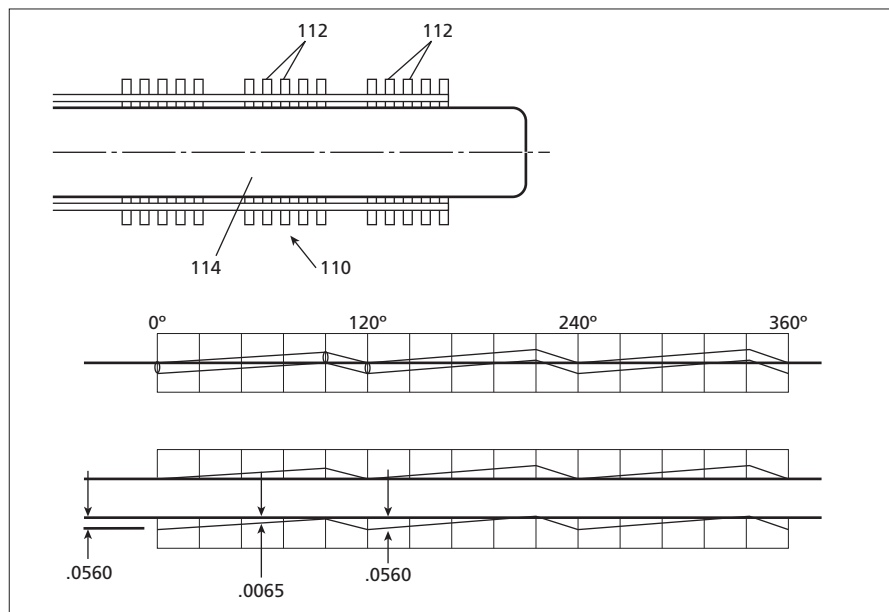


Fig. 54.6 Three groups of five washers surrounding the tip of an endoscope and the profile of the cam used to drive one set of washers. (From Allred [41].)

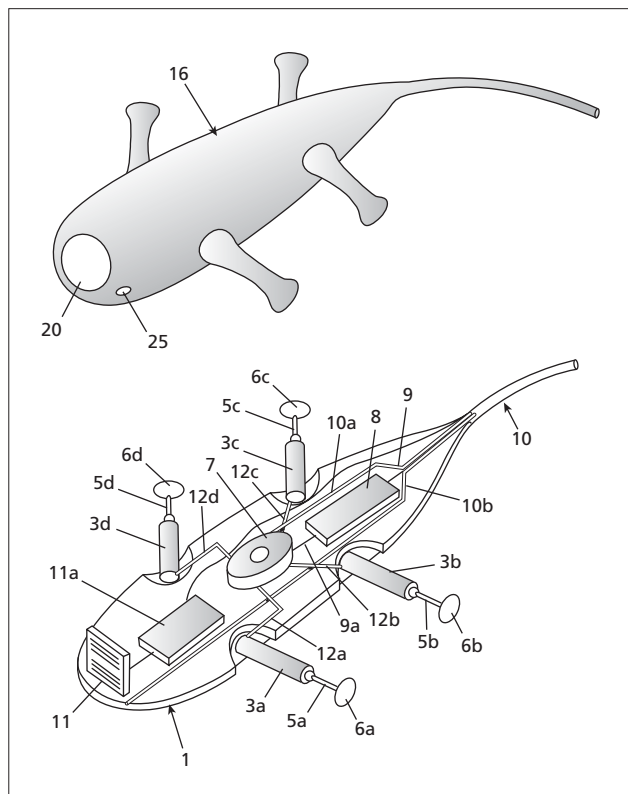


Fig. 54.7 Four-legged endoscope. (From Treat & Trimmer [42].)

Water jet: octopus

The octopus escapes from predators by squeezing water from its mantle and jetting away. The physical principle is that the mass is accelerated by forcing fluid through a small orifice and the force required to do this produces a reaction that pushes the octopus in the opposite direction. It is the same principle that drives a rocket or a jet engine.

Our group [34] has developed a water-jet-propelled endoscope. A spray head with a number of backward-facing nozzles can be attached to an endoscope so that the endoscopist can use bursts of water to pull the endoscope out of a loop when further pushing only serves to enlarge the loop. We have found that it is practical to produce sufficient thrust without introducing

an excessive amount of water in the bowel or an excessively sharp water jet. This propulsion force is helpful in advancing the endoscope along models made from plastic and rubber and also excised porcine colon as well as small bowel and has produced no visible damage in excised or *in vivo* pig colon.

Ginsburgh and colleagues [44] proposed that this principle could be used to propel a “borescope” for inspection of metal tubes such as drains or in other engineering applications.

Wheels and belts

With the introduction of wheels and tracks, the animal analogy must be dropped. Goh and colleagues [43] have published a picture of a device that looks like a toy car and have shown photographs of a robot similar to a model of a First World War tank using miniature motors, which drive caterpillar tracks.

Takada [45] has patented a more conventional looking endoscope that has belts running along its shaft that are supposed to act like the tracks of a tank (Fig. 54.8). It is suggested that the grip from the belts onto the bowel wall will be sufficient to pull the colonoscope smoothly and painlessly into the patient.

Wireless capsule colonoscopy

Wireless capsule endoscopy [46–49] has changed the way we think about enteroscopy. The system is strikingly successful in imaging patients with persistent gastrointestinal bleeding from the small intestine. Will wireless capsule technology change the future of colonoscopy? There is little doubt that many patients fervently wish that a painless swallowed device might make the discomfort of colonoscopy a thing of the past. Good images, especially of the right side of the colon, are often obtained. There are a number of technical issues that require solution if wireless capsule technology is going to image the colon as well as it currently images the small intestine. Power management is a problem. With two small silver oxide batteries, approximately 7 h of imaging is obtained. The capsule usually takes much longer to pass through the whole colon, on average about

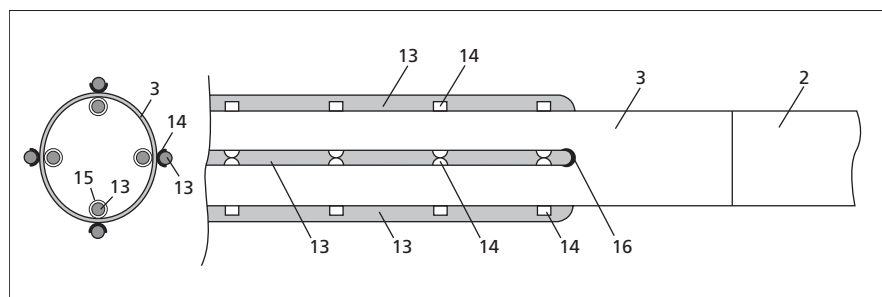


Fig. 54.8 Cross-section and side views of an endoscope with belts to pull it into and along the bowel: 13, belts; 14, guides to retain belts. (From Takada [45].)

24 h. More batteries, time delay, and external transmission of power might solve the power problem. Methods of better preparation, feedback illumination, coping with intermittent rapid movements and prolonged periods of stasis, and better viewing of the whole mucosal surface of the colon, which is larger than the small intestine, need to be found. Electrostimulation has been used to move ovoid (capsule-shaped) devices in the gut. Independent wireless devices have been used to drive experimental devices in the small intestine and colon [50,51].

Future needs in other areas related to colonoscopy

The response to sedation is variable. There is a need for better drugs than the opiate and benzodiazepine mixtures most commonly used. The use of propofol in colonoscopy is still controversial. The rapid onset of deep sedation and quick recovery are desirable but its occasional severe suppression of respiration and hypotension are negative features. The positive and negative features of propofol relate to its lack of protein binding, unlike the other medications used. In the future we need better and safer sedatives.

Preparation is often suboptimal. For some patients the preparation can be violent and uncomfortable. For the colonoscopist the preparation is frequently inadequate. Preparation in patients with severe bleeding is often difficult.

Cleaning colonoscopes still remains a concern. One potential future mishap waiting to occur might be a small epidemic of hepatitis C or HIV associated with poor cleaning of endoscopes. Publicity about such events might impact very seriously on the practice of colonoscopy. In the UK, colonoscopes and all colonoscopies in patients are tracked to assess the possible transmission of prion ("mad cow") disease. Any suggestion that colonoscopy could transmit prion disease might damage colonoscopy irretrievably or change its nature substantially.

It is hard to predict the impact that optoelectronic aids to colonoscopy will have in the future. Magnification, optical coherence tomography, and various types of spectroscopy may alter the practice of diagnostic colonoscopy. Most of these relate to taking the diagnosis of cancer or neoplasia from the histology laboratory to the tip of the endoscope. It is probable that imaging methods that can visualize structures in or beyond the wall of the colon will become an increasing part of colonoscopy. Endoscopic ultrasound in the colon will be used more commonly to stage tumors and direct therapy.

Future of therapeutic colonoscopy

The future of flexible endoscopic surgery in the colon depends on the development of better surgical tools. The

development of transanal microsurgical techniques that allow full-thickness excision of large villous adenomas and cancers with subsequent stitched closure of the defect has been shown to improve outcomes when compared with conventional surgical approaches. The development of safe and effective methods to perform such surgery at flexible colonoscopy is feasible. It is likely that submucosal resection of tumors will be more widely practiced and that as tools and techniques improve, full-thickness resection with closure of the defect and even anastomosis will become routine. Better sewing and stapling methods for use during flexible colonoscopy are needed.

Summary

The contents of this chapter might be regarded as a junkyard of ideas about improvements in colonoscopy; perhaps many will be rapidly discarded and forgotten. It could be that in the future colonoscopy will change very little. There are things about the procedure that stimulate the imagination to hope for better methods of colonoscopy in the future.

Acknowledgments

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Note: page numbers in *italics* refer to figures.

CRC, colorectal cancer; FAP, familial adenomatous polyposis; HNPCC, hereditary non-polyposis colorectal cancer.

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