4 Evidence-Based Endoscopy

John M. Inadomi and Ma Somsouk

Background

Evidence-based medicine provides a framework for using the medical literature to solve clinical problems and provide better patient care [1]. While many practitioners are skeptical about the value of this approach, which they perceive as being “cookbook” and dismissive of clinical judgment, the value of practicing evidence-based medicine is as much about understanding how little evidence is available to support our daily decision-making as it is about guiding medicine—is as much about understanding how little evidence is available to support our daily decision-making as it is about guiding practice based on results of quality clinical studies. “EBM” stands for evidence-based medicine—but it is meant to complement experience-based medical practice, not replace it.

This chapter will provide the foundation for understanding the principles of evidence-based medicine, using practical examples from endoscopy to illustrate the application of EBM. We will identify the critical components necessary to validate studies of therapy, diagnosis, harm, and prognosis. Armed with these tools, it is hoped that the reader will understand which aspects of his or her practice are based on firm evidence, which are based on guidelines or standards that may not be derived from solid evidence, and which are simply dogma based on experience. As my mentor Dr. Marvin Slesinger is fond of saying, “It’s not what we don’t know that will kill us but rather what we think we know that is wrong.”

Each of the following sections will focus on a different type of clinical problem, opening with a clinical scenario to frame the question, followed by the accepted components of a study that would provide valid evidence, and closing with recommendations about how to incorporate study results into clinical practice. The basis of these concepts has been presented previously by the Evidence-Based Medicine Working Group and published in a series of articles in JAMA entitled “Users’ Guides to the Medical Literature.” These comprehensive resources are listed as references, and interested readers can pursue details of the concepts of evidence-based medicine through these publications [1–7].

The template for discussing evidence-based methods includes three universal questions, each of which has subtopics, that ask: firstly, are the results of the study valid? Secondly, what are the results? And thirdly, will the results help me in caring for my patients? Since the second and third questions are irrelevant if the first question is not answered affirmatively, emphasis is placed on determining whether the study methods are valid. The whole essence of a valid study design boils down to a simple goal: reduce bias. What is bias? In technical terms, it is “the consistent, repeated divergence of the sample statistic from the population parameter in the same direction.” In plain English, it is the presence of something that causes the study to provide an answer that is not correct. Most often, it results from the presence of confounders, which are measured or unmeasured factors that are associated with both the predictor or exposure under scrutiny and the outcome. Instead of going through the mathematical or statistical derivations of bias, we will explore these ideas through various examples in this chapter.

Studies of Therapy

Clinical Scenario

You are consulted by your hospitalist to evaluate a patient with coffee-ground emesis and melena. Upper endoscopy revealed a large duodenal ulcer with a visible vessel that was not actively bleeding. Initial treatment was complicated by active bleeding, but you achieved hemostasis with epinephrine injection, thrombo- coagulation, and continuous infusion of a proton-pump inhibitor. Unfortunately, rebleeding occurred within 24 h. You feel that you have given it your best shot and feel wary about repeating an endoscopy. You question whether or not repeated endoscopy is warranted after initial endoscopy, or whether you should refer the patient for surgery.

Are the Results Valid?

The issues that need to be addressed in order to determine whether a study of therapy is valid are shown in Table 4.1 and consist of: 1. randomization; 2. blinding; 3. concealed allocation; 4. complete follow-up; 5. intention-to-treat analysis; and 6. co-interventions [5].

Randomization refers to the process of randomly assigning patients to one group versus another. If this were done by deliberate assignment, it could result in unequal distribution of patients, with confounders in the study groups based on investigator bias. For example, assignment of patients with peptic ulcer hemorrhage could be biased if the investigators preferentially assigned patients without stigmata of recent hemorrhage to a new endoscopic therapy while assigning patients with stigmata to medical therapy. In this case, the confounder would be stigmata of hemorrhage, which could drive the outcome of recurrent hemorrhage more heavily than the intervention. While it would be possible to manually assign patients in equal numbers to each arm of a trial and thus reduce bias, the advantage of randomization is that it can adjust for unknown factors.

Table 4.1 Studies of therapy

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<th>Are the results of the study valid?</th>
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<td>2. Blinding</td>
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<td>3. Concealed allocation</td>
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<td>4. Complete follow-up</td>
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<td>5. Intention-to-treat analysis</td>
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<td>6. Co-interventions</td>
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<th>What were the results?</th>
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<td>1. Magnitude of the treatment effect</td>
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<th>Will the results help me in caring for my patients?</th>
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<td>1. Application of the study to my patients</td>
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<td>2. Clinically important outcomes</td>
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<td>3. Treatment benefits versus harms and costs</td>
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confounders as easily as known confounders, while manual assignment can only adjust for the latter. A nice example of this occurred with studies of ulcer hemorrhage, where prior to our knowledge of *Helicobacter pylori* we could not have specified enrollment based on this important etiologic factor; however, randomization would have ensured equal distribution of patients with and without *H. pylori* into competing arms of any trial.

**Blinding.** Study investigators may treat patients or assess them differently if they know that they are on a new medication versus a standard medication or placebo. Patients themselves may report different outcomes if they know whether they are on an active therapy or placebo. For these reasons, it is essential to blind the patients and investigators or study observers responsible for assessing outcomes.

**Concealed allocation and baseline differences.** Despite randomization, it is possible that study groups may differ in important prognostic factors at baseline. This tends to occur more commonly in small trials, where there is an increased risk of imbalance between study groups in the number of patients with different potential confounders. More importantly, group differences may occur at the time of enrollment prior to randomization, in the absence of concealed allocation. This term refers to the blinding of the person responsible for enrolling patients to the sequence of group assignment. If an investigator is enrolling patients into a study comparing a new intervention versus standard therapy, there may be conscious or subconscious efforts to enroll healthier patients if it is known that the strategy to which they would be randomized is the new intervention, while excluding other potentially “sicker” candidates from enrollment on the basis of subjective exclusion criteria. Typically, the first table in a study of therapy will list baseline characteristics and identify significant differences between study groups to ensure that baseline differences are minimized. If significant differences remain, it is still possible to adjust for the differences statistically, but the power to detect significant outcomes may be reduced.

**Complete follow-up.** If a substantial proportion of patients enrolled in a trial are not followed to its conclusion, the possibility of biased ascertainment of end points may occur. Patients whose outcome is unknown could have dropped out because they were doing so well they did not feel the need to return; conversely, they might have been unable to attend for follow-up because they were too ill or had in the meantime died. A general rule of thumb is that if the dropout rate is less than 10%, the conclusions are not likely to be ascribed to the intervention under investigation, not differences in other factors (termed “co-interventions”). Double-blinding assists in this process, but it is possible that certain interventions, such as surgical procedures, do not allow complete blinding. Careful adherence to study protocols to reduce co-interventions will therefore be necessary.

If the study methods are deemed valid after each of the steps mentioned above has been confirmed, then it is appropriate to assess the results and determine the potential impact on the clinical care of patients [2].

### What Are the Results?

**Magnitude of treatment effect.** To assess the results of a study of therapy, one needs to determine the magnitude and precision of the treatment effect. In general, the results of a study of therapy report the proportion of patients who achieve the primary end point in the intervention group in comparison with the control or standard therapy group. In this case, there will be a comparison of proportions between these groups and some determination of the statistical and clinical importance of the differences. The differences can be described as the absolute risk reduction, which is simply the difference between rates. Alternatively, one may report the relative risk reduction, which is the percentage reduction in risk between strategies ([baseline risk – intervention risk]/baseline risk). The relative risk reduction can be somewhat misleading, as it may appear to magnify the actual reduction in risk. For example, assume a baseline risk of pancreatitis after endoscopic retrograde cholangiopancreatography (ERCP) of 2%. A new therapy that results in a 1% risk of post-ERCP pancreatitis nets an absolute risk reduction of 1%; however, the results can also be stated as a 50% relative risk reduction ([2% − 1%]/2%).

**Precision of treatment effect.** One must remember that a study can only identify a “point estimate” of the treatment effect, since only a sample of the entire population at risk for the outcome has been assessed in a clinical trial. If the study were to be repeated multiple times, the results might differ, and this variation in results reflects the precision. The confidence interval is used to describe the variation in study results that could be expected with repeated studies. By convention, a 95% confidence interval is used to report the range of values within which the risk reduction is expected to fall 95% of the time if such a study is repeated over and over again. In general, the larger the sample size of the study, the narrower the range of the confidence interval. Thus, when assessing the “power” of a study, which is the ability to detect a significant difference in treatment outcomes between competing strategies, the confidence interval is useful to determine whether the study is large enough to provide a
Introduction

Video capsule endoscopy (VCE) became a clinical reality in 2001, with Food and Drug Administration (FDA) approval of the M2A capsule (Given Imaging, Inc., Yoqneam, Israel) on the basis of a study comparing push enteroscopy with the capsule in patients with obscure gastrointestinal bleeding [1]. For clinicians interested in disorders of the small intestine, the arrival of capsule endoscopy was timely. Conventional endoscopic technology was severely limited; push enteroscopy allowed examination of up to 100 cm distal to the ligament of Treitz; ileoscopy allowed examination of the distal ileum; intraoperative enteroscopy was and still is the “gold standard” for small-bowel examination, but is far from perfect and is invasive [2]. The indications and limitations of VCE are now quite well understood around the world. In 2007, the FDA approved the EndoCapsule (Olympus America, Inc., Center Valley, Pennsylvania, USA) [3]. Capsules developed in China and the MiRo capsule from Korea have also been demonstrated [4], but are not yet clinically available in Western countries. With the concurrent development of other novel enteroscopic devices—double-balloon endoscopes [5] (Fujinon Inc., Wayne, New Jersey, USA), single-balloon enteroscopes [6] (Olympus America), and spiral overtubes [7] (Endo-Ease Discovery SB; Spirus Medical, Inc., Stoughton, Massachusetts, USA) for diagnosis and/or therapy—interest in the small intestine has undergone a renaissance. This chapter reviews the technology of VCE, the indications for the procedure, and its complications and provides a perspective on it in relation to other enteroscopic techniques.

Technology

The PillCam SB, EndoCapsule, and MiRo capsule are similar in size, shape, weight, and imaging capabilities. The MiRo capsule uses electrical field propagation to transmit images (Table 13.1). Both the PillCam and EndoCapsule are single-ended imaging devices that are able to take two images per second for a total of about 55,000 images over the life of the silver oxide battery. The images created by the VCE are transmitted to a portable hard drive worn on the patient’s belt, via eight sensor arrays adherent to the abdominal skin. After an 8-h period, the recorder is transferred from the patient to a workstation, and the images are processed into a video. The image quality of the two FDA-approved devices is excellent, but subjectively different. The slightly larger field of view of the PillCam SB has yet to be shown to be clinically useful. The images are magnified 1:8, allowing resolution of individual villi (Fig. 13.1). Since there is clear succus entericus in the lumen for much of the length of the small bowel, conditions are met for immersion enteroscopy. The villi are often seen to be “floating,” analogous to seaweed on a submerged rock. There is considerable variation in the normal characteristics of the villi. In at least 75% of studies, the entire length of the intestine is visualized. In the remaining 25%, transit of the capsule is incomplete after 8 h, but fewer than 1% of capsules are retained for a long period. Transient retention usually occurs at the ileocecal valve.

### Table 13.1 Comparison of video capsules

<table>
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<tr>
<th></th>
<th>EndoCapsule</th>
<th>PillCam SB</th>
<th>MiRo</th>
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<tbody>
<tr>
<td>Length</td>
<td>26</td>
<td>26</td>
<td>24</td>
</tr>
<tr>
<td>Diameter</td>
<td>11</td>
<td>11</td>
<td>10.8</td>
</tr>
<tr>
<td>Weight</td>
<td>3.8</td>
<td>3.45</td>
<td>3.3</td>
</tr>
<tr>
<td>Frame rate</td>
<td>2 fps</td>
<td>2 fps</td>
<td>2 fps</td>
</tr>
<tr>
<td>Image sensor</td>
<td>CCD</td>
<td>CMOS</td>
<td>CMOS</td>
</tr>
<tr>
<td>Field of view</td>
<td>145</td>
<td>156</td>
<td>150</td>
</tr>
<tr>
<td>Illumination</td>
<td>6 white LEDs</td>
<td>6 white LEDs</td>
<td>6 white LEDs</td>
</tr>
<tr>
<td>Antennas</td>
<td>8 body leads</td>
<td>8 body leads</td>
<td>Electrical field propagation</td>
</tr>
<tr>
<td>Real-time viewing</td>
<td>VE-1 viewer</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>Documentation</td>
<td>DVD</td>
<td>CD</td>
<td>?</td>
</tr>
</tbody>
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CCD, charge-coupled device; CD, compact disk; CMOS, complementary metal oxide semiconductor; DVD, digital video disk; fps, frames per second; LED, light-emitting diode.
Relatively recently, the PillCam ESO (Given Imaging, Inc., Yoqneam, Israel) has been approved by the FDA [8,9] for screening patients for Barrett’s esophagus and detecting esophageal varices. The device is the same size as the other capsules described above, but is double-ended and is used to take seven frames per second at each end. It has now been upgraded to take nine frames per second. Optimal imaging is obtained by placing the patient in the left lateral position. After rinsing out the mouth, the patient swallows the capsule with 15 mL of water, followed every 30 s by 15 mL of water ingested from a large-tipped syringe [10]. This position eliminates gravity and minimizes bubbles, and esophageal motility is such that that several minutes of imaging of the esophageal mucosa is possible. The battery life is only 30 min, but excellent views of the gastric mucosa and proximal small bowel can also be obtained. Images front the front and back are reviewed in parallel, and as the length of the capsule is known, it becomes possible to measure the length of abnormalities. However, at current pricing levels the device is not cost-effective and it has not caught on in the clinical arena. One study has reported sensitivity, specificity, and positive and negative predictive values for Barrett’s esophagus in comparison with esophagogastroduodenoscopy (EGD) as 97%, 100%, 100%, and 98%, respectively. However, a second study including 96 patients only showed a sensitivity of 67% and a specificity of 84% [9,11].

This capsule has also been approved for detection of varices. In this context, it has potential value in very ill patients with decompensated liver disease who are reluctant to undergo endoscopy, to check whether they have esophageal varices [12].

A colon capsule has been developed and is undergoing trials in Europe [13]. This is larger, 30 mm long, and is again double-ended. Unfortunately, the withdrawal of the prokinetic agent tegaserod (Novartis), has put the trials in the USA on hold pending the availability of a new small-bowel prokinetic agent.

The Agile patency capsule (Given Imaging, Inc., Yoqneam, Israel) has undergone development to the point that it is now a useful tool. It consists of a plastic film encasing a lactose–barium mixture and a small transponder [14,15]. At each end of it there is a dissolvable plug, which starts to disintegrate after about 36 h of contact with digestive juice. The concept is that this type of device can be useful when there is a suspected stricture that cannot be demonstrated by other means. The capsule is swallowed, and 30 h later the abdomen is scanned with a device to detect the transponder, or using a plain abdominal film. If the capsule is not detected or is in the colon, there is sufficient lumen for the video capsule to pass. The video capsule may still not complete its passage through the small bowel before the battery runs out. This device is particularly useful in patients known to have Crohn’s disease, in whom there is a capsule retention risk of up to 13%. In patients without Crohn’s disease or those in whom it is only suspected, the retention rate is 1% or less. The device was originally designed with a single plug, which dissolved erratically and was associated with a few cases of obstruction.

Preparation of the patient remains controversial. Many small studies have been performed, but all have the fundamental problem of not being able to objectively measure what constitutes good preparation. Furthermore, it is not clear whether there is an increased diagnostic yield if the preparation is better; preparation may wash away small amounts of blood and thereby reduce the diagnostic value of the procedure [16].

The use of simethicone as a bubble-reducing agent is also controversial, as are prokinetics. There is some evidence that placing the bed–ridden patient in the right lateral decubitus position reduces gastric transit time, but this has not been confirmed in ambulatory patients. Clinically, the most commonly used preparations are nothing by mouth for 12 h before the procedure or 2 L of a polyethylene glycol solution the night before the procedure. The present author does not routinely use preparation, except in patients in whom there is evidence of reduced motility.

The PillCam SB is approved for use in children down to the age of 10, but anecdotally it has been used in children as young as 2 years of age without mishap. Children who are unable to swallow the capsule need to have the capsule placed endoscopically under general anesthesia (Fig. 13.2).

**Limitations**

The technology is not perfect. In the majority of patients, 75% of the full length of the small bowel may be visualized, but the mucosal surface is incompletely seen. The duodenal sweep is usually poorly imaged, and the ampulla of Vater is seen about 5% of the time (Fig. 13.3). This is for two reasons—firstly, the lumen is not dis tended, so that it is not possible to see deeply between the plicae; and secondly, the capsule has been shown to tumble. This was demonstrated in the FDA trial for the Olympus capsule, in which a PillCam SB and EndoCapsule were swallowed by the same patient 40 min apart [3]. In some of the patients, the second capsule caught up with the first and imaged the leading capsule in a variety of postures, including tumbling and with the lens hood buried in the mucosa. This possibility was alluded to in an early paper in which beads were attached in a dog’s intestinal mucosa. Subsequent study with VCE did not detect all the beads [17].

Interpretation is a major issue. The American Society for Gastrointestinal Endoscopy has recommended credentialing guidelines, which should be regarded as minimalist. There is the problem of the learning curve, particularly learning the range of normal variation. There is considerable confusion in interpreting abnormalities associated with intraluminal bubbles and what constitutes a submucosal mass. Thirdly, there is disagreement, even between experts, as to when a red spot becomes an angiectasia; the level of disagreement may be as high as 25% [3]. The capsule is also not the perfect tool for detecting small-bowel polyps or tumors, but is still better...
Introduction

Robert H. Hawes

The development of laparoscopic cholecystectomy has had a significant influence on the practice of surgery, as well as on surgeons’ mindset, making them more aware of new ways of operating less invasively. Endoscopists—both physicians and surgeons—have always taken a less invasive approach, as therapeutic endoscopy primarily developed as an alternative to more invasive surgical procedures. As a result, the introduction of natural orifice surgery by Kalloo et al. in 2000 \cite{1,2} created excitement in both disciplines. For surgeons, natural orifice transluminal endoscopic surgery (NOTES) offers new opportunities for less invasive procedures, while for endoscopists it has the potential to allow transluminal therapy and also promises to accelerate the development of devices facilitating a whole range of new endoluminal procedures.

Since the first description of NOTES, there has been considerable speculation—and indeed concern—about how it will develop. The chaos in the early days of laparoscopic cholecystectomy is still vivid in our memories. Although natural orifice surgery is considered to have great potential, guidance and direction in its implementation is needed in order to ensure that patients are protected and that it develops in a responsible way. Toward this end, the Society of American Gastrointestinal Endoscopic Surgeons (SAGES) and the American Society for Gastrointestinal Endoscopy (ASGE) established a joint committee to support basic research, promote education, and create a registry for human NOTES procedures. In addition, an organization called the Natural Orifice Surgery Consortium for Assessment and Research (NOSCAR) was formed, with its membership drawn from teams of laparoscopy and flexible-endoscopy experts from around the world. The joint ASGE/SAGES committee, in cooperation with the NOSCAR group, was charged with setting standards for conduct in the field of NOTES—such as insisting that all human NOTES procedures be conducted under the guidance and oversight of institutional review boards—and establishing guidelines for practice when appropriate. Groups with organizational structures and goals similar to those of NOSCAR have also emerged in Europe, Asia, and South America. This paradigm of cooperation between societies to provide leadership in the development of new techniques will surely be one of the most powerful legacies of natural orifice surgery.

It is very important to view natural orifice surgery as a movement toward less invasive therapies, rather than as a series of new surgical procedures. It has already had a significant influence and will undoubtedly continue to have an impact on therapeutic endoscopy for many years to come:

- It has brought endoscopists and laparoscopic surgeons together—each with their own unique perspectives. Together, they will accelerate innovation in endoscopy.
- It has brought representatives of medical-device manufacturers together—including companies that had previously concentrated on innovative devices only in their own markets. Now, companies specializing in laparoscopic devices, flexible endoscopes, and accessories for flexible endoscopes are exploring opportunities outside their own markets and are leveraging their knowledge and experience in order to solve the unique problems faced in natural orifice surgery.
- The improved relationship between surgeons and endoscopists, combined with innovative technologies from industry, will greatly accelerate the development of intraluminal therapies for obesity management, reflux disease, full-thickness resection of intramural tumors, and endoscopic submucosal dissection.

These direct effects of the NOTES movement will create a legacy that goes well beyond the new generation of minimally invasive surgical procedures. To appreciate the real impact of NOTES, these developments should be seen as a whole, without focusing exclusively on an announcement of the NOTES equivalent of laparoscopic cholecystectomy, for example. There is no question that procedures will eventually be performed using natural orifices as access points. Medical historians will look back and document the broad influence that the introduction of natural orifice surgery had on therapeutic endoscopy.

This trend toward procedures with access via natural orifices has tremendous implications for future practice and may well stimulate the development of a “comprehensive digestivist”—an individual trained in minimally invasive gastrointestinal therapy, regardless of whether it involves a laparoscope or a flexible endoscope, and one who is equally comfortable with intraluminal, transluminal, and transabdominal access. While the future may see the development of combined medical/surgical specialists in gastrointestinal therapy, this will take time. At present, speculation is continuing on whether it will be surgeons or gastroenterologists who will take the lead with NOTES. Initially, teams combining endoscopists and surgeons were the driving force in basic NOTES research. Even now, most research is being conducted with close cooperation between gastroenterologists and surgeons. However, the first NOTES procedures in humans have been carried out with laparoscopic assistance. Access has been primarily transvaginal, with dissection and organ removal via a natural orifice but with traction, insufflation, clipping (of the cystic duct and artery)—and in the case of transgastric access, closure—accomplished with laparoscopic access. Surgeons have clearly taken the lead in these developments and in the end it is likely that natural orifice surgery will be performed, with few exceptions, by surgeons who either already possess or have acquired skills in flexible endoscopy. This development has several important implications for the practice of natural orifice surgery:

- Firstly, surgeons are developing a greater appreciation of therapeutic endoscopy. As they acquire the skills in flexible endoscopy needed to perform natural orifice surgery, they will probably also take advantage of the opportunities developing for intraluminal therapies such as antireflux procedures, obesity therapies, full-thickness resection, and mucosal resection.

23 Laparoscopic, Natural Orifice, and Laparoscopy-Assisted Surgery: New Paradigms in Minimally Invasive Therapy

Robert H. Hawes, Stefan von Delius, D. Nageshwar Reddy, and Hubertus Feußner
Transgastric Tubal Occlusion

A similar transgastric approach can be used for tubal occlusion (Fig. 23.6). A transvaginal uterine elevator is used to assist the procedure [38]. The procedure is done using a single-channel 9-mm gastroscope. Resolution clips are doubly applied over the fallopian tubes, which are divided in between using a needle-knife. Alternatively, an Endoloop can be used to occlude the tubes. Methylen blue is injected at the end of the procedure to confirm tubal occlusion on the table.

The hybrid technique. Hybrid procedures involve performing NOTES with laparoscopic assistance [56]. While some groups have limited the assisting laparoscopic port to an independent visualization port [57] in the form of a needlescope to monitor the pneumoperitoneum, others have used it as a retraction port [58] or even as a working port [59]. The hybrid technique provides better visual information independently of the endoscope that is being used to carry out the procedure. During dissection with the working instruments, the endoscopic image is constantly in motion and even shifts away from the operative field. The laparoscopic image, however, is stable and the operated field can always be kept at the center of it. In particular, this ensures the safety of the initial puncture and incision and greatly facilitates advanced NOTES procedures, as it provides a wide field of vision and sufficient illumination. The hybrid technique is also a useful bridge to performing “pure” NOTES procedures.

Natural orifice (transvaginal or transanal) extraction of a laparoscopically dissected specimen has also been described as a modification of hybrid NOTES [60]. The dual-lumen or rendezvous technique [61,62] is another variant of hybrid NOTES. The transgastric and transvaginal routes are used simultaneously here to provide the same advantages of the hybrid technique while avoiding an external scar.

Transvaginal Cholecystectomy

The transgastric route for cholecystectomy requires the scope to be positioned in a retroflexed position. The resulting difficulties in working with a retroflexed scope can be avoided by using a more direct transvaginal route. The other advantage of this route is that it is easy to close the colpotomy using manual suturing under vision [63]. The richness of the vaginal flora in comparison with the gastric flora is a cause for concern. From the gynecological point of view, other potential disadvantages of this route include the formation of adhesions, spread of preexisting endometriosis, infertility, and dyspareunia [64].

The patient receives preoperative antibiotics, which are continued for 48 h postoperatively. The vagina is disinfected with povidone–iodine. The patient is placed in a lithotomy position, with the surgeon positioned between her legs. The cholecystectomy is usually assisted with a needlescope placed transabdominally to guide the initial puncture and to monitor the pneumoperitoneum. Some surgeons have also used the laparoscopic port for organ retraction and clip placement [65]. A triangular area between the uterosacral ligaments, which is avascular and without innervation, is chosen for port placement [38] (Fig. 23.7). An incision is sited on the posterior vaginal cul-de-sac [66]. A double-channel endoscope is introduced into the peritoneum after adequate pneumoperitoneum has been achieved (Fig. 23.8). The dissection is commenced in the Calot triangle, separating the peritoneum off the cystic duct. The combination of grasping and cutting with the endoscopic instruments and the deflection movements of the tip of the endoscope are used to accomplish the dissection (Fig. 23.9). Once sufficiently skeletonized, the cystic duct and artery are clipped and divided with endoscopic scissors. The gallbladder is then dissected from the liver and placed in a retrieval bag. The gallbladder bed is checked for hemostasis. The specimen is then removed transvaginally. The colpotomy is closed with absorbable sutures transvaginally.

A recent systematic review shows that the NOTES operation performed most often to date in humans is transvaginal cholecys-
Normal Stomach—Anatomical Variants—Mucosal Prolapse and Tearing

Normal Stomach

Normal stomachs have a variety of shapes. Some are long and vertical, others are transverse. At endoscopy, the stomach is gently inflated with air so that the entire mucosal surface can be inspected. Observations are made of the color of the mucosa, the degree of luster, and whether blood vessels can be seen in a not overly distended stomach. The rugae or folds are inspected for caliber, regularity, and pliability, and whether they flatten and disappear as the stomach is inflated. The entire gastric surface is inspected for lesions, including erosions, ulcers, nodules, polyps, tumors, tears, etc.

The stomach has three compartments: the antrum, gastric body (corpus), and fundus. The fundus is the dome-shaped area immediately above the gastric body and abutting the diaphragm. The folds or rugae begin in the upper part of the stomach, and run distally toward the antrum (Fig. 43.1a). Folds or rugae are normally soft and pliable. Usually, they will almost completely flatten with distension of the stomach. Four vertical fairly straight parallel folds run along the lesser curve toward the angle.

The antrum is usually smooth and free of folds. Gastric peristalsis begins in the mid-gastric body, and progresses down to the antrum (Fig. 43.1b). The pylorus is usually open. When the contraction wave reaches it, the pylorus closes. This is probably important for mixing and grinding of food, and to allow only liquid and small particles to pass into the duodenum. Peristaltic contractions normally occur at a frequency of three per minute. It is useful to watch a contraction wave move from the gastric body to the antrum, to determine whether there is a lack of symmetry or whether there is an area that is less pliable. The pylorus opening is normally round or oval (Fig. 43.1c). Occasionally, a fold traverses the opening. Passage of the instrument into the bulb usually occurs after gentle
pressure is exerted with the well-centered tip of an end-viewing endoscope into the pyloric channel. This maneuver may occasionally have to be repeated several times, because of displacement of the flexible tip as a consequence of antral motor activity.

When the endoscope is retroflexed, detailed observation of the lesser curvature, cardia, and fundus is possible. The retroflexed endoscope can be pulled up close to the cardia and upper fundus (Fig. 43.1 d).

Visualization of the antrum and pylorus is occasionally not immediately apparent after introduction of the endoscope, especially when there is acute angulation of the antrum and gastric body. Problems with orientation also occur when there is cascade formation, in which the upper part of the stomach appears to be separated from the distal part by a tissue bridge. With some maneuvering of the endoscope, it is usually possible to advance the instrument along the lesser curve into the distal stomach and antrum.

There are several organs adjacent to the stomach that can cause extrinsic compression on the gastric lumen. Impression by the spleen is usually seen in the posterior greater curvature area. Normally, the gastric lining has a uniform salmon color. With careful inspection, one can observe the areae gastricae, and with high magnification the pit pattern. The pit pattern is different in the antrum (with a sulcus or grooved pit pattern) in comparison with the gastric body (with a foveolar or round pit pattern) (Fig. 43.2). The areae gastricae are irregular or absent in patients with atrophic gastritis or with intestinal metaplasia, and enlarged in patients with acid hypersecretion. Blood vessels are normally not seen in a healthy stomach.

■ Hiatal Hernia

The normal cardia fits snugly around the endoscope when viewed in retroflexion. When there is a hiatal hernia, this snug apposition is lost, and a pouch or cupola may be seen entering the thorax through the hiatal ring (Figs. 43.3–43.5). A commonly used definition of hiatal hernia is based on dislocation of the esophagogastric junction above the pinchcock of the diaphragm during quiet breathing and in the absence of retching or vomiting. Three landmarks are helpful in indentifying the esophagogastric junction: the proximal extent of the gastric folds, the distal extent of the esophageal palisade vessels, and the pinch of the lower esophageal sphincter. A ring-like narrowing, causing dysphagia when the diameter is less than 13 mm, at the level of the squamocolumnar mucosal junction is called a Schatzki ring (Fig. 43.6). A hiatal hernia is often combined with evidence of reflux esophagitis or esophageal columnar metaplasia. Mild inflammatory changes may also be seen around the proximal extent of the gastric folds in the hiatal sac. In rare circumstances, there is polypoid thickening of this fold—known as the “sentinel polyp” (Fig. 43.7). Riding ulcers (Cameron ulcers) may develop as a consequence of the constant to-and-fro movement of the gastric mucosa across the pinchcock of the diaphragm, causing mechanical
Colorectal Polyps

Gastrointestinal tract polyps are typically limited protrusions that form on the mucosal lining. The majority of colorectal polyps are sporadic and solitary. However, some are hereditary—particularly multiple polyps—and give rise to polyposis syndromes. The clinical description of polyps and their treatment includes several elements, including the shape (pedunculated, sessile, or flat), size (in centimeters), location (the region of the colon or the distance from the anus on withdrawal of a colonoscope), the technique of polyp removal, and its endoscopic completeness. For a more detailed shape description, the Paris–Japanese classification, including depressed lesions, can be used (Table 47.1) [1].

Three main groups of polyps can be distinguished histopathologically: neoplastic, nonneoplastic, and submucosal (Table 47.2). Single, nonneoplastic polyps do not have malignant potential. Hyperplastic polyps occur most frequently. Diminutive hyperplastic polyps (<5 mm) located in the rectum have no clinical significance; however, it is important to distinguish them from adenomas by histopathology. In contrast, large hyperplastic polyps may have malignant potential. A hyperplastic polyposis syndrome is suspected when hyperplastic polyposis are numerous (n > 20), large (> 1 cm), and localized in the right colon.

Among intestinal polyps, adenomas are the most important from the clinical point of view [2]. Adenomas represent 70% of all polyps removed during colonoscopy. Four types of adenoma can be distinguished histopathologically: tubular, tubulovillous, villous, and “serrated” (Table 47.2). A common feature among adenomas is epithelial cell dysplasia, which involves cytological and architectural changes that unequivocally indicate a neoplastic abnormality. Dysplasia is divided into low-grade and high-grade types. Cells with high-grade dysplasia may penetrate through the muscularis mucosa into the submucosal layer, resulting in invasive carcinoma.

Colorectal adenomas can be diagnosed at any age, but there is a clear increase in the incidence among adults over 30, and the incidence increases to about one-third in those over the age of 50. Colorectal adenomas are significant, as they are regarded as precursor lesions in the large bowel. The majority of adenomas are less than 1 cm in diameter, with low malignant potential. The potential is significantly increased in advanced adenomas that are 1 cm or larger in diameter, contain a villous element (at least 20%), or show high-grade dysplasia. It is estimated that development into a medium-sized adenoma takes roughly 5 years, while development to invasive cancer takes about 10 years. In an asymptomatic population of adults over 50 years old, the incidence of advanced adenoma is about 5–10%, while that of invasive cancer is about 1%. Advanced adenoma plus cancer is known as advanced neoplasia.

The most frequent symptom of polyps is rectal bleeding. Less frequently reported symptoms include mild anemia, tenesmus, or the presence of mucus in the stool. The majority of polyps are completely asymptomatic, especially when small (< 1 cm in diameter). Polyps can be diagnosed with endoscopy or radiography. The barium enema has limited diagnostic value, particularly when performed without using the double-contrast method. Even in referral centers, the sensitivity is not more than 60–70% for lesions 1 cm or larger. Better results can be obtained with computed-tomographic colonography; spiral computed tomography (CT) allows detection of 90% of polyps 1 cm or larger, but it is not widely used for polyp diagnosis. Endoscopy is most commonly used to diagnose adenomatous polyps and makes it possible to carry out treatment with endoscopic polypectomy simultaneously. Approximately two-thirds of adenomas lie within reach of flexible sigmoidoscopy, which is also used for screening purposes, especially in the United Kingdom. Small polyps (<7 mm) that are detected during flexible sigmoidoscopy screening are biopsied to examine the histology. According to current opinion, when only hyperplastic polyps without adenomas are detected, the diagnostic process is completed; the risk of advanced proximal adenoma is estimated to be only 1–3%. However, when an adenoma is detected in the rectum or sigmoid colon, independent of its diameter, the risk of advanced proximal adenoma increases to 5–7%, and a total colonoscopy is indicated. The sensitivity of total colonoscopy is over 90% for detecting polyps ≥7 mm. Characterization of the polyp type (neoplastic, nonneoplastic, type of adenoma, etc.) is based on the histopathologist’s assessment and currently cannot be predicted macroscopically with sufficient probability, even with modern visualization techniques.

Detection of a colorectal polyp as a result of diagnostic work-up or incidental discovery nearly always requires its removal. Pedun-
Collected and semipedunculated polyps larger than 7 mm should be removed with a diathermic snare. Smaller polyps can be removed with biopsy forceps or cold snaring, which is performed without activating the diathermic current. Other techniques are also available, including piecemeal polypectomy, endoscopic mucosal resection (EMR), or endoscopic submucosal dissection (ESD). Only a minority of polyps (very large polyps with visible signs of malignancy) may require a laparotomy. Typical shapes and sizes of colonic polyps, including pedunculated, semipedunculated, and flat polyps, as well as the value of image enhancement using the narrow-band imaging technique (NBI), are illustrated in Figs. 47.1–47.5.