Steven D. Wexner
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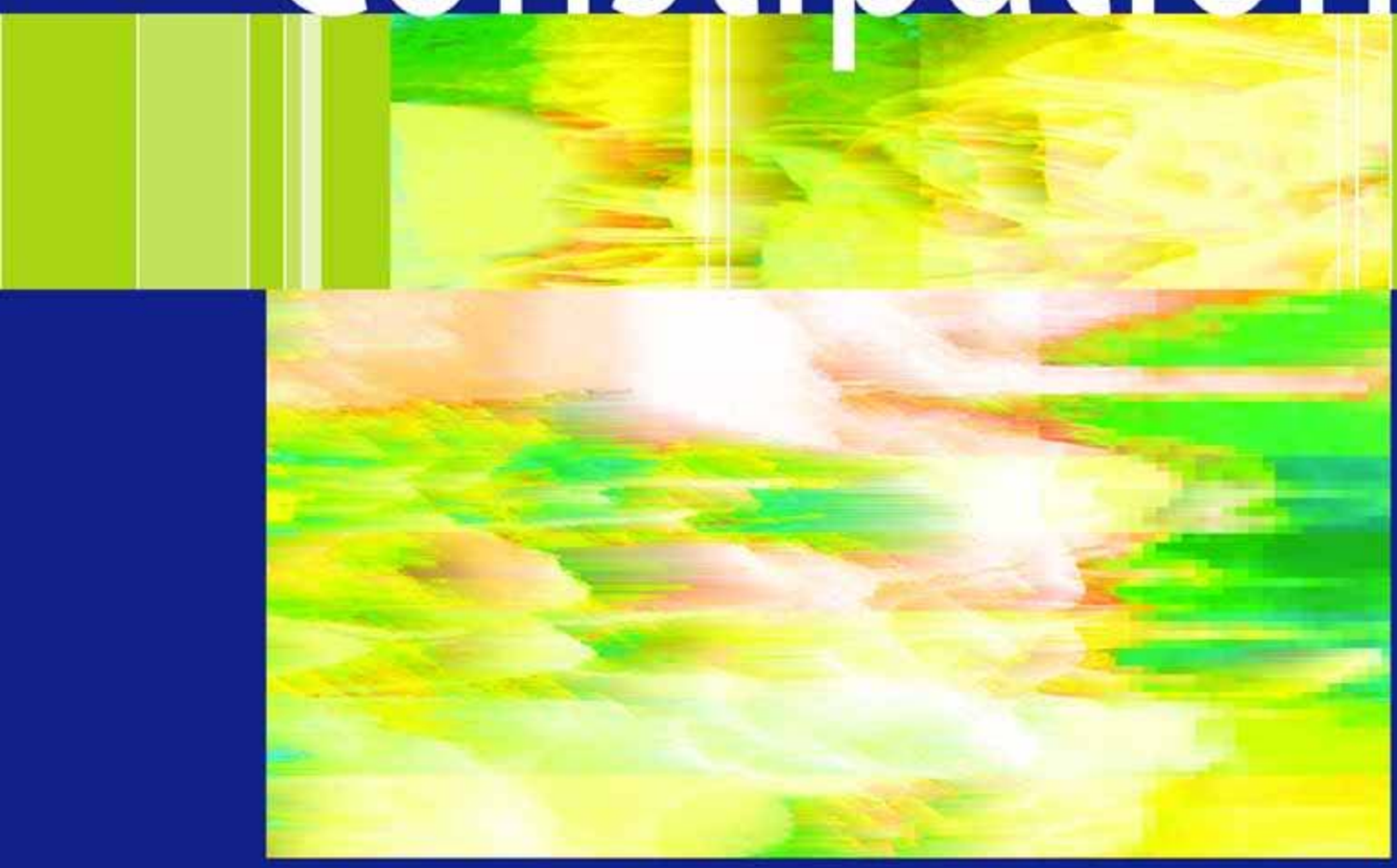
Constipation



Etiology, Evaluation, and Management

Second Edition

Springer

Constipation

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Steven D. Wexner and Graeme S. Duthie (Eds)

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Foreword by David C.C. Bartolo, MS, FRCS, FRCSE

Springer

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This book is dedicated to my parents, Justice Ira H. Wexner and Arlene L. Wexner, whose guidance, love, and encouragement kept me focused on my goals. Their nurturing, caring, and support have enabled me to help patients and practitioners throughout the world. Their teachings and values have been the cornerstones of my professional career and, in fact, my entire life.

Steven D. Wexner

Foreword

Constipation may simply be a symptom that signifies an obsessive desire to defecate with regular frequency. The authors of this text, however, have demonstrated admirably that this nebulous condition often has a multifaceted etiology. I enjoyed reading this excellent text, which covers the gamut of topics related to the etiology, assessment, investigation, and management of constipation. The editors have recruited an international team of exemplary ability and have amassed a very comprehensive and consistent text. The chapters merge imperceptibly with minimal repetition. Novel treatments and the more accepted approaches have been presented in considerable detail. This book should be considered the standard for health care professionals managing functional bowel and allied disorders. It provides a benchmark on how to approach and treat the constipated patient. The majority of the authors have been my esteemed colleagues for a number of years; thus it is with particular pleasure that I am able to share their opinions so ably expressed in their respective chapters. This book demonstrates that coloproctology remains a dynamic specialty that provides a holistic approach to constipation. Managing constipation without understanding the psyche and emotions, together with the background of emotional and physical traumas of life, would be analogous to walking blindfolded.

It has been my pleasure and privilege to have been associated with the editors for some nineteen years and to watch their reputations grow in the international arena. It has been an honor to write the foreword for this book which deserves great success.

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Preface

The subject of constipation has been discussed in a variety of textbooks. Some works have been authored and edited in the field of gastroenterology, some in colorectal surgery, and still others in general surgery. The purpose of the first edition of *Constipation: Etiology, Evaluation, and Management*, which has also been continued in this second edition, was to provide multidisciplinary coverage of a rather difficult and sometimes controversial subject. In addition, rather than culling authors from a specific geographic area, the authors for this work have been selected from throughout the world. As such, excellent contributions and perspectives within this book emanate from throughout Scandinavia, the United Kingdom, North and South America, Asia, and Australia. This very comprehensively written, authoritatively referenced, and visually enhanced work has strived not only to update the preexisting chapters, but has thoroughly improved upon the subject matter with more current and relative information. The interdisciplinary, intercontinental approach has led to the most complete and comprehensive of all available information regarding the evaluation and management of constipation. We trust that you will find this book worthwhile and hope that you join us in expressing our very sincere appreciation to the authors for their superlative material.

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Definitions and Epidemiology of Constipation

John F. Johanson

Constipation is among the most common gastrointestinal disorders. It is so prevalent, in fact, that it has been considered endemic in the elderly population. In the United States alone, more than 3 million prescriptions are written for cathartics yearly and over $800 million is spent for over-the-counter (OTC) laxatives.[1] It is clear that constipation represents a major public health problem.

Despite its significant impact, the etiology of constipation remains largely unknown. The variety of symptoms and risk factors associated with constipation suggest that its etiology is likely to be multifactorial. Although epidemiologic studies cannot establish etiologic relationships, consistent epidemiologic distributions may suggest potential causative risk factors. The more uniform the epidemiologic pattern, the more likely an environmental agent(s) may be contributing to its etiology. Elucidation of the epidemiology of constipation, therefore, is helpful both in suggesting potential etiologic risk factors and in identifying populations that are at highest risk of developing this condition. Once high-risk populations are identified, they can be targeted for treatment or possibly even for interventions that might prevent the development of this often debilitating condition.

Disease Definition

A description of the epidemiology of constipation is clearly dependent on how the disorder is defined. Attempts to provide an objective definition of constipation date back to the 1960s. In a commonly cited study, Connell and colleagues[2] surveyed the bowel frequency of factory workers in England and found that more than 99% had bowel frequencies ranging between three per day and three per week. These data provided an easily measurable and reproducible definition that did not rely on an individual's subjective impressions of their bowel function. As a result, constipation began to be defined as less than three bowel movements per week, and this definition continued as the predominant definition for the past 30 years. Unfortunately, infrequent bowel movements only capture a small percentage of individuals with constipation. A population-based survey of young adults done by Sandler and Drossman[3] indicated that patients consider other symptoms to also represent constipation. Of those who completed the survey, 52% believed that constipation meant straining to pass stool, whereas 44% believed that constipation was present if the stools were hard. Other definitions included the inability to defecate when desired (34%) and abdominal discomfort associated with defecation. Infrequent bowel movements were considered constipation by only 32% of survey respondents. Thus, there appears to be a divergence between physicians' and patients' perspectives as to what constitutes constipation.

These differences, as well as the recognition that there are additional components to constipation, are the main reasons for the development of the Rome criteria for defining constipation. The initial intent of the Rome criteria for functional bowel diseases was to provide a consistent method of identifying individuals to facilitate enrollment of comparable patients into clinical trials. However, these criteria have increasingly

been applied to clinical practice to better identify patients with constipation. The original Rome criteria have been updated, and now the Rome II criteria for functional constipation comprise two or more of the following abnormalities, which must be present at least 3 months during the previous year: less than three bowel movements per week, hard or lumpy stool, straining, a sensation of incomplete evacuation, a feeling of anorectal obstruction, or the need for manual maneuvers (digital disimpaction). Additionally, criteria for irritable bowel syndrome (IBS) must not be present; specifically, significant abdominal pain or discomfort must not be a primary complaint.[4]

Even when using the Rome II criteria to define constipation in epidemiologic studies, many patients with this condition may not be captured. Defining constipation as hard stools, straining with defecation, or even infrequent defecation may be inadequate because individuals often complain of being constipated even though they do not have any of the established symptoms. Many individuals feel constipated based solely on the perception that their own expectations for bowel habits are not being met. This often manifests as a complaint that an individual is not having a daily bowel movement. Regardless of whether one meets the accepted definition of constipation, they are likely to seek treatment either by use of OTC products or by visiting a physician and requesting recommendations for therapy. Since constipation is a symptom-based disorder, patients' perceptions that they are constipated make them constipated whether or not they demonstrate objective criteria to support the diagnosis.

Although this definition may seem to rest on a discussion of semantics, it is important when studying the epidemiology of constipation. The most reliable data sources for elucidation of the epidemiology of various diseases are population-based data. These sources, particularly the large databases, typically rely on International Classification of Diseases (ICD-9) diagnosis codes that ultimately are based on physician coding. If a physician's perception is that constipation is present only when defecation frequency is less than three per week, the observed prevalence rates may underestimate the true prevalence of this condition. Even when epidemiologic studies utilize the Rome criteria to define constipation, they may underestimate the true prevalence of constipation. This possibility is supported by the findings of a recent systematic review of constipation where the prevalence of self-reported constipation was consistently higher than that defined by either the Rome I or Rome II criteria.[5] On the other hand, relying solely on individuals' perceptions that their bowel habits are not normal may lead to an overestimation of the true prevalence of constipation.

Nevertheless, reliable criteria are necessary to define constipation in order to examine its epidemiology in an organized manner. There are a number of methods to define constipation, and each definition has its own strengths and limitations. There is not a single best method to define constipation. For purposes of interpretation and application of the findings of epidemiologic studies of constipation, however, it is important to know the definition upon which the results were based. This will enable practitioners' to apply the results to their own patient population. For this discussion, the epidemiologic patterns of constipation will be discussed in the context of the specific definition upon which they were based.

Clinical Presentation and Natural History

Constipation may be associated with a number of different diseases or conditions. The known etiologies of constipation include mechanical obstruction, metabolic disturbances, neurologic disorders, and medication side effects. A large proportion of patients with constipation do not have a known cause and suffer from idiopathic constipation.

The symptoms of constipation may start at any time, although they typically begin later in life. Constipation usually commences insidiously without any obvious inciting event. Early in its course, infrequent or difficult defecation may represent the only symptom. As constipation progresses in severity, patients usually develop bloating and crampy abdominal discomfort that may be worse after meals. The pain is often constant, located in the lower abdomen and is not generally relieved with defecation, which distinguishes chronic constipation from IBS. The pain is also generally less severe than that seen in patients with IBS. Those who have suffered with constipation for many years may additionally

note fatigue, malaise, anorexia, or other constitutional symptoms. The specific constipation symptoms vary according to the type of constipation. Slow-transit constipation, for example, is often associated with infrequent defecation, bloating, fatigue, and malaise. By contrast, disordered defecation commonly presents with hard stools, straining, rectal pressure, and feelings of incomplete evacuation.

There has been little if any study of the natural history of constipation. Consequently, the course of constipation remains unclear. It would appear that constipation represents a slowly progressive disorder that rarely if ever resolves. This is partly supported by Talley and colleagues,[6] who estimated the stability of the symptoms of constipation among residents of Olmstead County, Minnesota. They compared the results of two surveys completed 15 months apart, finding that 89% of the population surveyed had no change in their symptoms of constipation during the intervening months. Furthermore, the typical clinical presentation of a patient with severe constipation is of one who has been self-medicating for years with OTC laxatives, often requiring increasing doses to achieve consistent relief.

Despite its apparent progressive course, however, constipation rarely leads to severe morbidity. Hospitalization for constipation is uncommon and mortality from constipation is quite rare.[7] Potential complications of chronic constipation include fecal impaction, fecal incontinence, sigmoid volvulus, and stercoral ulcerations of the sigmoid colon or rectum.[7–9]

Epidemiology

Incidence

It is difficult to estimate the incidence of this common disorder because of the widespread availability of OTC therapies. The overwhelming majority of patients self-medicate when they initially develop symptoms of constipation, making it difficult to capture these individuals at the time they initially develop constipation. Since incidence defines the number of new cases per specified time period, it is essential to determine the frequency and time frame of new cases.

Two studies have provided estimates of the incidence of constipation. Talley and colleagues[6] observed onset rates of 40/1000 person-years when resurveying white residents of Olmsted County a median of 15 months after an initial survey of the same population. The corresponding constipation symptom disappearance rate was 309/1000 person-years. A study by Everhart et al[10] showed that over a 10-year period between the first National Health and Nutrition Examination Surrey (NHANES I) and National Health and Nutrition Evaluation Survey Epidemiologic Follow-up Study (NHEFS), there was a 27.3% increase in the number of patients self-reporting constipation.

A third study examined the incidence of constipation among nursing-home patients. Although this investigation may not provide insight into the incidence of constipation in the general population, it does provide interesting comparative data because nursing home patients represent a high-risk population. In this retrospective database study of nursing home residents, the incidence of constipation after admission to a nursing-home facility was estimated to be 7% in the first 3 months.[11] This correlates to an incidence rate of 280/1000 person years, sevenfold higher than that seen in ambulatory Olmstead county residents. While the population studied was biased toward a high-risk population, such as the elderly, immobile, and disabled, the investigators captured data on 21,012 Medicare and Medicaid beneficiaries to obtain this estimate of incidence.

Prevalence

The prevalence of constipation ranges from 3.4% to 27.2% depending on the definition of constipation utilized (Table 1.1). This wide range is the result of both differing case definitions of constipation and the effects of varied ascertainment methods. A recent systematic review of all population-based epidemiologic studies of constipation in North America identified 10 different studies demonstrating an average preva lence rate of 14.8%.[5] In these studies, differing case definitions of constipation were employed, including self-reported constipation and answers to questions defining Rome I or Rome II criteria for constipation. Interestingly, one of the studies in this systematic review compared the three different definitions of constipation among the same individuals, finding that self-report led to the highest prevalence of constipation (27.2%), whereas Rome I (14.9%) and Rome II criteria (16.7%) provided similar

Table 1.1. Prevalence of constipation by gender

Study	Population source	Year	Constipation definition	Overall prevalence (%)	Males (%)	Females (%)
Sandler[17]	NHANES I	1971–75	Self-report	12.8	7.0	18.2
Everhart[10]	NHANES I	1971–75	Self-report	15.8	8.0	20.8
Johanson[7]	NHIS	1983–87	Self-report	1.9	0.9	2.8
Harari[15]	NHIS	1989	Self-report	3.4	1.3	4.9
Talley[12]	Olmsted county	1991	Strain and hard Or <3/wk	17.4	13.9	20.8
Talley[13]	Olmsted county	1993	Self-report	5.0	2.7	7.3
			Rome I FC	19.2	18.3	20.1
			Rome I DD	11.0	5.2	16.5
Drossman[23]	Householder	1993	Rome I FC	3.6	2.4	4.8
			Rome I DD	13.8	11.5	16.0
Stewart[21]	U.S. EPOC	1997	Rome II FC	14.7	12.0	16.0
Pare[20]	Canada	2000	Self-report	27.2	18.4	35.4
			Rome I	16.7	12.0	21.0
			Rome II	14.9	8.3	21.1

DD, Disordered defecation; EPOC, Epidemiology of Constipation (study); FC, Functional constipation; NHANES, National Health and Nutrition Examination Survey; NHIS, National Health Interview Survey.

prevalence rates. However, the overall average prevalence of constipation among the 10 studies was quite similar to that identified by Rome I or Rome II.

Although population-based surveys tend to be the most reliable, case ascertainment is frequently based on ICD-9 coding, which provides the opportunity for significant variability in case definition. A number of regional studies have been performed that benefit from the ability to more precisely define constipation. These studies even allow analysis of the epidemiology of the different subsets of constipation such as normal-transit (functional) and slow-transit constipation or disordered defecation constipation.

Talley et al[12,13] performed two mail surveys of white adults between the ages of 30 and 64 residing in Olmsted County, observing prevalence rates ranging from 11% for cases defined by Rome I outlet obstruction to 19% for cases defined by Rome I functional constipation. In the same manner, a meta-analysis of 30 regional epidemiologic studies revealed a broad range of prevalence rates, again depending on the specific definition of constipation employed. Prevalence rates ranged from 1.4% for infrequent defecation (less than three bowel movements weekly) to 16.9% for straining.[14]

Based on an analysis of all the published population-based data, the overall prevalence of constipation is approximately 15% corresponding to 42 million people in the United States alone.

Demographic Distributions

Age

The relationship between age and constipation prevalence has been evaluated in numerous studies. Unfortunately, most of these studies have divided age groups differently, with some being much more aggressive in subdividing elderly subjects by age. In general, however, constipation demonstrates a progressive increase in prevalence with increasing age. Harari et al[15] and Johanson et al,[7,16] observed a trend toward increased constipation with increasing age in the National Health Interview Survey (NHIS) data, as did Sandler et al[17] in the NHANES I data. This same age distribution is seen in other large databases. Physician visits data such as the National Ambulatory Medical Care Survey (NAMCS) and the National Disease and Therapeutic Index (NDTI) as well as hospitalization data sources such as the National Hospital Discharge Survey (NHDS) likewise demonstrate a clear and progressive increase in constipation associated with increasing age.[7,18]

Gender

The majority of epidemiologic studies that have examined the prevalence of constipation by gender report a higher prevalence of

constipation in females (Table 1.1), with female-to-male ratios ranging from 1.01:1 to 3.77:1. This was true across a range of case criteria, although the higher ratios were typically observed in the studies that used self-reported constipation (average 2.65) rather than Rome criteria (average 1.75).[5,12,13,15–17,19–21]

Race

The prevalence of constipation is higher among non-Caucasian populations with nonwhite-to-white ratios ranging from 1.13 to 2.89.[5] Self-report again generated the highest ratio,[10] and Rome II criteria the smallest.[21] The prevalence of constipation among different racial or ethnic groups is more difficult to identify. Nonwhite racial groups are not typically broken down any further for analysis because of small numbers of nonwhite participants among population-based North American studies. Moreover, it is difficult to compare prevalence rates of constipation among different countries to examine the influence of race or ethnicity since the definitions of constipation can vary significantly.

Socioeconomic Status

The influence of socioeconomic status on the prevalence of constipation also appears to be constant among published studies. Although the specific breakdown by income groups was different across studies, subjects with lower incomes consistently demonstrated significantly higher rates of constipation than their wealthier counterparts.[7,17,20,21] This effect was usually less dramatic in studies defining constipation using the Rome criteria.[5]

Education

An inverse correlation of years of education with prevalence of constipation has also been reported. There appears to be a trend toward increased prevalence with less education in the NHANES I data.[17] A similar trend toward increasing self-reported constipation with less education was seen in the NHIS data set by Johanson.[7] An association of constipation with lower education is less consistent in several other studies, particularly among those defining constipation using the Rome criteria.[5] This finding, therefore, may simply represent a surrogate marker for socioeconomic status.

Geographic Distribution

Constipation demonstrates a distinctive geographic distribution. Analysis of the prevalence of self-reported constipation by region in the United States reveals that constipation is more common in the South and Midwest.[16] A more refined analysis of Medicare data examining the prevalence of constipation by individual states revealed that constipation was more common in rural states, northern or mountainous states, and poorer states.[22] The latter finding is not surprising given the socioeconomic distribution of constipation observed in other epidemiologic studies. The uniformity of findings among the different studies serves to support the validity of the observed geographic distribution.

This unique geographic pattern of constipation seems to suggest the influence of three global environmental factors: rural living, colder temperatures, and lower socioeconomic status. How these factors influence the development of constipation remains speculative. However, these factors likely act through effects on the diet. Conceivably, poorer individuals living in colder climates may consume less fresh fruits and vegetables related to diminished availability or increased cost. It may be hypothesized, then, that the absence of fresh fruits and vegetables may play an important role in the development of constipation.

Special Populations

Patients Seeking Health Care

A number of studies have utilized health care databases to examine various aspects of the epidemiology of constipation. Although these databases have been used at times to provide estimates of the prevalence of constipation, they are not true population-based data sources. These data sources may be biased and underestimate the true prevalence of constipation because entrance is dependent on health care seeking. Since a large proportion of patients with

self-reported constipation self-medicate rather than seek health care for their constipation, they would never be included in a health care database.[12,17,23] Nevertheless, studies from individuals seeking health care are still helpful in examining the demographic distributions of constipation because there are not likely to be any systematic differences among individuals who self-medicate and those who seek medical attention for their symptoms of constipation. Referral population studies are beneficial in corroborating the demographic patterns of constipation observed in population-based prevalence data. For example, the identification of similar male-to-female ratios of constipation in physician visit data serves to substantiate the validity of similar findings in other data sets. Another benefit of studies of referral populations is their ability to evaluate large numbers (millions) of subjects and generate hypotheses regarding causality.

Utilizing data from the NHIS, the NHDS, and the NDTI, Johanson and colleagues[7,16,18] found associations between constipation and increasing age, female gender, low income, and decreased education. Although these databases were not specifically population based, the demographic distributions identified by analysis of these databases were analogous to those observed in population-based studies, adding support to the validity of these distributions.

Patients with Concomitant Disease

Neurologic Diseases

Constipation occurs commonly among patients with other diseases. In many instances, these conditions are the actual cause of an individual's constipation. For example, hypothyroidism is well known to cause constipation. In other cases the associations may be coincidence or may be the result of shared etiologic risk factors. To investigate this possibility, Johanson et al[24] examined the Health Care Financing Administration (HCFA) database comprising 11 million Medicare beneficiaries to assess the association of constipation with other coexisting diseases. Not surprisingly, a number of recognized causes of constipation were found to be strongly associated with constipation including laxative abuse [odds ratio (OR) 18.8], Hirschsprung's disease (OR 6.5), intestinal obstruction (OR6.3), and hypothyroidism (OR 1.6). These findings served to corroborate the validity of the results.

Subsequent analysis revealed the largest group of conditions associated with constipation was neurologic and psychiatric disorders. A number of dramatic associations between constipation and neuropsychiatric and spinal diagnoses were observed, including herpes zoster (OR 5.1), depression (OR 6.5), multiple sclerosis (OR 3.9), Parkinson's disease (OR 3.2), vertebral column fracture (OR 10.1), and sprains and strains of the sacroiliac (OR 7.7) region.[24] These associations suggest a potential link between central nervous system (CNS) function and constipation. Of particular interest was the strong association between herpes zoster and constipation. The zoster virus resides in the posterior root ganglia and can damage the ganglionic or spinal neurons. This association hints at a possible viral contribution to the onset of constipation among some patients with idiopathic constipation.

The prevalence of constipation among populations of patients with specific neurologic disease has also been studied. Hinds et al[25] observed a constipation prevalence rate of 43%, among 280 outpatients with multiple sclerosis regardless of the severity of their disability. Han et al[26] examined 72 spinal cord injury patients and found that 31% demonstrated severe constipation and 24% had difficulty evacuating their stool. Han et al further found that anal massage was used by 35%, abdominal massage by 29%, and manual digitation by 18% to assist bowel movements. De Looze et al[27] also studied spinal cord injury patients. They found that 58% had constipation and required manual maneuvers or laxatives to facilitate successful defecation. Both quadriplegia, as compared to paraplegia, and anticholinergic medication usage significantly increased the risk of constipation, while the presence of intact rectal sensation did not reduce the risk. Looking at the association between constipation and neurologic disease from another perspective, a population-based study of a cohort of 51- to 75-year-old men in Hawaii found that less than one bowel movement per day predicted future onset of Parkinson's disease with an OR of 2.7 at 24 years of follow-up, with an average onset at 12 years after the initial assessment.[28]

Finally, a recent study of developmentally delayed individuals demonstrated a high prevalence of constipation among this population as

well. Bohmer and colleagues[29] studied the bowel habits and laxative use patterns of a random population of 215 individuals with IQs less than 50. The authors defined constipation as less than three bowel movements per week or the need to use laxatives more than three times per week. Even with this relatively strict definition of constipation, they found that 70% of these individuals were constipated. When compared to a control group, the constipated patients were more likely to have cerebral palsy, be nonambulatory, use anticonvulsants, and have an IQ less than 35. This study further supports the possibility of a shared risk factor between individual neurologic diseases and constipation.

Diabetes

Constipation is also widely believed to be associated with diabetes mellitus. This association has been observed in studies by Talley's group[30] in Australia, Lithner's group[31] in Sweden, and Enck et al[32] in Germany. However, the only population-based study specifically examining the prevalence of gastrointestinal symptoms among diabetics was performed by Locke's group[33] at the Mayo Clinic. They surveyed random samples of Olmsted County residents with type 1 and type 2 diabetes as well as two age- and gender-stratified control groups without diabetes. They did not observe any difference in the prevalence of constipation among patients with type 1 (12% vs. 14%) or type 2 (10% vs. 12%) diabetes, when compared with controls. There was a trend toward constipation and/or laxative use being more common among individuals with type 1 diabetes particularly among men ($p < .15$), but this difference was observed only in those individuals using calcium channel blockers, which are known to cause constipation as a side effect of the medication.

Other Conditions

Pappagallo[34] surveyed 76 opioid-using pain clinic patients with chronic noncancer pain and found that 40% had less than three stools per week, despite 80% of them taking medications to prevent constipation. Leroi et al[35] interviewed 344 Canadian gastrointestinal (GI) clinic patients with functional lower GI disorders, and found that 40% reported a history of sexual abuse, compared to 10% of those being seen for organic disorders. Of those who reported a history of sexual abuse, 88% reported constipation. A more recent study by Hobbis et al[36] used a matched case-control design to find that in two sets of age- and gender-matched controls (Crohn's disease patient controls and healthy controls) there were no differences in the rates of abuse between patients with functional bowel disorders and controls.

Thus, constipation appears to be strongly associated with a number of neurologic diseases, with opioid use, and possibly with a history of sexual abuse, although the association between constipation and sexual abuse remains to be confirmed.

Conclusion

The epidemiology of constipation demonstrates a consistent pattern with several key points. No true population-based incidence or natural history studies have been published to date. The prevalence of constipation ranges from 3% to 27%, averaging approximately 15%, the variance resulting from differing case definitions of constipation and the effects of varying ascertainment methods. Constipation increases progressively with age, and this increase is particularly marked after the age of 65 years. It is twice as common in females than males and is also more common in nonwhites than whites, although the distribution by race is less consistent than the distributions by age or gender. Constipation is also more common among those with lower socioeconomic status and education levels.

Constipation demonstrates a distinct geographic distribution, being more common in rural states, northern or mountainous states, and poorer states. The unique geographic pattern of constipation seems to suggest the influence of three global environmental factors: rural living, colder temperatures, and lower socioeconomic status. Finally, constipation is more common among patients with a wide variety of neurologic diseases, indicating the possibility of a shared environmental risk factor.

References

1. Lembo T, Camilleri M. Chronic constipation. N Engl J Med 2003;349:1360–1368.

2. Connell AM, Hilton C, Irvine G, Lennard-Jones JE, Misiewicz JJ. Variation of bowel habit in two population samples. Br Med J 1965;5470:1095–1099.
3. Sandler RS, Drossman DA. Bowel habits in young adults not seeking health care. Dig Dis Sci 1987;32: 841–845.
4. Thompson WG, Longstreth GF, Drossman DA, Heaton KW, Irvine EJ, Muller-Lissner SA. Functional bowel disorders and functional abdominal pain. Gut 1999;45(suppl 2):II43–47.
5. Higgins PDR, Johanson JF. Epidemiology of constipation in North America: a systematic review. Am J Gastroenterol 2004;99:750–759.
6. Talley NJ, Weaver AL, Zinsmeister AR, Melton LJ 3rd. Onset and disappearance of gastrointestinal symptoms and functional gastrointestinal disorders. Am J Epidemiol 1992;136:165–177.
7. Johanson JF. Constipation. In: Everhart JE, ed. Digestive Diseases in the United States: Epidemiology and Impact. U.S. Department of Health and Human Services, Public Health Service, National Institutes of Health, National Institute of Diabetes and Digestive and Kidney Disease. NIH publication no. 94-1447. Washington, DC: U.S. Government Printing Office, 1994:567–594.
8. Devroede G. Constipation: mechanisms and management. In: Sleisenger MH, Fordtran JS, eds. Gastrointestinal Disease: Pathophysiology, Diagnosis, Management, 3rd ed. Philadelphia: WB Saunders, 1983:288–307.
9. Wrenn K. Fecal impaction. N Engl J Med 1989;321: 658–662.
10. Everhart JE, Go VL, Johannes RS, Fitzsimmons SC, Roth HP, White LR. A longitudinal survey of self-reported bowel habits in the United States. Dig Dis Sci 1989;34:1153–1162.
11. Robson KM, Kiely DK, Lembo T. Development of constipation in nursing home residents. Dis Colon Rectum 2000;43:940–943.
12. Talley NJ, Zinsmeister AR, Van Dyke C, Melton LJ 3rd. Epidemiology of colonic symptoms and the irritable bowel syndrome. Gastroenterology 1991;101:927–934.
13. Talley NJ, Weaver AL, Zinsmeister AR, Melton LJ 3rd. Functional constipation and outlet delay: a population-based study. Gastroenterology 1993;105:781–790.
14. Sonnenberg A, Everhart JE, Brown DM. The economic cost of constipation. In: Kamm MA, Lennard-Jone JE, eds. Constipation. Peters, UK: Wrightson Biomedical Publishing, 1994:19–29.
15. Harari D, Gurwitz JH, Avorn J, Bohn R, Minaker KL. Bowel habit in relation to age and gender. Findings from the National Health Interview Survey and clinical implications. Arch Intern Med 1996;156:315–320.
16. Johanson JF, Sonnenberg A, Koch TR. Clinical epidemiology of chronic constipation. J Clin Gastroenterol 1989;11:525–536.
17. Sandler RS, Jordan MC, Shelton BJ. Demographic and dietary determinants of constipation in the US population. Am J Public Health 1990;80:185–189.
18. Johanson JF, Sonnenberg A. The prevalence of hemorrhoids and chronic constipation: an epidemiologic study. Gastroenterology 1990;98:380–386.
19. Hammond E. Some preliminary findings on physical complaints from a prospective study of 1,064,004 men and women. Am J Public Health 1964;54:11–23.
20. Pare P, Ferrazzi S, Thompson WG, Irvine EJ, Rance L. An epidemiological survey of constipation in canada: definitions, rates, demographics, and predictors of health care seeking. Am J Gastroenterol 2001;96: 3130–3137.
21. Stewart WF, Liberman JN, Sandler RS, et al. Epidemiology of Constipation (EPOC) study in the United States: relation of clinical subtypes to sociodemographic features. Am J Gastroenterol 1999;94:3530–3540.
22. Johanson JF. Geographic distribution of constipation in the United States. Am J Gastroenterol 1998:93:188–191.
23. Drossman DA, Li Z, Andruzzi E, et al. U.S. householder survey of functional gastrointestinal disorders. Prevalence, sociodemography, and health impact. Dig Dis Sci 1993;38:1569–1580.
24. Johanson JF, Sonnenberg A, Koch TR, McCarty DJ. Association of constipation with neurologic diseases: an epidemiologic study of the concordant occurrence of diseases in the Medicare population. Dig Dis Sci 1992;37:179–186.
25. Hinds JP, Eidelman BH, Wald A. Prevalence of bowel dysfunction in multiple sclerosis. A population survey. Gastroenterology 1990;98:1538–1542.
26. Han TR, Kim JH, Kwon BS. Chronic gastrointestinal problems and bowel dysfunction in patients with spinal cord injury. Spinal Cord 1998;36:485–490.
27. De Looze D, Van Laere M, De Muynck M, Beke R, Elewaut A. Constipation and other chronic gastrointestinal problems in spinal cord injury patients. Spinal Cord 1998;36:63–66.
28. Abbott RD, Petrovitch H, White LR, et al. Frequency of bowel movements and the future risk of Parkinson's disease. Neurology 2001;57:456–462.
29. Bohmer CJ, Taminiau JA, Klinkenberg-Knol EC, Meuwissen SG. The prevalence of constipation in institutionalized people with intellectual disability. J Intellect Disabil Res 2001;45:212–218.
30. Bytzer P, Talley NJ, Leemon M, Young LJ, Jones MP, Horowitz M. Prevalence of gastrointestinal symptoms associated with diabetes mellitus: a population-based survey of 15,000 adults. Arch Intern Med 2001;161: 1989–1996.
31. Spangeus A, El-Salhy M, Suhr O, Eriksson J, Lithner F. Prevalence of gastrointestinal symptoms in young and middle-aged diabetic patients. Scand J Gastroenterol 1999;12:1196–1202.
32. Enck P, Rathmann W, Spiekermann M, et al. Prevalence of gastrointestinal symptoms in diabetic patients and non-diabetic subjects. Z Gastroenterol 1994;32:637–641.
33. Maleki D, Locke GR 3rd, Camilleri M, et al. Gastrointestinal tract symptoms among persons with diabetes mellitus in the community. Arch Intern Med 2000;160(18):2808–2816.
34. Pappagallo M. Incidence, prevalence, and management of opioid bowel dysfunction. Am J Surg 2001;182:11S–18S.
35. Leroi AM, Bernier C, Watier A, et al. Prevalence of sexual abuse among patients with functional disorders of the lower gastrointestinal tract. Int J Colorectal Dis 1995;10:200–206.
36. Hobbis IC, Turpin G, Read NW. A re-examination of the relationship between abuse experience and functional bowel disorders. Scand J Gastroenterol 2002;37:423–430.

2

Etiology of Congenital Colorectal Disease

Massarat Zutshi and Tracy L. Hull

Developmental disorders related to colorectal disease are for the most part identified with Hirschsprung's disease (HD) in children and adults, and hereditary conditions related to chronic megacolon. Other disorders result from structural abnormalities that manifest as anorectal malformations. Conditions that are rare and others that arise from surrounding structures are listed in Table 2.1.

Incidence

The incidence of HD is reported as approximately 1 in 5000 live births.[1] The disease has a male-to-female ratio of 4.1 : 1, though this ratio is decreased as the length of the aganglionic segment increases. Familial incidence has been reported in 15% to 20% of the patients with total aganglionosis of the colon and 50% of those with total aganglionosis of the intestine. Aganglionosis has been confined to the rectosigmoid in 75% of the patients and to the sigmoid, splenic flexure, and the transverse colon in 17%.[2] No clear genetic inheritance patterns have been identified in spite of the genetic factors that have been implicated. There is an increased risk for siblings of affected persons at 4% as compared with that of the general population, and also association with other genetic abnormalities and syndromes. There has been no racial predominance of the disease. Intestinal neuronal dysplasia (IND) described by Meier-Ruge in 1971,[3] resembles HD in the clinical presentation; however, it differs in histology, which shows hyperplasia of the submucosal and myenteric plexus[4] as opposed to aganglionosis in HD. Intestinal neuronal dysplasia is seen in about 25% to 35% of patients with HD, and HD occurs in 17.9% of patients with IND.[4]

Alternatively, structural anomalies also occur roughly in one in every 5000 live births with a slight male preponderance. The most common anomaly is an imperforate anus, which is a term used to denote all anorectal malformations ranging from simple to complex defects. These are often associated with anomalies of the urinary tract, trachea, esophagus, heart, gastrointestinal tract, and skeletal system. The other anomalies are duplications and malrotation, which are manifested in the neonatal period.

Evolution of the Enteric Nervous System

The enteric nervous system (ENS) is unique, as it can function without input from the brain or spinal cord. It also has all the neurotransmitters that are found in the central nervous system (CNS).[5,6] The evolution of the ENS has been long debated. Okamoto and Ueda[7] showed that the extramural parasympathetic innervation develops in the 5th and 6th weeks of embryogenesis. Studies in the chick and quail embryos have defined the embryogenesis of the ENS.[8] The ENS develops as a result of the migration of cells along defined pathways from the neural crest in a craniocaudal direction. These cells migrate to the vagal and sacral crest.[8,9] The vagal crest colonizes almost the entire bowel, whereas the sacral crest is responsible for the postumbilical bowel. In the absence of the vagal crest cells, the sacral neural crest cells are not capable of giving

Table 2.1. Classification of congenital colorectal disease

1. Structural and developmental malformations
   - Hirschsprung disease
   - Anorectal malformations
   - Congenital colonic varices
   - Rectal arteriovenous malformations
2. Myopathies
   - Familial and degenerative myopathy mimicking Hirschsprung's disease
   - Hereditary internal sphincter myopathy
   - Spastic pelvic floor syndrome
3. Retrorectal tumors
   - Developmental cysts
   - Chordoma
   - Anterior sacral meningocele

rise to the enteric ganglia. This migration takes place during the 9th to 12th week, which is much later than that which occurs in the small bowel in the 7th week. The selection of the pathway is most likely achieved by a balanced combination of molecules that promote and reduce cell adhesion.[10] Aganglionosis and hypoganglionosis are a result of factors that govern the migration, differentiation, and colonization of the sacral crest cells and is also due to the premature differentiation and early cessation of migration. Cessation of migration correlates with cell–cell and cell–matrix adhesion molecules, consistent with an adhesive basis.[11–13] The timing of inhibition of migration results in aganglionosis of different parts of the bowel. If the crest cells are inhibited in the 8th week, only the colon is affected and the ileum remains unaffected. Inhibition in the 9th week results in aganglionosis of the descending colon and rectosigmoid, and only the rectosigmoid is affected when it occurs between the 10th and 12th weeks.

Neurons are nonmigratory, and thus for ganglia to develop the bowel the neurons must be colonized by crest-derived neural precursors. The process of homing in of the neural crest precursors is dependent on the microenvironment of the smooth muscle cells, which are the ultimate target of the crest cells and tell the cells where to stop migration and form enteric ganglia.[14] This process is associated with an extracellular matrix called laminin, which is present in the mucosal and serosal epithelium of the smooth muscle cells and is the target for the neural crest cells.[15] The neural crest cells acquire a receptor for laminin asynchronously, which directs this homing process. This receptor is called laminin binding protein (LBP 110) and is necessary for laminin binding. Laminin promotes neuritic extension and axonal growth.[16] Laminin 1 promotes development of neurons from enteric cells of neural crest cells. There is a histologic difference between aganglionosis and denervation. An aganglionic segment is not denervated; what are missing are the cell bodies of the enteric neurons, which mediate the reflexes. An aganglionic segment may be hypernervated, and this is seen in HD, wherein an abundance of laminin 1 is seen. The ENS is essential for normal propulsive intestinal motility. The peristaltic reflex has long been recognized as one that is evoked by increased luminal pressure and results in a wave of excitation and relaxation that descends the bowel and is propulsive; however, its net effect is as a relaxant. This feature accounts for the contraction and narrowing that occurs in the hypoganglionic segment of bowel.

Etiology in Hirschsprung's Disease and Allied Disorders

The diseases grouped under this heading are defined as a congenital absence of neurons in the terminal portion of the gut. It encompasses HD, in which a segment of the bowel is totally aganglionic, and other diseases where the pathology is dysganglionosis. The diseases grouped under dysganglionosis include hypoganglionosis or hyperganglionosis as seen in intestinal neuronal dyplasias. Hirschsprung's disease is a multigene abnormality with a wide variety of mutations. The widely differing phenotypes, however, cannot account for the known mutations. Each gene involvement adds to the final HD disease phenotype and many of these abnormalities are as yet unknown. No one mechanism can explain the pathogenesis in HD due to the complexity of the mechanisms and multigenic nature of its evolution. Some of the gene abnormalities and their phenotype are listed in Table 2.2.

The animal models of aganglionosis are studied in lethal spotted (ls/ls) and piebald lethal mutant (s^l/s^l) mice. These mutations are inherited as autosomal recessive traits and provide the best models of HD.[17,18] Many observations have pointed to the role of inheritance in HD. The male-to-female ratio of 4:1, which is clearly imbalanced, the high rate of recurrences seen in siblings of affected individuals, the association of other genetic diseases with other genetic abnormalities, and the demonstration of the

Table 2.2. Hirschsprung's disease: genetic association

Gene	Phenotype	Chromosome
ret	AD HSCR	10
GNDF	HSCR	5
EDNRB	AR HSCR*	13
EDN3	AR HSCR*	20
Sox 10	AD HSCR*	22

* Shah Waardenburg.
AD, autosomal dominant; AR, autosomal recessive.

disease in several animal models are pointers of the pattern of inheritance. This pattern has been studied in the autosomal dominant form with incomplete penetrance and also in the autosomal recessive form. Badner et al[19] have studied the inheritance patterns and found that with aganglionosis beyond the sigmoid colon the mode of inheritance was that of a dominant gene with incomplete penetrance, while in those with aganglionosis that did not extend beyond the sigmoid colon the pattern was likely to be due to a recessive gene with very low penetrance.

C-*ret* (Rearranged During Transfection) and Glial Cell Line–Derived Neurotropic Factor (GNDF)

The c-*ret* proto-oncogene has been widely studied, and germline mutations have been responsible for HD and multiple endocrine neoplasia type II (MEN II). The enteric neurons are dependant on the c-*ret* for survival.[20] This has prompted studies in lethal spotted mice and knockout mice that have targeted the c-*ret* proto-oncogene. This gene encodes for a Ret protein tyrosine kinase (TK) for which the GNDF has been defined as a ligand.[21] Activation of the Ret receptor by GNDF is therefore a very important step for formation of the ENS. The GNDF-independent Ret forms ENS of the rostral foregut and sympathetic chain, except for the sympathetic chain and superior cervical ganglion.[6] When c-*ret* is totally knocked out in transgenic mice, the ENS fails to develop in the entire bowel except the rostral foregut, when the gene is homozygous. However, the heterozygous mice have a normal ENS, and all *ret* mutations in humans are heterozygous and this could be explained by effects of additional genes or environmental factors.[6]

The *ret* proto-oncogene is mapped on chromosome 10 and plays a role in the control of proliferation, differentiation, and migration of subsets of the neural crest cells. The location of the Ret protein was reported by Martucciello et al[22] in 1995, and this study supports the hypothesis that HD may be due to a loss in functional effect of Ret. In HD the autosomal dominant form has been demonstrated with functional loss of one copy of *ret*. Only a small number of HD patients, however, present a total deletion or disruption of the *ret* proto-oncogene. Identical *ret* abnormalities, however, can result in dissimilar lengths of involvement of aganglionosis.

Other gene abnormalities are linked to genes encoding endothelin 3 (*EDN3*) or its receptor endothelin B (*EDNRB*). These genes are located on chromosome 13 and play a critical role in the development of ENS. The detection of this abnormality was a result of the analysis of the effect of knockout of the gene that encodes these molecules in mice.[23] When *EDNRB* is knocked out, an agangliosis develops that is similar to that seen in s^l/s^l mice.[24] When *EDN3* is mutated in ls/ls mice, arginine is replaced with a tryptophan residue in the C terminus of big *EDN3*.[23] This results in a more localized abnormality wherein only the terminal colon is aganglionic. This effect is not well understood, and it is postulated that because *EDN1/N2* do not compensate for the loss of *EDN3*, its effect must be quite local. The effect of *EDN3* on crest-derived precursors by itself does not result in aganglionosis; however, in combination with factors controlling the microenvironment it may cause premature differentiation of the precursors as neurons, resulting in distal aganglionosis.

Ret mutations account for 50% of all familial mutations and 15% to 20% of the sporadic cases of HD. Currently it is estimated that 50 *ret*[25] and 13 *EDRNB*[26] mutations have been reported. Of these 95% of *EDRNB* and 25% of *ret* mutations result in short segment aganglionosis.

Etiology of Other Congenital Diseases Mimicking Hirschsprung's Disease

Hypoganglionosis in adults is acquired or inflammatory in its origin and is rare as an isolated condition. The acquired form can be

caused by various conditions that include anoxemia or toxic or autoimmune processes, which result in neuronal depletion. The inflammatory type is also due to an autoimmune process, in which selective neurons are attacked by mononuclear cells.

Isolated intestinal neuronal dysplasia type B is found in 58.5% of constipated adults.[27] A milder form was seen in about 14.6% of all patients, and these patients may subsequently develop diverticulosis.[27] Type A is rare, occurring in less than 5% of cases, and is characterized by aplasia or hypoplasia of the adrenergic innervation.

The specific etiology of degenerative hollow visceral myopathy mimicking HD is unknown. The inheritance pattern may be autosomal dominant with high or low penetrance.[28] The genetic defect is as yet unknown; however, a link with a defect in synthesis of a contractile protein[29] has been postulated. Involvement of the muscle layer that develops at 12 weeks of gestation may be an indication that the insult is during the first trimester. A mitochondrial DNA mutation has been postulated as a probable lesion in familial visceral myopathy.[30]

Diseases Associated with Hirschsprung's Disease

Congenital anomalies associated with HD have been reported from various series and have an overall incidence of about 14.7% in 2856 patients.[31] Down syndrome is the most common chromosomal abnormality associated with HD, and the genetic modifiers have been located on chromosome 21q 22.[32] The diagnosis of HD in Down syndrome is often delayed because other associated anomalies take precedence and because constipation is often present in these patients due to hypotonia and hypothyroidism.

Cardiac abnormalities have been reported in the range of 0.5% to 1.0% of the general population, and the incidence is increased in patients with Down syndrome. The common defects are endocardial cushion defects and patent ductus arteriosus. Hirschsprung's disease is often associated with other neurocristopathy manifestations, such as pheochromocytoma, neuroblastoma, neurofibromatosis, and MEN II. Waardenburg syndrome, caused by a gene on chromosome 2, is also associated and is characterized by pigment abnormalities, cranial and spinal nerve anomalies, and bowel dysfunction. Micro-ophthalmia and anophthalmia are also congenial disorders that are associated with HD. Associated gasterointestinal tract anomalies include malrotation, intestinal atresia anorectal malformations, Meckel's diverticulum, and pyloric stenosis.

Conclusion

Hirschsprung first described HD in 1886, and since then many theories have been postulated to explain the genesis of this rather complex disease. Recent advances and studies in animal models have furnished a better understanding of the embryogenesis of the human enteric nervous system and the pathophysiology of HD. Genetic studies have identified various factors that can collectively influence the disease phenotype in HD. In humans *ret*, *EDRNB*, and *EDN3* have been implicated in the etiology of HD. No one factor, however, can be singled out, as HD is a complex multigenic disorder. Future studies in identification of abnormal genes that cause dysganglionosis could help in the prevention and treatment of many of the disorders that have a genetic etiology. At this stage genetic counseling is still based on the length of the aganglionic segment. Future research will provide a better understanding of this complex genetic disorder and better means of counseling affected families. Understanding of the pathophysiology and its link to the disease phenotype of HD and its related diseases will also modify treatment options and help future generations of affected families.

References

1. Passarge E. The genetics of Hirschsprung's disease. N Engl J Med 1967;276:138–143.
2. Kleinhaus S, Boley SJ, Sheran M, Sieber WK. Hirschsprung's disease: a survey of the members of the surgical section of the American Academy of Pediatrics. J Pediatr Surg 1979;14:588–597.
3. Meier-Ruge W. Classification of malformations of colorectal innervation. Vech Dtsch Ges Pathol 1971;506:55.
4. Puri P, Lake BD, Nixon HH, et al. Neuronal colonic dysplasia: an unusual association of Hirschsprung's disease. J Pediatr Surg 1977;12:681–685.
5. Furness JB, Costa M. The enteric nervous system. 1987:65–69. New York Churchill Livingstone.

6. Gershon MD, Kirchgessner AL. Functional anatomy of the enteric nervous system. In Physiology of the gastrointestinal tract. 3rd Ed. Edited by Johnson LR, Alpers DH, Jocobson LR and Walsh JH. New York: Raven Press Vol. 1, 1994, 381–422.
7. Okamoto E, Ueda T. Embryogenesis of intramural ganglia of the gut and its relationship to Hirschsprung's disease. J Pediatr Surg 1967;14:437–443.
8. LeDourin NM. Experimental analysis of the migration and differentiation of neuroblasts of the autonomous nervous system and neuroectodermal mesenchymal derivatives using a biochemical marking techniques. Dev Biol 1973;41:162–184.
9. LeDourin NM. The migration of neural crest cells to the wall of the digestive tract in avian embryo. J Embryol Exp Morphol 1973;30:31–48.
10. Erickson CA. Control of neural crest cell migration in avian embryo. Dev Biol 1985;111:138–157.
11. Weston JA. The migration and differentiation of neural crest cells. Adv Morphol 1970;8:41–114.
12. Newgreen DF. Control of the directional migration of migration of mesenchyme cells and neurites. Semin Dev Biol 1990;1:301–311.
13. Akitaya T, Bronner-Fraser M. Expression of cell adhesion molecules during initiation and cessation of neural crest migration. Dev Dynam 1992;194:12–20.
14. Pomeranz HD, Sherman DI, Smalheiser NR, et al. Expression of a neurally related laminin binding protein by neural crest-derived cells that colonize the gut: relationship to the formation of enteric ganglia. J Comp Neurol 1991;313:625–642.
15. Bilozur ME, Hay ED. Neural crest migration in 3D extracellular matrix utilizes laminin, fibronectin or collagen. Dev Biol 1988;125:19–33.
16. Engvall E, Davis GE, Dickerson K, et al. Mapping of domains in human laminin using monoclonal antibodies: localization of the neurite promoting site. J Cell Biol 1986;103:1321–1329.
17. Bolande RP. Animal model of human disease. Hirschsprung's disease, aganglionic or hypoganglionic megacolon: animal model. Aganglionic megacolon in piebald and spotted mutant mouse strains. Am J Pathol 1975;79:189–192.
18. Lane PW. Association of megacolon with recessive spotting genes in the mouse. J Hered 1966;108:29–31.
19. Badner JA, Sieber WK, Garver KL, Chakravarti A. A genetic study of Hirschsprung's disease. Am J Hum Genet 1990;46:568–580.
20. Pachynis V, Mankoo B, Constantini F. Expression of c-ret protooncogene during mouse embryogenesis. Development 1993;119:1005–1017.
21. Jing S, Wen D, Yu Y, et al. GDNF-induced activation of the Ret protein tyrosine kinase is mediated by GDNFR-alpha a novel receptor for GDNBF. Cell 1996;85: 1113–1124.
22. Martucciello G, Favre A, Takahashi M, Jasonni V. Immunohistochemical localization of Ret protein in Hirschsprung's disease. J Pediatr Surg 1995;30:433–436.
23. Baynash AG, Hosoda K, Giaid A, et al. Interaction of endothelin 3 with endothelin b receptor is essential for development of epidermal melanocytes and enteric neurons. Cell 1994;79:1277–1285.
24. Hosoda K, Hammer RE, Richardson JA, et al. Targeted and natural (piebald-lethal) mutation of endothelin-B receptor gene in mutagenic Hirschsprung's disease. Cell 1994;79:1267–1276.
25. Charkravarty A. Endothelin receptor mediated signalling in Hirschsprung's disease. Hum Mol Genet 1996;5:303–307.
26. Kusafuka T, Wang YP. Novel mutation of the endothelin-B receptor gene in isolated patients wih Hirschsprung's disease. Hum Mol Genet 1996;5:347–349.
27. Stoss F, Meier-Ruge W. Experience with neuronal intestinal dysplasia (NID) in adults. Eur J Pediatr Surg 1994;4:298–302.
28. Schuffler MD, Pagon RB, Schwartz R, Bill AH. Visceral myopathy of the gastrointestinal tract. Gasteroenterology 1988;94:892–898.
29. Ionasescu V, Ionasescu R, Anuras S. Alterations in synthesis of contractile protein in fresh and cultured stomach smooth muscle in familial visceral myopathy. Gasteroenterology 1981;80:1182.
30. Lowsky R, Davidson G, Wolman S, et al. Familial visceral myopathy associated with mitochondrial myopathy. Gut 1993;34:279–283.
31. Brown RA. Disorders and Congenital Malformations Associated with Hirschsprung's Disease. Harwood Academic Publishers, Amsterdam, 2000.
32. Puffenberger EG, Hosada K, Washington SS. A missense mutation of the Endothelin-B receptor gene in multigenic Hirschsprung's disease. Cell 1994;79:1257–1266.

3

Etiology of Acquired Colorectal Disease: Constipation

Peter J. Deveaux and Susan Galandiuk

Functional constipation is defined by the Rome II Coordinated Committees as a group of functional disorders that present with resistant, difficult, infrequent, or seemingly incomplete defecation.[1] Previous definitions have included a regular occurrence (in more than 25% of defecations) of excessive straining, lumpy or hard stools, a sense of incomplete evacuation, a sensation of anorectal obstruction or blockage, or less than three bowel movements per week over at least 12 consecutive weeks in the preceding 2 years. Such disorders may be congenital, as in Hirschsprung's disease, or acquired later in life as a result of lifestyle or behavior, infection, or because of anatomic or physiologic abnormalities (Fig. 3.1). The causes of constipation, even after an exhaustive evaluation, often remain unclear and, in many cases, multifactorial. This chapter discusses the etiology of acquired constipation.

Lifestyle

Diet

Western-style societies have the highest incidence of constipation as compared to less developed societies. Dietary composition, especially fiber content, may be a leading contributing cause of constipation. Inadequate dietary fiber intake produces stools that are less bulky, lower in water content, lower in volume, and more difficult to eliminate. In societies such as western Africa where the average dietary fiber intake is as much as 35 g of insoluble fiber, individuals have two to three large soft bowel movements per day on average, and reports of constipation are uncommon.[2] In the United States, dietary fiber intake averages less than 12 g per day, and complaints of constipation may affect 3% to 5% of the population at any given time.[2] Insoluble dietary fiber acts by drawing water into the intestinal lumen, resulting in bulky, soft, large stools that have higher water content. Colonic peristaltic movements, in turn, are in part stimulated by colonic distention.

Frenetic Pace of Life

Strange as it may seem, a hectic schedule and lack of time to eliminate is an increasingly frequent cause of constipation, particularly in individuals trying to manage more than one job.

Medications

Numerous medications (anticholinergics, antidepressants, narcotics) may lead to iatrogenic constipation by impeding neural signaling, resulting in impaired colonic muscular coordination (Table 3.1). Initial treatment of constipation with an identified pharmacologic cause consists of discontinuing the offending drug or replacing the drug with a nonconstipating alternative, if available. Psychiatric disorders such as depression, psychosis, and anorexia nervosa, as well as their pharmacologic treatments, may contribute to or worsen constipation. This has become a real clinical problem with the increasing and almost ubiquitous prescription of

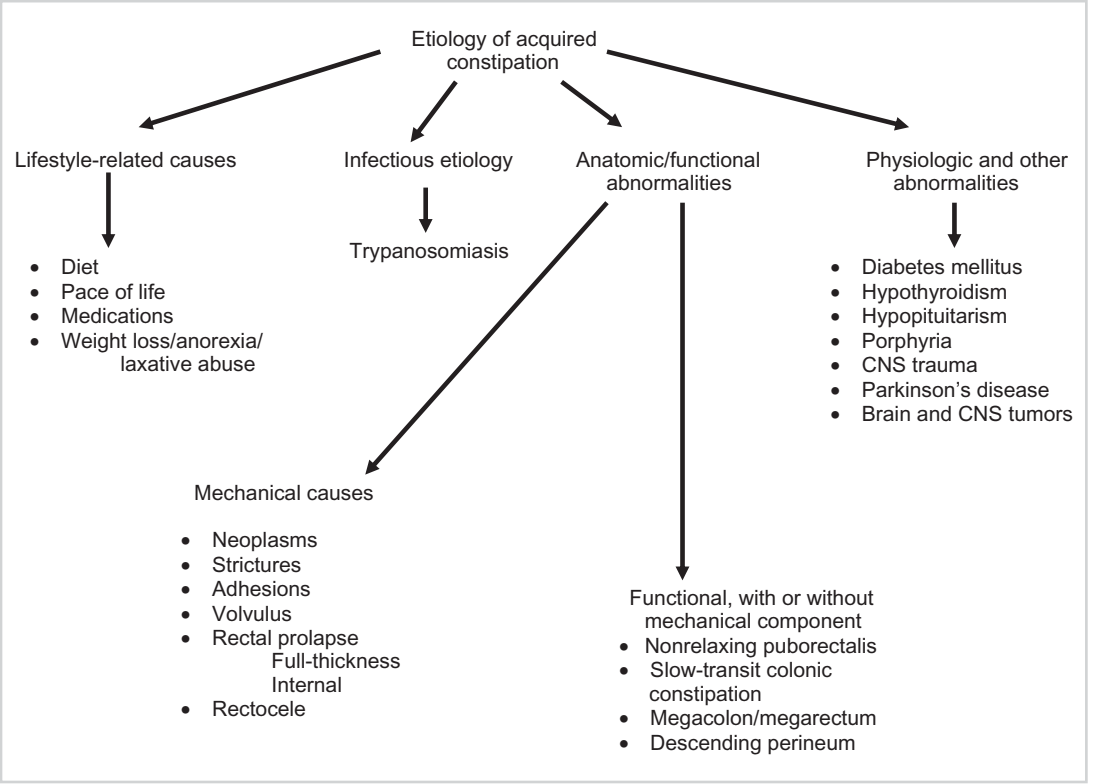


Figure 3.1. Algorithm describing etiologies of various acquired constipation.

Table 3.1. Pharmacologic causes of constipation

Amiodarone
Antacids (e.g., aluminum)
Anticholinergics
Anticonvulsants
Antidepressants
Antihypertensives
Calcium channel blockers
Diuretics
Ganglionic blockers
Antiparkinsonians
Bismuth
Bromocriptine
Bulk laxatives with inadequate hydration
Carboplatin
Cholestyramine
Erythropoietin
Filgrastim [granulocyte colony-stimulating factor (G-CSF)]
Iron
Lovastatin
Mesalamine
Narcotics/opiates
Pravachol
Sandostatin
Valproic acid
Vincristine

antidepressants and psychotropic drugs by many physicians.

Weight Loss, Eating Disorders, and Laxative Abuse

Lack of oral intake, or bulimia, can be associated with reduced fecal volume. By their mechanism of action, overuse of laxatives may result in constipation due to dehydration, hypokalemia, or hypermagnesemia, altering neural transmission and function. The role of laxatives in damaging enteric neurons is uncertain. Long-term use has been associated with changes in neurons of the myenteric plexus and smooth muscle of the colon.[3] Findings such as loss of neurons, morphologic changes of argyrophilic cells, including clubbing and shrinkage, and replacement of ganglia by Schwann cells have been histologically demonstrated.[4] Similar morphologic findings have been discovered in patients with inflammatory bowel disease and diabetic

neuropathy, and may not be specific for laxative use.[5]

Infection

The most common infectious cause of constipation is American trypanosomiasis, or Chagas disease. Caused by the parasitic protozoan *Trypanosoma cruzi*, Chagas disease affects an estimated 17 to 24 million individuals throughout Central and South America and Mexico and leads to 50,000 deaths annually. The disease is endemic in South America, especially in Chile, Brazil, and Argentina. Wild and domesticated mammals harboring *T. cruzi* and infected reduviid insects are found in patchy distributions from the southern United States to southern Argentina. Chagas disease is particularly a public health problem among the poor in rural areas of Central and South America. Acute Chagas disease in the United States is rare. Because enormous numbers of Central and South Americans have immigrated to the United States since the 1980s, the number of cases of chronic Chagas disease in North America will undoubtedly increase over time.

Trypanosoma cruzi is transmitted to mammalian hosts by one of several species of hematophagous triatomine insects known as reduviids. Reduviids become infected by ingesting blood from mammals that have circulating parasites. Common sites of infection include the mucous membranes, conjunctiva, and breaks in the skin. The ingested parasites multiply in the gut of reduviid insects, and infective forms are transmitted in the feces of reduviids while feeding on host blood. Trypanosomes multiply in smooth muscle, among other tissues, eventually causing destruction of these muscle cells. Migration of trypanosomes to regional lymph nodes and into systemic circulation occurs, reaching nearly all host organs.

The pathogenesis of Chagas disease is poorly understood. In its acute form, Chagas disease is generally a mild febrile illness marked by periorbital edema. Children are particularly susceptible to the disease, especially in endemic regions. Following resolution of the acute illness, the great majority of individuals remain in the indeterminate phase of Chagas disease for life, characterized by parasitemia and the absence of symptoms.[6] In a minority of infected patients, cardiac and gastrointestinal lesions result in significant illness and death. Symptoms include abdominal pain, bloating, chronic constipation, and weight loss. The heart is most commonly affected. As the disease progresses in the gastrointestinal tract in 7% to 11% of infected patients, parasitic infestation of the smooth muscle layers of the gut results first in myositis and then in destruction of Auerbach's plexus. Fibrosis of the myenteric plexus occurs as ganglion cells are destroyed,[7] leading to parasympathetic denervation. The affected segment of colon does not achieve peristalsis in a coordinated fashion. The resulting dyskinesia leads to a functional obstruction, whereby the proximal bowel becomes dilated and elongated. Uninfected areas of gut musculature hypertrophy in an attempt to overcome the functional obstruction.

The diagnosis of Chagas disease is made serologically by detecting antibodies that bind to *T. cruzi* antigens (Guerro-Machado complement fixation test). Evaluation with contrast studies usually demonstrates dilation of the colon and rectum.

Anatomic Abnormalities

Anatomic alterations of the colon, rectum, and anus may also cause constipation. These problems can be divided into disorders associated with obstruction, either mechanical or functional, above the level of the pelvis or at the level of the pelvis, and disorders of transit with increased length of the colon. While functional colonic motility may be normal in the individual with constipation, the mechanical obstruction of the passage of stool by extrinsic or intrinsic causes may have an important role.

Mechanical Obstruction

Neoplasms

Neoplasms of the colon, rectum, and anus may cause gradual changes in elimination as they enlarge and obstruct the passage of stool. These lesions are usually readily identified by radiographic or colonoscopic evaluation, and the clinical suspicion of neoplasm is often aroused by the patient's clinical status and constellation of symptoms.

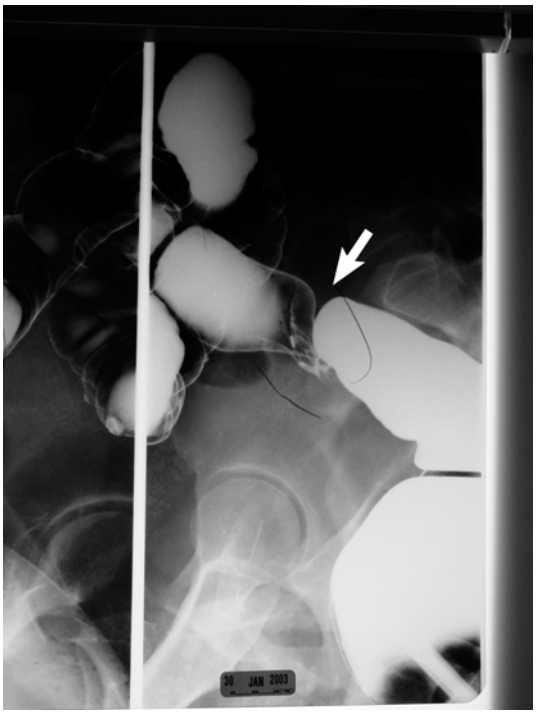


Figure 3.2. Sigmoid colon stricture due to endometriosis.

Benign Strictures

Strictures of the colon, rectum, and anus may mimic symptoms of constipation. The etiology of such strictures may be due to inflammatory processes such as ulcerative colitis, Crohn's disease, endometriosis (Fig. 3.2), or diverticular disease. Adjuvant radiation therapy may also result in stricture or obstruction. Strictures may also occur at areas of prior anastomosis. The most common cause of anal stricture is previous surgery (i.e., hemorrhoidectomy) or inflammatory bowel disease.

Volvulus

Occasionally, patients who suffer from chronic constipation may, in fact, have volvulus. Volvulus may occur at the level of the sigmoid or transverse colon or cecum. Generally, the onset of volvulus is abrupt and presents with the same signs and symptoms as obstruction. On occasion, older patients may have crampy abdominal pain, nausea, and constipation that spontaneously resolves. Diagnosis is often delayed because symptoms have resolved and radiographic findings do not capture the acute event. Symptoms may be ascribed to irritable bowel syndrome or changes associated with aging. A high degree of suspicion should exist for patients who present with this constellation of symptoms and a torturous, redundant transverse or sigmoid colon.

Functional Obstruction

Rectocele

A rectocele may be an important cause of obstructive defecation that presents as constipation. A rectocele is a herniation of the anterior wall of the rectum into the lumen of the vagina. A rectovaginal septum weakened by multiple childbirths and the aging process may enable stool to become trapped in this herniation, leading to a sense of incomplete evacuation. Continued straining may further weaken the rectovaginal septum and lead to progressive enlargement of the herniation. Because patients with a rectocele believe that they cannot completely evacuate during a bowel movement, despite a normal urge to do so, digital manipulation, enemas, or suppositories are often used to assist defecation. These patients typically have rectal fullness, bleeding, pain, and soiling. A bimanual examination discloses a defect of the anterior rectal wall above the level of the anal sphincter. Radiographically, a pocket-like protrusion of the rectovaginal septum into the vagina is noted on lateral or oblique views. This is best observed during defecating proctography by retained contrast within the rectocele at the end of defecation (Fig. 3.3).

Rectoceles are a relatively common finding on physical examination, occurring in up to 81% of all women.[8] However, only half of these patients report symptoms of constipation or difficulty with defecation. Thus, many women with rectoceles are asymptomatic, and the presence of a rectocele is not an indication for repair. Rectoceles found on defecography that measure less than 2 cm are generally considered to be clinically insignificant, whereas rectoceles larger than 3 cm are usually considered clinically significant.[8] Interestingly, the size of a rectocele has been shown not to correlate with the severity of symptoms clinically.[9–11] Furthermore, the size of a rectocele as measured by the amount of

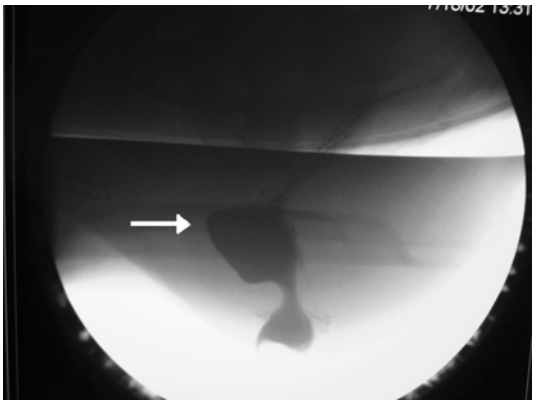


Figure 3.3. An anterior rectocele (arrow) retains contrast during defecating proctography.

barium trapped radiographically has not been proven to correlate with the success of rectocele repair.[9]

Controversy exists as to whether rectoceles are the cause or result of excessive straining. Repeated trauma, as in obstetrical injury or repeated vaginal delivery, appears to play a role in weakening the rectovaginal septum. Typically, the sphincter is shortened and the perineal body is thinned. Beven[12] has speculated that thinning of the rectovaginal septum and/or pelvic denervation seen following hysterectomy may contribute to rectocele formation. Johansson et al[13] has noted that some patients have associated paradoxical sphincter contraction and elevated mean resting rectal pressures. Because rectoceles commonly present in the fourth and fifth decade of life, the postmenopausal hormonal milieu with supporting tissue laxity may play a role in the pathogenesis of rectocele.

Descending Perineum Syndrome

Weakness of pelvic floor support may result in the descending perineum syndrome. This muscular weakness is reportedly related to injury of the sacral nerves or pudendal nerves or due to damage to the musculature itself during childbirth or chronic straining while defecating. Obstruction to defecation may occur through widening of the anorectal angle, weakening of the perineal body, and a more vertical orientation of the rectum, which are all results of pelvic floor weakness.[14] A perineal descent of greater than 4 cm on straining as identified radiographically suggests a weakened perineum. Prolonged latency on stimulation of the pudendal nerve is characterized on electrophysiology studies. Over time, prolapsed anterior rectal wall mucosa may become irritated and bleed as it protrudes through the anal canal. Mucus secretion, soilage, and pruritus are later findings. Patients usually relate a sensation of incomplete evacuation during defecation, followed by a feeling of obstruction due to the prolapsing of the anterior rectal wall mucosa. Manual reduction with a finger in the anal canal may temporarily reduce this obstruction and allow defecation.

Nonrelaxing Puborectalis Syndrome (Anismus)

The constellation of symptoms associated with rectoceles (prolonged repeated straining at bowel movements, sensation of incomplete evacuation, and the need for digital manipulation) is also seen in puborectalis syndrome. Synonyms include nonrelaxing puborectalis syndrome, paradoxical puborectalis syndrome, spastic pelvic floor syndrome, and anismus. During normal evacuation, distention of the rectum by fecal matter induces relaxation of the internal anal sphincter, followed by contraction of the external anal sphincter mechanism. At the time of defecation, the external sphincter relaxes, as does the puborectalis muscle. This has the effect of straightening the anorectal angle, thereby facilitating elimination. The failure of the puborectalis muscle to relax (or paradoxically, to contract) in nonrelaxing puborectalis syndrome results in continued maintenance of the anorectal angle. The effect is anal outlet obstruction.

The symptoms of these two syndromes are so similar that the history alone cannot discriminate between the two. While paradoxical contraction of the puborectalis muscle during the Valsalva maneuver can be evaluated on physical examination, electromyography (EMG), balloon expulsion studies, and defecography are typically more reliable and reproducible means for diagnosing this condition. Diagnosis may require the use of several modalities, and each test has its limitations. Patient inhibition may lead to nonrelaxation of the pelvic floor on defecography. Pain during EMG due to probe placement may also result in nonrelaxation during testing, resulting in a false-positive finding. Prospective studies suggest that EMG

has a sensitivity of 67%, positive predictive value of 70%, and specificity of 83%, whereas these values for defecography are 70%, 67%, and 80%, respectively.

Whether paradoxical contraction of the puborectalis muscle during defecation is a cause of constipation or a coincidental finding is unclear. A study by Jorge et al[15] evaluated 112 constipated patients with EMG and defecography. One third of these patients displayed findings consistent with paradoxical puborectalis contraction as measured by these techniques. However, the correlation between EMG and defecography was poor: 33% of patients displaying findings of anismus on defecography had a normal EMG, and 30% of patients with an EMG suggesting anismus had normal defecography. Treatments directed at inhibiting contraction of the puborectalis muscle, such as injection of botulinum toxin or division of the puborectalis muscle, have yielded mixed results.

It may be that the isolated finding of contraction of the puborectalis muscle represents an abnormal learned response that has been hypothesized to result in some patients from sexual assault[16] or abuse.[17] The passage of large painful bowel movements in children is also thought to contribute to the development of paradoxical puborectalis contraction.

Rectal Prolapse

Internal rectal intussusception is an early stage of rectal prolapse, where the proximal rectum has prolapsed into the ampulla but has not progressed through the anal canal. Symptoms include constipation and an incomplete sense of evacuation. Less commonly reported are incontinence, pain, and soiling. Endoscopy may reveal a solitary rectal ulcer on the anterior rectal wall 8 to 10 cm above the anal verge. Defecography is the diagnostic test of choice and shows the rectum intussuscepting several centimeters above the level of the levators. Classically, a funnel-shaped pattern is seen reflecting circular prolapse of the rectal wall. Rectal intussusception previously had been thought to be a common cause of obstructed defecation. However, because operative repair of rectal intussusception has met with little success, current thought suggests that intussusception may be the result of, and not the cause of, obstructed defecation.

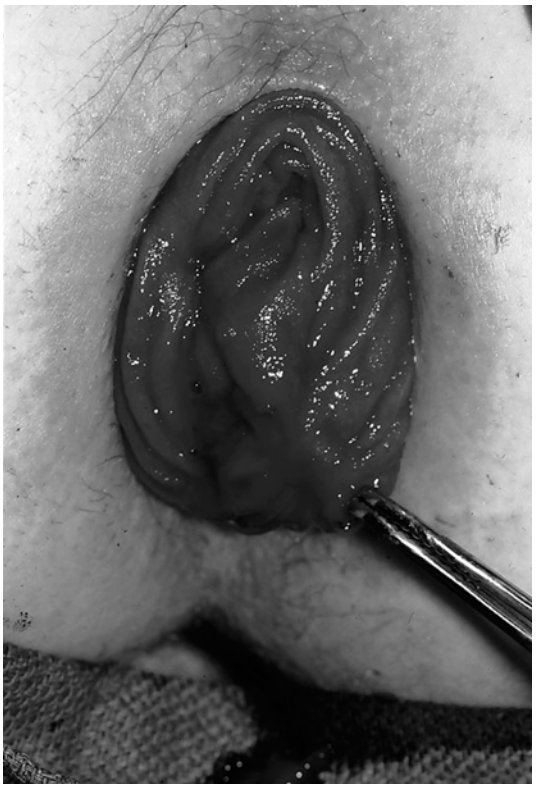


Figure 3.4. Full-thickness rectal prolapse.

Full-thickness rectal prolapse is the protrusion of the full thickness of the wall of the rectum through the anal canal (Fig. 3.4). Symptoms correlate with the degree of prolapse through the anal canal. With complete prolapse through the anal canal, the extruded rectum becomes excoriated, resulting in ulceration, bleeding, and mucous discharge. In this latter stage, fecal incontinence is the rule. A history of constipation is a common finding. Physical examination discloses a protruding mass of reddened friable tissue. Digital rectal examination may easily reduce the prolapse, and a widely patent, poorly contractile, anal canal is noted. Concentric folds of colonic mucosa are observed in contrast to the radial folds seen in patients with prolapsed internal hemorrhoids. Uterine prolapse or cystocele may be identified concomitantly.

Slow-Transit Constipation Without Megacolon

Patients with slow-transit constipation are almost always women, usually presenting in

their second or third decade. They have two or fewer bowel movements per week. Malaise, bloating, nausea, and abdominal cramping are frequent complaints. Symptoms are typically unresponsive to bulk laxatives and stool softeners. There is often a strong association with gynecologic complaints such as irregular menstrual cycles, ovarian cysts, and galactorrhea. Many patients have delayed gastric emptying, biliary dyskinesia, and delays in small bowel transit, suggesting the presence of a panenteric motility disorder.[18–20] A diagnosis of colonic inertia is made only after excluding systemic neurologic processes such as diabetes mellitus or multiple sclerosis, or a pelvic floor abnormality as a cause.

Investigation typically reveals a normal-caliber but often very redundant colon on barium enema (Fig. 3.5). Defecography and manometry are essential to exclude pelvic floor dysfunction as an etiology of constipation. Colonic transit studies show markedly delayed transit of ingested radiopaque markers. Interestingly, there are two categories of transit studies. The first displays pancolonic inertia, as markers have delayed transit beginning in the cecum and continuing throughout the remainder of the colon. The second shows passage of markers without delay through the ascending and transverse colon and a slowing of transit through the left colon and rectosigmoid.

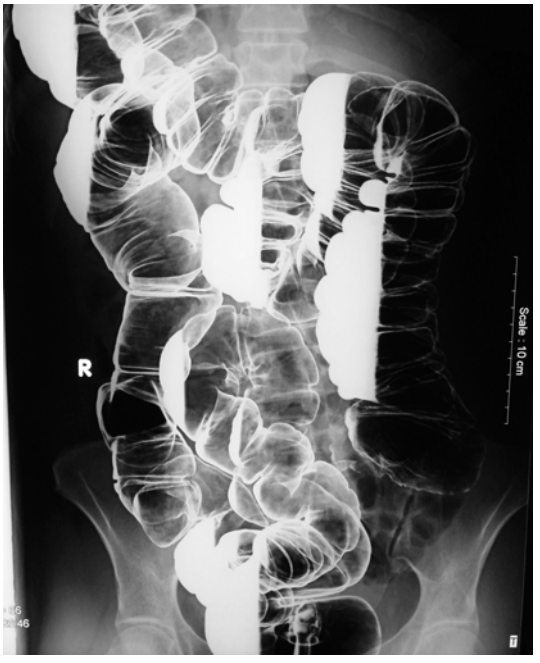


Figure 3.5. Slow-transit constipation as observed following barium enema. Note the appearance of a normal-caliber, but often very redundant, colon, in this patient with situs inversus.

Studies in animal models suggest that colonic transit can be accelerated by serotonin, serotonin analogues, or both. Zhao et al[21] evaluated the distribution, density, and staining intensity of enterochromaffin and serotonin cells in the colonic mucosa of patients with colonic inertia compared to controls. The number of enterochromaffin cells and serotonin-producing cells was increased in the group with colonic inertia, with a greater number found in the left colon. Compared with controls, these cells contained fewer hormones as measured by the intensity of staining but were present in greater numbers. It is unknown whether an increased level of serotonin is the cause of motility impairment or a consequence.

The mechanism by which serotonin exerts an effect on colonic motility is not completely understood. Work by Haga et al[22] indicates that serotonin, both endogenously produced and exogenously applied, stimulated acetylcholine release via 5-hydroxytryptamine ($5\text{-}HT_3$) receptors, resulting in increased colonic transit.

Alterations of hormones at the enteric level also may play a role in the etiology of idiopathic slow-transit constipation. Substance P levels have been found to be decreased in the mucosa and submucosa of patients with slow-transit constipation.[23] Altomare et al[18] and others have suggested that slow-transit constipation is a manifestation of autonomic nervous system dysfunction, pointing out that such disorders are characterized by abnormalities in diverse systems such as cardiovascular, urinary, sexual, and digestive. A recent review found that more than 70% of patients suffering from slow-transit constipation also showed some degree of autonomic dysfunction, such as biliary dyskinesia and delayed small bowel transit. This group has also shown that women with slow-transit constipation exhibit impaired sweat production after acetylcholine application. Impaired extrinsic autonomic control of mechanisms controlling colonic motility via acetylcholine and serotonin-regulated pathways may result in multisystem dysregulation and subsequent clinical symptoms. Pharmacologic treatment of such patients will be a rapidly expanding field in the future.

Slow-Transit Constipation with Megarectum/Megacolon

In contrast to the condition previously described, some patients with constipation present with a markedly dilated colon and rectum. Males and females are affected equally. This condition usually presents in childhood or adolescence. Patients often require chronic laxative use to maintain bowel function. The symptoms of chronic constipation with abdominal pain, bloating, and often fecal incontinence can have a significant adverse affect on lifestyle.[24]

Radiographic evaluation shows dilatation of the colon and rectum to the pelvic floor. Although any part of the colon may be affected, the process usually begins in the rectum or involves the rectum. A rectal diameter of 6.5 cm at the pelvic rim on lateral view defines megarectum.[25] Colonic transit studies are abnormal, with marked delay in the dilated segment of affected bowel.[26] Small bowel transit studies are generally normal. The diagnosis of idiopathic megacolon and megarectum is a diagnosis of exclusion, made only after other causes of constipation such as Hirschsprung's disease have been ruled out (Fig. 3.6). This syndrome can be distinguished from Hirschsprung's disease by the presence of anorectal inhibitory reflex, the absence of a normal caliber or stenotic length of distal bowel, and the presence of ganglion cells on rectal biopsy. Subtle histologic abnormalities have been identified in both smooth muscle and intrinsic innervation. There is thickening of the bowel wall due to smooth muscle hypertrophy and fibrosis of the muscularis mucosa, circular muscle, and longitudinal muscle layers. These findings, however, are not specific to this syndrome.

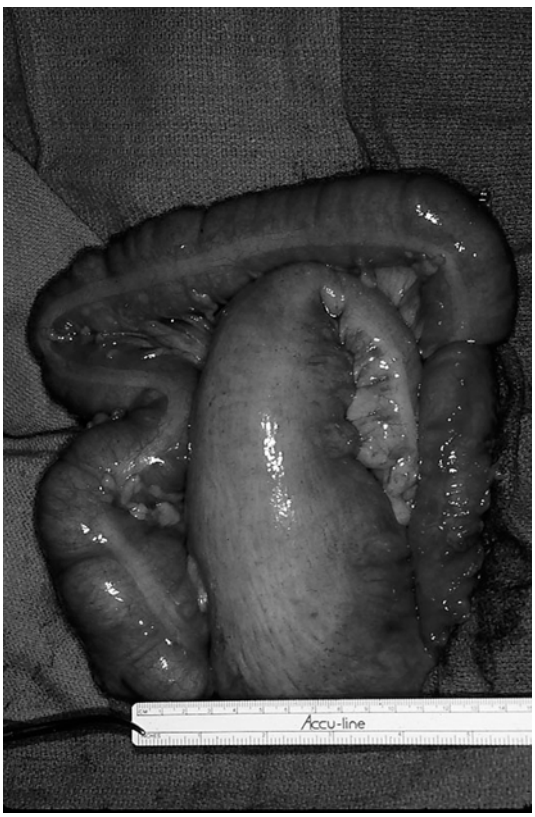


Figure 3.6. Intraoperative photograph of a megarectum. Note that the rectum extends up to the level of the transverse colon.

Several investigators have found decreased vasoactive intestinal peptide levels in the muscularis externa in patients with idiopathic megacolon,[27,28] suggesting a loss of inhibitory nerves that normally innervate colonic smooth muscle. Other researchers have noted reduced numbers of argyrophilic neurons and structural abnormalities in these neurons, such as decreased neuronal processes and variable-size nuclei in the ganglia.

Physiologic Abnormalities

Other than the anatomic and functional causes of constipation described above, a host of other, less common medical problems may present with constipation. Systemic illness such as diabetes mellitus, multiple sclerosis, hypothyroidism, hypopituitarism, and porphyria may cause or exacerbate constipation. Neurologic disorders, including brain and spinal cord neoplasms, central nervous system trauma, and Parkinson's disease, are known to be associated with constipation, significantly altering the quality of life.

Conclusion

There are many causes of acquired constipation, and unfortunately, many patients have constipation due to a combination of these. A careful patient history and evaluation is necessary in order to determine the etiology, which is outlined in succeeding chapters. It is wise to begin with the least invasive and safest treatment and then proceed with further treatment, only if this initial treatment fails. The next few years will

likely see the development of more effective pharmacotherapy for slow-transit colonic constipation, and thereby greatly facilitate the treatment of affected individuals.

References

1. Rome II: The functional gastrointestinal disorders: diagnosis, pathophysiology and treatment—a multinational consensus. In: Drossman DA, Talley NJ, Corazziari ES et al., 2nd ed. McLean, VA: Degnon Associates, 2000:382.
2. Whitehead WG, Drinkwater D, Cheskin LJ, et al. Constipation in the elderly living at home: definition, prevalence and relationship to lifestyle and health status. J Am Geriatr Soc 1989;37:423–429.
3. Xing JH, Soffer EE. Adverse effects of laxatives. Dis Colon Rectum 2001;44:1201–1209.
4. Krishnamurthy S, Schuffler MD, Rohrmann CA, et al. Severe idiopathic constipation is associated with a distinctive abnormality of the colonic myenteric plexus. Gastroenterology 1985;88:26–34.
5. Riemann JF, Schmidt H. Ultrastructural changes in the gut autonomic nervous system following laxative abuse and in other conditions. Scand J Gastroenterol Suppl 1982;71:111–124.
6. Hudson L, Britten V. Immune response to South American trypanosomiasis and its relationship to Chagas' disease. Br Med Bull 1985;41:175–180.
7. Olivares-Villagomez D, McCurley TL, Vnencak-Jones CL, et al. Polymerase chain reaction amplifications of three different Trypanosoma cruzi DNA sequences form human chagasic cardiac tissue. Am J Trop Med Hyg 1998;59:563–570.
8. Halligan S, Bertram CI. Is barium trapping in rectoceles significant? Dis Colon Rectum 1995;38:764–768.
9. Van Dam JH, Ginai AZ, Crosselink MJ, et al. Role of defecography in predicting clinical outcome of rectocele repair. Dis Colon Rectum 1997;40:201–227.
10. Kelvin FM, Magliate DD, Hornback JA. Pelvic prolapse: assessment with evacuation proctography (defecography). Radiology 1992;184:547–551.
11. Siproudhis L, Robert A, Lucas J, et al. Defecatory disorders, anorectal and pelvic floor dysfunction: a polygamy? Radiologic and manometric studies in 41 patients. Int J Colorectal Dis 1992;7:102–107.
12. Beven JT. Female Pelvic Floor Disorders: Investigation and Management. New York: W.W. Norton, 1992: 380–389.
13. Johansson C, Nilsson BY, Holmstrom B, et al. Association between rectocele and paradoxical sphincter response. Dis Colon Rectum 1992;35:503–509.
14. Karasick S, Karasick D, Karasick SR. Functional disorders of the anus and rectum: findings on defecography. AJR 1993;160:777–782.
15. Jorge JM, Wexner SD, Ger GC, et al. Cinedefecography and electromyography in the diagnosis of nonrelaxing puborectalis syndrome. Dis Colon Rectum 1993;36: 668–676.
16. Shelton AA, Welton ML. The pelvic floor in health and disease. West J Med 1997;167:90–98.
17. Leroi AM, Berkelmans I, Denis P, et al. Anisumus as a marker of sexual abuse. Consequences of abuse on anorectal motility. Dig Dis Sci 1995;40:1411–1416.
18. Altomare DF, Portincasa P, Rinaldi M, et al. Slow-transit constipation: a solitary symptom of a systemic gastrointestinal disease. Dis Colon Rectum 1999;42:231–240.
19. van der Sijp JR, Kamm MA, Nightingale JM, et al. Disturbed gastric and small bowel transit in severe idiopathic constipation. Dig Dis Sci 1993;38:837–844.
20. Donald A, Baxter JN, Bessent RG, et al. Gastric emptying in patients with constipation following childbirth and due to idiopathic slow transit. Br J Surg 1997;84: 1141–1143.
21. Zhao R, Baig MK, Wexner SD, et al. Enterochromaffin and serotonin cells are abnormal for patients with colonic inertia. Dis Colon Rectum 2000;43:858–863.
22. Haga K, Arsano K, Fukuda T, et al. The function of 5-HT3 receptors on colonic transit in rats. Obes Res 1995;5:801S–810S.
23. Goldin E, Karmelli F, Selinger Z, et al. Colonic substance P levels are increased in ulcerative colitis and decreased in chronic severe constipation. Dig Dis Sci 1989;34: 754–757.
24. Kamm MA. Investigation and management of megarectum and megacolon. Hosp Update 1993;19:280–288.
25. Preston DM, Lennard-Jones JE, Thomas BM. Towards a radiologic definition of idiopathic megacolon. Gastrointest Radiol 1985;10:167–169.
26. Gattuso JM, Kamm MA, Morris G, et al. Gastrointestinal transit in patients with idiopathic megarectum. Dis Colon Rectum 1996;39:1044–1050.
27. Koch TR, Schulte-Bockholt A, Telford GL, et al. Acquired megacolon is associated with alteration of vasoactive intestinal peptide levels and acetylcholinesterase activity. Regul Pept 1993;48:309–319.
28. Gattuso JM, Hoyle CH, Milner P, et al. Enteric innervation in idiopathic megarectum and megacolon. Int J Colorectal Dis 1996;11:264–271.

4

Extracolonic Causes of Constipation

Noel R. Fajardo and Lawrence A. Szarka

Lifestyle

Dietary Fiber

In clinical practice, it is commonly accepted that fiber therapy and stool-bulking agents are the main therapeutic agents of choice in the initial management of primary constipation.[1] Several clinical trials have been performed on the effects of fiber therapy and constipation. Meta-analyses of these trials have had discordant conclusions. In one study, a total of seven double-blind, placebo-controlled trials were analyzed; five of the studies resulted in improvement in overall symptoms, an increase in fecal weight and frequency, and decreased transit time.[2] However, another meta-analysis reviewed 13 clinical trials, and only four found beneficial results. Moreover, the improvements noted were in several nonspecific outcomes, such as ease of stool passage and frequency of satisfaction with bowel movements, and no significant improvement was noted in the more specific symptoms such as stool frequency, abdominal pain, and bloating.[3] Reviews of fiber therapy have pointed out that the most common reason for failure of fiber treatment is noncompliance.[4] In an ongoing prospective study among female registered nurses in the United States, a total of 3327 out of 62,036 women reported constipation. Intake of dietary fiber based on a self-reported food-frequency questionnaire was correlated with the prevalence of constipation. Multiple logistic regression analysis demonstrated that higher dietary fiber intake was associated with a decreased prevalence of constipation. The study has shown that women who had approximately 20 g daily of fiber had a threefold lower prevalence of constipation compare to women who had about 7 g daily of fiber.[5] In light of the conflicting evidence regarding the benefit associated with higher fiber intake and its efficacy in the management of constipation, the current recommendation is that since increasing dietary fiber and hydration is safe and can be prescribed as placebo, it is an important therapeutic modality in the empiric management of constipation.[6]

Physical Activity

The effect of exercise and physical activity on the gastrointestinal system is an area of emerging interest.[7] A major function of colonic motor activity is the propulsion of colonic contents in the aborad direction; the available literature on the net effects of exercise and physical activity on colonic transit is, at present, controversial.[8] Along with increased ample hydration and high-fiber diet, regular physical exercise has been advocated as the standard, first-line treatment of primary constipation.[4] This recommendation is based on the observation that patients who have decreased mobility are more susceptible to constipation, and from studies suggesting that exercise accelerates gastrointestinal transit, yet there has been no conclusive evidence supporting the use of exercise as therapy for constipation.[9] In one study, information concerning bowel habits was gathered from a representative sample of

14,407 United States adults in the first National Health and Nutrition Examination Survey in 1971 to 1975 and approximately 10 years later among the same individuals. The prevalence of self-reported constipation and infrequent defecation (three or fewer bowel movements per week) increased with aging, and women were more likely than men to report constipation (20.8% vs. 8.0%, $p < .05$) and infrequent defecation (9.1% vs. 3.2%, $p < .05$). The study concluded that along with female gender, black race, fewer years of education, and symptoms of depression, low physical activity was one of the independent risk factors for impairment in bowel function.[10]

Bi and Triadafilopolous[9] critically analyzed two studies that reported a significant reduction in transit time after aerobic exercise. In one study that was reviewed, the authors were critical of the methodology, noting that a standardized diet was not given to the cohorts, suggesting that this feature might have affected colonic transit time.[11] The other study that has shown an increase in gastrointestinal transit after aerobic exercise was criticized for lack of dietary control, and the serial nature of 1-week crossover trial among cycling, running, and rest.[11]

Meshkinpour et al[12] studied eight subjects, seven of whom were women with chronic idiopathic constipation, for a 6-week study period that included 2 weeks of rest and 4 weeks of regular exercise. The subjects exercised 1 hour each day, 5 days per week, using a pedometer to objectively assess their overall physical activity. A diary was kept to record the number and consistency of their bowel movements and the amount of straining required for defecation. Results of the study revealed that patients covered 1.9 ± 0.3 and 3.2 ± 0.3 miles/day in the rest period and during the exercise period ($p < .007$). Despite this level of exercise, the authors noted that the subjects did not improve their constipation indices, which were 9.1 ± 0.7 and 8.6 ± 1.1 in the rest and exercise periods, respectively (p = ns). Thus, the authors concluded that physical activity does not play a role in the management of chronic idiopathic constipation. Using solid-state manometry catheters, Rao et al[8] studied 12 healthy subjects, six of whom were females. These subjects were then instructed to exercise on a stationary cycle ergometer for a period of 15 minutes alternating with 15 minutes of rest. Colonic motor activity, illustrated by number of waves, mean amplitude of waves, and area under the curve, was analyzed before and after the exercise period. The results of the study were contrary to popular belief, as the data have suggested that the incidence of pressure waves and the area under the pressure curve waves were significantly lower during exercise. Moreover, the authors found that with a higher intensity of exercise, there was an associated greater reduction in motor activity.

In summary, the benefits of physical activity and exercise may be related to cardiovascular enhancement, and future studies focusing on the effect of physical activity may elucidate the risk of constipation associated with physical inactivity.

Social Habits

Although it may be intuitive that personal and social habits, which include sleeping, bowel hygiene, and lifestyle, are likely to influence an individual's bowel habits, a literature review found that these factors are not as systematically studied as possible etiologies of constipation. A study on the effect of transatlantic travel on the bowel habits of 77 individuals, 40 of whom were women, hypothesized that with the social changes associated with travel, such as varied diet, different timetables, and problems related to lavatory use, travelers would be more prone to constipation. The participants recorded their regular bowel habits by answering an 11-item questionnaire 1 month before, during, and after the trip. Stool consistency using the Bristol Stool Form Scale, jet lag caused by the trip using the Columbia Jet Lag Scale questionnaire, and colonic transit time using radiopaque markers before and during the trip were the outcome variables of interest. The authors found that there was a difference in bowel movements per day (before the trip, 0.97 ± 0.07 vs. after the trip, 0.68 ± 0.06), where there was a significant decrease after the trip ($p < .05$). However, comparing the colonic transit time between the two periods did not reveal any significant differences (before the trip, 36.7 ± 4.2 hours vs. after the trip, 36.2 ± 2.8 hours, p = ns). The authors concluded that traveling may induce changes in bowel movements, and that indeed, a significant proportion of the subjects did complain of having constipation. The authors have suggested that

the defecatory frequency decrease associated with traveling may be related to jetlag and changes in physical activity and diet, and may be normal consequences of flying.[13]

Psychological

In clinical practice and studies, it is recognized that there is a strong relationship between gastrointestinal symptoms and psychiatric, mood, and eating disorders.[14–16] Acknowledging that there may a referral bias associated with these studies, a survey questionnaire was used to determine the relationship between psychiatric disorders and gastrointestinal symptoms.[17] The authors analyzed questionnaires returned by 62,651 persons (66.5% response rate). It was found that the prevalence of anxiety disorder and depression were 15.3% and 10.4%, respectively. The authors' analysis revealed that anxiety was more strongly associated than depression with gastrointestinal complaints (constipation, diarrhea, and heartburn), but the association was significant in both groups, and that demographic factors, lifestyle factors, and extragastrointestinal complaints could not explain the effect of anxiety disorders and depression on these gastrointestinal symptoms. No conclusion could be made about causality, whether anxiety or depression results from worry about constipation, or whether this symptom can be an expression of the anxiety or depression disorder.

A study by Nehra et al[18] demonstrated the prevalence of psychological impairment in patients with rectal evacuation disorders. In the 60 patients included in the study (55 women), psychological disorders were identified in 39 (65%). These disorders were subdivided into the following categories: eating disorders in five, rumination syndrome in three, pain disorder in six, and anxiety-depression in 10, a combination of depression and pain disorder in three, and a combination of eating disorder with anxiety-depression and pain disorder in 12. Since these patients were evaluated as they were undergoing pelvic floor retraining, the association between the psychological status of the patient and the outcome of the retraining was also analyzed. The authors demonstrated that the prevalence of psychological impairment among patients seen for constipation in a tertiary care practice is significant and has a negative impact on the outcome of behavioral treatment.

Eating disorders affect an estimated 5 million Americans every year, and they typically occur in adolescent girls or young women. These illnesses, which include anorexia nervosa, bulimia nervosa, binge-eating disorder, and their variants, are characterized by disturbances in eating, either with restriction of intake or bingeing, as well as excessive concern and distress about body shape and weight. Among the abnormalities associated with eating disorders, somatic indications include diarrhea or constipation, that may be a result of inadequate dietary intake or related to the purging behavior that may be induced by laxatives, enemas, diuretics, anorexic drugs, caffeine, or other stimulants.[19]

Physiological Factors

Metabolic

Measurement of serum electrolytes is an important diagnostic modality in evaluating patients who present with constipation. It is known that electrolyte abnormalities such as hypokalemia, hypo- and hypercalcemia, and metabolic derangements seen in uremia are associated with symptoms of constipation.[20]

Endocrine Disorders

Endocrine disorders are associated with gastrointestinal complications, for example, constipation. Among the endocrinopathies discussed here are diabetes mellitus, hypothyroidism and hyperparathyroidism, multiple endocrine neoplasia type IIb (MEN IIb), and pregnancy.

The prevalence of gastrointestinal symptoms in individuals with diabetes mellitus is higher as compared to the general population.[21] The impact of diabetes mellitus on gastrointestinal function and quality of life was assessed by Talley et al[22] in a total of 1101 Australian diabetics. Among the gastrointestinal symptoms that were assessed, 24.5% of patients reported having constipation, which was the most prevalent symptom reported among all diabetics, both types 1 and 2. The authors concluded that gastrointestinal morbidity among diabetics is high and is associated with a significant impairment

of quality of life. This finding was echoed in another study that concluded that diabetic autonomic neuropathy is a serious and common complication of diabetes, and constipation is the most common lower gastrointestinal symptom.[23] Gastrointestinal function of individuals who have diabetes mellitus and constipation were assessed by scintigraphic colonic transit studies, anal sphincter vector manometry, balloon expulsion defecatory dynamics, and scintigraphic measurement of anorectal angles. Among diabetics with constipation, the study concluded that, compared with community controls, diabetics have a higher prevalence of abnormal evacuation and colonic motor abnormality as manifested by prolonged colonic transit.[24]

The prevalence of bowel dysfunction in hypothyroidism was assessed by a colon transit study among patients who manifested with clinical hypothyroidism. The authors found a significant delay in the whole-gut transit in this population. The authors concluded that hypothyroidism may clinically manifest as a decrease in bowel movements, and is improved by replacement with thyroid hormones.[25] Constipation is a common symptom of hypercalcemia, secondary to hyperparathyroidism.[26]

Delayed orocecal transit studies were reported in pregnancy.[27] There is an increased incidence of constipation and symptomatic hemorrhoids, especially during the latter phases of pregnancy, either as a result of alterations in hormones or secondary to mechanical compression caused by an enlarging uterus.[28]

It is known that the syndrome of MEN IIb comprises mucosal ganglioneuromatosis, medullary thyroid carcinoma, pheochromocytoma, and skeletal anomalies. In patients who were found to have ganglioneuromatosis of the alimentary tract, constipation was described as a clinical manifestation of the disorder; megacolon occurred in five of a series of 16 patients.[29]

Other less common endocrinopathies that have been associated with constipation include hyperparathyroidism,[26] panhypopituitarism, pheochromocytoma,[30] and glucagonoma.[31,32]

Drugs (Table 4.1)

The following pharmacotherapeutic agents are associated with constipation: analgesics, which include opiates and to a much lesser extent nonsteroidal antiinflammatory drugs; anticholinergic medications that are commonly used as antispasmodics, antidepressants, and antiparkinsonism drugs; antacids that contain the elements aluminum and calcium; α-adrenergic agonists, beta-blockers, calcium channel blockers, and diuretic antihypertensives; and other medications such as anticonvulsants, iron, and bismuth.

Table 4.1. Constipating medications

Medication class	Common medications
Analgesics	Opiates, nonsteroidal antiinflammatory drugs
Anticholinergic medications	Antispasmodics, antidepressants, and antiparkinsonism drugs
Antacids	Aluminum hydroxide and calcium carbonate
Antihypertensives	α-adrenergic agonists, beta-blockers, calcium channel blocker, and diuretics
Others	Anticonvulsants, iron, bismuth

Neurologic

Neurohumoral integrity is essential for normal gastrointestinal motility, and this is subdivided into intrinsic and extrinsic components. The intrinsic component involves the enteric nervous system; the extrinsic component involves the vagus nerve and splanchnic nerves to the stomach and upper intestine, and the pelvic nerves that supply the distal intestinal segments.[33] In patients with neurologic diseases, colorectal dysfunction is caused by a combination of lesions of the central or peripheral nervous systems, immobility, altered dietary habits, or use of medications such as opioid analgesics and spasmolytics.[34]

Central Nervous System

A variety of colorectal dysfunction can be attributed to lesions of the central nervous system. Those disorders that are seen most commonly in clinical practice will be discussed, namely cerebrovascular accidents, spinal cord injury, multiple sclerosis, Parkinson's disease, and spina bifida.

The impact of gastrointestinal (GI) complications after an episode of cerebrovascular accident is determined by the extent of the functional impairment related to the event. Initially

after the event of a stroke, fecal incontinence is more frequent (31–40%) and is associated with the severity of the stroke; after 6 months, the frequency of fecal incontinence is reduced to 3% to 9%.[34] The frequent association of constipation with disorders involving neuronal malfunction suggests that disruption of the neural modulation of colonic motility may play an important role in the development of constipation. In a study of 8.8 million Medicare patients in the United States, the closest associations were observed between constipation and neurologic diseases.[35] A prospective study to determine the incidence of constipation was conducted on a population of 152 inpatients at a stroke rehabilitation center. The authors found that constipation occurred in 60% of the patients, and that the incidence of constipation was not related to age or gender but was strongly related to functional status of patients as assessed by the Barthel Index.[36]

The prevalence of individuals with spinal cord injury is estimated to be between 183,000 to 230,000, with approximately an 11,000 annual incidence.[37] The pervasive effect of spinal cord injury on the individual involves many systems and results in a variety of impairments that limit adaptive compensation. The impact of gastrointestinal, specifically neurogenic bowel, dysfunction after spinal cord injury can be particularly life limiting.[38] Neurogenic bowel dysfunction is defined as the life-altering impairment of gastrointestinal and anorectal function resulting from a lesion of the nervous system that can lead to life-threatening complications.[39] These symptoms result from interruption of supraspinal control of the sacral parasympathetic supply to the colon, pelvic floor, and anal sphincters.[40,41] In addition, paralysis and sensory deficits of the limbs can limit independence in the adaptive habits required to compensate for a neurogenic bowel.[38]

Among the plethora of complications associated with neurogenic bowel dysfunction, constipation and difficulty with evacuation have the strongest negative impact on the quality of life of the individual, as it affects as many as 80% of people with spinal cord injury.[42] One of the main impediments in the management of neurogenic bowel dysfunction is that common therapeutic modalities used in addressing constipation, such as fiber therapy, do not lead to optimal results and may even exacerbate colonic impairment.[43] Studies assessing the colonic transit in individuals after spinal cord injury, both with the use of colonic markers[44] and colonic scintigraphic studies,[45] have demonstrated that there is a significant delay in individuals with this injury as compared to healthy control groups. In both of these studies, it has been suggested that the significant delay occurs in the rectosigmoid and the descending colon, whereas the transverse, ascending colon, and cecum did not show any significant delays. The authors have suggested that this finding is likely due to the damage to the reflex arches between the colorectum and the sacral spinal cord, thus significantly reducing emptying of the rectosigmoid and descending colon during defecation.

Through the use of solid-state manometric catheters, Fajardo et al[46] evaluated the colonic motor function of the colon of individuals with spinal cord injury and healthy controls. Ambulatory monitoring was made technically possible by attaching the manometric sensors on the colon through the use of endoclips.[47] Prolonged colonic manometric recordings, that is, >24 hours, were made distal to the splenic flexure. The authors concluded that resting colonic motor activity, defined by the motility index, is significantly affected after spinal cord injury when compared to healthy subjects (8.3 ± 3.2 vs. 2.6 ± 0.6, $p < .01$).

It has been suggested in the literature that colonic motor dysfunction after spinal cord injury is impaired partly due to reduced postprandial colonic motor activity in these individuals.[48,49] However, it has been demonstrated that although significantly reduced as compared to healthy subjects, there is a significant increase in the motility index of those individuals with spinal cord injury after meal ingestion (2.6 ± 0.6 vs. 4.6 ± 0.7, $p < .01$). The interesting finding in this study is that there appears to be regional variation in the postprandial response of the colon. The increase in colonic motor activity after meals was seen only in the proximal descending colon (2.8 ± 0.8 vs. 5.8 ± 0.9, $p < .03$) and not in the distal descending colon (2.5 ± 0.8 vs. 3.2 ± 1.0, p = ns), or rectosigmoid. These observations may help reconcile previous findings including a significant delay of colonic transit in the rectosigmoid area and lack of postprandial increase in colonic motor activity, by demonstrating the importance of the location of the recording system with respect to the likelihood of detecting a gastrocolic response after spinal cord injury. The authors concluded that

prolonged transit time in persons with spinal cord injury may be explained by decreased colonic activity, colonic contractions, and intraluminal pressure. These findings may help to explain the difficulty with bowel evacuation after spinal cord injury, and relief from neurogenic bowel dysfunction should be directed toward modalities that increase colonic motility in general.

The imbalance between the sympathetic-parasympathetic systems resulting from spinal cord injury may lead to disturbances in normal colonic motility, but the specific pathophysiologic mechanism has not yet been defined. The enteric nervous system and the autonomic nervous system, in general, modulate colonic function. Parasympathetic stimulation results in increased colonic contractility, motility, and tone. Thus, it may be inferred that agents or devices that enhance parasympathetic tone (such as neuroprosthetic stimulation of the sacral nerves or pharmacologic interventions) may be important adjuncts in the management of neurogenic bowel dysfunction.

The incidence and prevalence of multiple sclerosis in the United States are estimated to be 3.2 per 100,000 persons and 58.3 per 100,000 persons, respectively.[50] The prevalence of gastrointestinal complaints in individuals afflicted with multiple sclerosis is high and is associated with neurogenic dysfunction of other organ systems.[51] Bowel symptoms are common; at least 52% of patients in one series had constipation, fecal incontinence, or both,[52] while other studies have shown that the prevalence of constipation varies from 2% to 20%.[53] As in individuals with spinal cord injury, neurogenic bowel dysfunction secondary to multiple sclerosis is a source of considerable psychosocial impairment.[54] Indeed, among individuals with multiple sclerosis, bladder and bowel symptoms were rated as the third most important factors, after spasticity and incoordination, associated with the limitations on their ability to work.[55]

Colonic transit time in individuals with multiple sclerosis was assessed by means of radiopaque markers and was found to be significantly delayed,[56] suggesting either a disturbance in decreased colonic motor activity or outlet dysfunction. Colonic compliance was found to be reduced in individuals with multiple sclerosis as colonometrograms demonstrated a more rapid pressure rise in the multiple sclerosis group than in the control group; likewise, the multiple sclerosis group failed to demonstrate the postprandial increase in colonic motor and myoelectrical activity that was observed in the control group.[57] The authors suggested that these findings may be features of visceral neuropathy in patients with multiple sclerosis and severe constipation.

Pelvic floor dysfunction has been demonstrated in individuals who have constipation and multiple sclerosis. Anorectal physiology testing of individuals with multiple sclerosis and constipation revealed that paradoxical puborectalis contraction is common among these individuals, and it was proposed that such is a feature of the disturbed voluntary sphincter control mechanism, analogous to detrusor sphincter dyssynergia in the bladder.[58] In addition to the physiologic abnormalities of the gastrointestinal tract that are reputed to be associated with multiple sclerosis, medications such as anticholinergics and muscle relaxants are possible contributors to constipation.[55] Bowel management in multiple sclerosis is challenging and is currently empirical, mainly because the underlying illness is progressively debilitating and is not reversible. Treatment of constipation is important, as a distended rectum may worsen bladder symptoms, and constipation may lead to increased limb spasticity.[51] Empiric recommendations are the starting point of therapy, which include maintaining a high-fiber diet, high fluid intake, and physical exercise.[55,59]

Gastrointestinal impairment, specifically constipation, in individuals with Parkinson's disease is common and prevalent,[60–64] occurring in as many as two thirds of the patients diagnosed with the disease.[65,66] In a study by Siddiqui et al[67] involving 68 patients diagnosed with Parkinson's disease, autonomic dysfunction was assessed by comparing gastrointestinal, urinary, sexual, cardiovascular, and thermoregulatory symptoms with a matched control group. The study found that patient's with Parkinson's disease experienced a higher frequency and severity of autonomic dysfunction, and that among the gastrointestinal symptoms that were assessed, patients reported decreased bowel movements as compared to controls (20.4% vs. 0%, $p < .02$).

The cause of the disturbances in gastrointestinal function after Parkinson's disease is uncertain.[59] The effect of antiparkinsonian medication as a possible etiology for gastrointestinal dysfunction in Parkinson's disease is largely overestimated, although it certainly has an influence

and should be adapted accordingly in patients with GI motility disorders; in particular, anticholinergic drugs should be avoided.[68] Recent evidence suggests that the gastrointestinal symptoms seen in Parkinson's disease are related to the Parkinson's disease process itself rather than to the medications.[59] The effects of the disease on skeletal muscles parallel the severity and duration of the dysfunction seen in the oropharynx, anorectum, and pelvic floor, and are thus implicated as possible etiologic factors for the morbidity.[60] Evidence suggests that neuropathologic abnormalities in the enteric nervous system analogous to those anomalies regarded as pathognomonic of the parkinsonian process in the central nervous system demonstrate parallel pathologic changes in a number of disease processes previously regarded as confined to the central and somatic nervous systems.[66] Depletion of dopamine-containing neurons in the central nervous system is a basic defect in Parkinson's disease.

Immunohistochemistry staining of myenteric and submucosal neurons for dopamine, tyrosine hydroxylase, and vasoactive intestinal polypeptide (VIP) in Parkinson's disease patients revealed that the number of dopaminergic myenteric neurons is significantly decreased. When compared with controls, patients with Parkinson's disease had a mean (in percentage) of 0.4 ± 0.2 vs. 6.9 ± 2.3 in controls. The authors have suggested that the identification of this defect of dopaminergic neurons in the enteric nervous system in Parkinson's disease may offer a plausible explanation for the disturbances in gastrointestinal function in these individuals.[69]

Patients with tethered cord syndrome, whether secondary to myelodysplasia, presacral mass, or sacral hemivertebrae, were found to have a higher prevalence of constipation and fecal and urinary incontinence. Untethering of the cord was performed in 18 patients, and none noted improvement in their bowel symptoms.[70]

Peripheral Nervous System

Gastrointestinal dysfunction, specifically slow-transit constipation, generally is a moderate to severe disorder, and more often than not is of unknown etiology. The involvement of the peripheral nervous system (somatic-sensory and autonomic nervous system) is implicated as a conceivable etiology of this dysfunction. Among the disorders of the peripheral nervous system that will be discussed are familial autonomic neuropathy, neurofibromatosis, and paraneoplastic and antineuronal visceral neuropathy.

Autonomic neuropathy can be familial in nature. In a cohort of patients who have slow-transit constipation of unknown etiology, quantitative sensory and autonomic tests revealed that there is evidence of small fiber neuropathy. There is also a high incidence of a positive family history, particularly a possible association with Hirschsprung's disease. The authors suggest investigation for possible genetic basis, and the exact mechanism of the disease remains unknown.[71]

Neurofibromatosis is a group of autosomal dominant diseases that occur in three principal forms: (1) hyperplasia of the submucosal and myenteric nerve plexuses and mucosal ganglioneuromatosis, which leads to disordered gut motility (discussed in the endocrine disorders); (2) gastrointestinal stromal tumors showing varying degrees of neural or smooth muscle differentiation; and (3) a distinctive glandular, somatostatin-rich carcinoid of the periampullary region of the duodenum that contains psammoma bodies.[72] Neurofibromatosis has been described as diffusely involving the entire gastrointestinal tract, which can lead to a disorder in gut motility manifesting as constipation, luminal obstruction, or intussusception.[73,74]

It has been reported that antineuronal antibodies were found in some patients with severe gut dysmotility of unknown etiology.[75] Postmortem analysis of the gastrointestinal tracts of individuals who had paraneoplastic visceral neuropathy is characterized by neuronal and axonal degeneration, lymphoplastic infiltration, and glial cell proliferation within the myenteric plexus. Often, these patients manifested with severe gastrointestinal dysfunction that included constipation, obstipation, and intestinal pseudo-obstruction.[76]

Connective Tissue Diseases

Connective tissue diseases are associated with a wide spectrum of disorders involving the gastrointestinal system. In a study by Trezza et al,[77] the impact of systemic sclerosis on bowel function was assessed by determining the frequency and severity of colorectal problems among patients with systemic sclerosis. Among 83

respondents (86%), 16% did not have a normal desire to defecate and 18% regularly needed digital stimulation or evacuation of the rectum. Among these respondents who complained of significant impairment associated with their systemic sclerosis, 20% reported that colorectal dysfunction caused some or a major restriction of social activities or their quality of life. The authors concluded that colorectal dysfunction is very common among patients with systemic sclerosis, and that this problem often leads to restriction of their social activities and significant impairment in their quality of life.

In a study that assessed gastrointestinal transit through the esophagus, stomach, and small and large intestine of patients with progressive systemic sclerosis, Wegener et al[78] noted differences in patients and controls. Using radiopaque markers, the authors found that in the subset of patients who complained of constipation, two of three had a whole-gut transit time outside the range of the control group, suggesting that in this disorder the complaint of constipation is associated with colonic motor dysfunction. In 1998 Weston et al[79] characterized gastrointestinal disturbances seen in a tertiary care referral center. A total of 62 patients, 45 of whom were women, with scleroderma (46 patients), mixed-connective tissue disease (eight patients), and polymyositis or dermatomyositis (eight patients) were included in the study. Among the gastrointestinal symptoms that were seen at the time of the patients' presentation, constipation was observed in 31% of the cohort. The authors likewise observed that there was a higher prevalence of constipation in those with more than 5 years of the diagnosis, and that there was a higher prevalence of pseudo-obstruction and small bowel dilatation or diverticulosis in patients with less than 5 years of the diagnosis.

Infiltrative Diseases

Infiltrative diseases, for example amyloidosis, of the colon as the etiology of constipation are typically rare. Amyloidosis refers to a group of disorders characterized by the extracellular accumulation of insoluble, fibrillar proteins (amyloid). In a case report in an elderly patient who presented with intestinal pseudo-obstruction and had a subsequent colectomy, immunohistochemical analysis of the resected transverse colon revealed massive deposits of amyloid proteins composed of lambda light chains in the interstitial, connective, perivascular tissue and muscula tunica, suggestive of a diagnosis of amyloidosis.[80] Common clinical features of amyloidosis include gastrointestinal disorders that often manifest as constipation.[81] In a cohort of women who were diagnosed with amyloidosis by detection of amyloid in subcutaneous fat tissue, 63% of these patients were found to have constipation, compared with 25% in the matched control group. In the same study, it was found that the prevalence of constipation was more common than the presence of proteinuria or renal insufficiency.[82] In a study that compared the clinical symptoms, specifically gastrointestinal disturbances of Swedish and Japanese patients with familial amyloidotic polyneuropathy, the authors reported that the initial gastrointestinal symptom in the majority of the Japanese patients is diarrhea, whereas in the Swedish patients the initial symptoms are commonly nausea, vomiting, and constipation.[83] However, at the final stages of the disease, patients are usually incapacitated, suffering from pronounced malabsorption, and death is usually caused by extreme malnutrition and infections.[84]

References

1. Drossman DA, Camilleri M, Mayer EA, Whitehead WE.AGA technical review on irritable bowel syndrome. Gastroenterology 2002;123:2108–2131.
2. Akehurst R, Kaltenthaler E. Treatment of irritable bowel syndrome: a review of randomised controlled trials. Gut 2001;48:272–282.
3. Jailwala J, Imperiale TF, Kroenke K. Pharmacologic treatment of the irritable bowel syndrome: a systematic review of randomized, controlled trials [comment]. Ann Intern Med 2000;133:136–147.
4. Camilleri M, Thompson WG, Fleshman JW, Pemberton JH. Clinical management of intractable constipation [comment]. Ann Intern Med 1994;121:520–528.
5. Dukas L, Willett WC, Giovannucci EL. Association between physical activity, fiber intake, and other lifestyle variables and constipation in a study of women. Am J Gastroenterol 2003;98:1790–1796.
6. Talley NJ. Pharmacologic therapy for the irritable bowel syndrome. Am J Gastroenterol 2003;98:750–758.
7. Peters HP, De Vries WR, Vanberge-Henegouwen GP, Akkermans LM. Potential benefits and hazards of physical activity and exercise on the gastrointestinal tract. Gut 2001;48:435–439.
8. Rao SS, Beaty J, Chamberlain M, Lambert PG, Gisolfi C. Effects of acute graded exercise on human colonic motility. Am J Physiol 1999;276(5 pt 1):G1221–1226.
9. Bi L, Triadafilopoulos G. Exercise and gastrointestinal function and disease: an evidence-based review of risks

and benefits. Clin Gastroenterol Hepatol 2003;1:345–355.
10. Everhart JE. A longitudinal survey of self-reported bowel habits in the United States. Dig Dis Sci 1989;34:1153–1162.
11. Cordain L, Latin RW, Behnke JJ. The effects of an aerobic running program on bowel transit time. J Sports Med Physical Fit 1986;26:101–104.
12. Meshkinpour H, Seold S, Movahedi H, Nami N, James N, Wilson A. Effects of regular exercise in management of chronic idiopathic constipation. Dig Dis Sci 1998;43:2379–2383.
13. Mearin F, Zarate N, Sardi A, Moreno-Osset E, Salis G. Traveler's constipation. Am J Gastroenterol 2003;98: 507–509.
14. Cheng C, Chan AO, Hui WM, Lam SK. Coping strategies, illness perception, anxiety and depression of patients with idiopathic constipation: a population-based study. Aliment Pharmacol Ther 2003;18:319–326.
15. Garvey M, Noyes R Jr, Yates W. Frequency of constipation in major depression: relationship to other clinical variables. Psychosomatics 1990;31:204–206.
16. Hadley SJ, Walsh BT. Gastrointestinal disturbances in anorexia nervosa and bulimia nervosa. Current Drug Targets CNS Neurol Disord 2003;2:1–9.
17. Haug TT, Mykletun A, Dahl AA. Are anxiety and depression related to gastrointestinal symptoms in the general population? Scand J Gastroenterol 2002;37:294–298.
18. Nehra V, Bruce BK, Rath-Harvey DM, Pemberton JH, Camilleri M. Psychological disorders in patients with evacuation disorders and constipation in a tertiary practice. Am J Gastroenterol 2000;95:1755–1758.
19. Becker AE. Eating disorders [comment]. N Engl J Med 1999;340:1092–1098.
20. Lembo A, Camilleri M. Chronic constipation. N Engl J Med 2003;349:1360–1368.
21. Schvarcz E, Palmer M, Ingberg CM, Aman J, Berne C. Increased prevalence of upper gastrointestinal symptoms in long-term type 1 diabetes mellitus. Diabet Med 1996;13:478–481.
22. Talley NJ, Young L, Bytzer P, Hammer J, Leemon M, Jones M, Horowitz M. Impact of chronic gastrointestinal symptoms in diabetes mellitus on health-related quality of life. Am J Gastroenterol 2001;96:71–76.
23. Feldman M, Schiller LR. Disorders of gastrointestinal motility associated with diabetes mellitus. Ann Intern Med 1983;98:378–384.
24. Maleki D, et al. Pilot study of pathophysiology of constipation among community diabetics. Dig Dis Sci 1998;43(11):2373–2378.
25. Deen KI, Seneviratne SL, de Silva HJ. Anorectal physiology and transit in patients with disorders of thyroid metabolism. J Gastroenterol Hepatol 1999;14(4):384–387.
26. Sharma S, et al. Colorectal manifestations of endocrine disease. Dis Colon Rectum 1995;38(3):318–323.
27. Wald A. Constipation, diarrhea, and symptomatic hemorrhoids during pregnancy. Gastroenterol Clin North Am 2003;32(1):309–322.
28. Wald A, et al. Effect of pregnancy on gastrointestinal transit. Dig Dis Sci 1982;27(11):1015–1018.
29. Munro KM. Ganglioneuromatosis of the sigmoid colon. Br J Surg 1971;58(5):350–352.
30. Short IA, Padfield PL. Malignant phaeochromocytoma with severe constipation and myocardial necrosis. Br Med J 1976;2(6039):793–794.
31. Lax E, et al. Neglected radiologic signs of the glucagonoma syndrome. Diagn Imaging Clin Med 1986;55(6):321–326.
32. Jones B, et al. Villous hypertrophy of the small bowel in a patient with glucagonoma. J Comput Assist Tomogr 1983;7(2):334–337.
33. Hansen MB. The enteric nervous system I: organisation and classification. Pharmacol Toxicol 2003;92(3):105–113.
34. Krogh K, Christensen P, Laurberg S. Colorectal symptoms in patients with neurological diseases. Acta Neurol Scand 2001;103(6):335–343.
35. Johanson JF, et al. Association of constipation with neurologic diseases. Dig Dis Sci 1992;37(2):179–186.
36. Robain G, et al. Incidence de la constipation dans une population de patients atteints d'hemiplegie vasculaire recente: etude prospective de 152 cas. Rev Neurol 2002;158(5 pt 1):589–592.
37. Collins JG. Vital and Health Statistics, series 10, no. 159. U.S. DOH 87–1587, 1999:10(159).
38. Stiens SA, Fajardo NR, Korsten MA. The gastrointestinal system after spinal cord injury. In: Lin VW, ed. Spinal Cord Medicine: Principles and Practice. New York: Demos Publishing, 2003:321–348.
39. Stiens SA, Bergman SB, Goetz LL. Neurogenic bowel dysfunction after spinal cord injury: clinical evaluation and rehabilitative management. Arch Phys Med Rehabil 1997;78(3 suppl):S86–102.
40. Stone JM, et al. Chronic gastrointestinal problems in spinal cord injury patients: a prospective analysis. Am J Gastroenterol 1990;85(9):1114–1119.
41. Sun WM, Read NW, Donnelly TC. Anorectal function in incontinent patients with cerebrospinal disease. Gastroenterology 1990;99(5):1372–1379.
42. Krogh K, et al. Colorectal function in patients with spinal cord lesions. Dis Colon Rectum 1997;40(10): 1233–1239.
43. Cameron KJ, et al. Assessment of the effect of increased dietary fibre intake on bowel function in patients with spinal cord injury. Spinal Cord 1996;34(5):277–283.
44. Nino-Murcia M, et al. Colonic transit in spinal cord-injured patients. Invest Radiol 1990;25(2):109–112.
45. Krogh K, et al. Colorectal transport during defecation in patients with lesions of the sacral spinal cord. Neurogastroenterol Motility 2003;15(1):25–31.
46. Fajardo NR, et al. Decreased colonic motility in persons with chronic spinal cord injury. Am J Gastroenterol 2003;98(1):128–134.
47. Fajardo N, Hussain K, Korsten MA. Prolonged ambulatory colonic manometric studies using endoclips [comment]. Gastrointest Endosco 2000;51(2):199–201.
48. Bruninga K, Camilleri M. Colonic motility and tone after spinal cord and cauda equina injury. Am J Gastroenterol 1997;92(5):891–894.
49. Glick ME, et al. Colonic dysfunction in patients with thoracic spinal cord injury. Gastroenterology 1984; 86(2):287–294.
50. Cooper GS, Stroehla BC. The epidemiology of autoimmune diseases. Autoimmun Rev 2003;2(3):119–125.
51. Hinds JP, Eidelman BH, Wald A. Prevalence of bowel dysfunction in multiple sclerosis. A population survey. Gastroenterology 1990;98(6):1538–1542.
52. Chia YW, et al. Prevalence of bowel dysfunction in patients with multiple sclerosis and bladder dysfunction. J Neurol 1995;242(2):105–108.

53. Heaton KW, et al. Defecation frequency and timing, and stool form in the general population: a prospective study. Gut 1992;33(6):818–824.
54. DasGupta R, Fowler CJ. Bladder, bowel and sexual dysfunction in multiple sclerosis: management strategies. Drugs 2003;63(2):153–166.
55. Wiesel PH, et al. Pathophysiology and management of bowel dysfunction in multiple sclerosis. Eur J Gastroenterol Hepatol 2001;13(4):441–448.
56. Nicoletti R, et al. Transito intestinale con marker radiopachi nei pazienti affetti da sclerosi multipla. Radiol Med 1992;83(4):428–430.
57. Glick ME, et al. Colonic dysfunction in multiple sclerosis. Gastroenterology 1982;83(5):1002–1007.
58. Chia YW, et al. Paradoxical puborectalis contraction is a feature of constipation in patients with multiple sclerosis. J Neurol Neurosurg Psychiatry 1996;60(1):31–35.
59. Stark ME. Challenging problems presenting as constipation. Am J Gastroenterol 1999;94(3):567–574.
60. Ashraf W, et al. Constipation in Parkinson's disease: objective assessment and response to psyllium. Mov Disord 1997;12(6):946–951.
61. Stocchi F, et al. Anorectal function in multiple system atrophy and Parkinson's disease. Mov Disord 2000;15(1):71–76.
62. Abbott RD, et al. Frequency of bowel movements and the future risk of Parkinson's disease [comment]. Neurology 2001;57(3):456–462.
63. Martignoni E, et al. Autonomic disorders in Parkinson's disease. J Neural Transm Suppl 1995;45:11–19.
64. Pfeiffer RF. Gastrointestinal dysfunction in Parkinson's disease. Clin Neurosci 1998;5(2):136–146.
65. Jost WH, Schimrigk K. Constipation in Parkinson's disease. Klin Wochensch 1991;69(20):906–909.
66. Quigley EM. Gastrointestinal dysfunction in Parkinson's disease. Semin Neurol 1996;16(3):245–250.
67. Siddiqui MF, et al. Autonomic dysfunction in Parkinson's disease: a comprehensive symptom survey. Parkinsonism Rel Disord 2002;8(4):277–284.
68. Jost WH. Gastrointestinal motility problems in patients with Parkinson's disease. Effects of antiparkinsonian treatment and guidelines for management. Drugs Aging 1997;10(4):249–258.
69. Singaram C, et al. Dopaminergic defect of enteric nervous system in Parkinson's disease patients with chronic constipation. Lancet 1995;346(8979):861–864.
70. Levitt MA, et al. The tethered spinal cord in patients with anorectal malformations. J Pediatr Surg 1997; 32(3):462–468.
71. Knowles CH, et al. Sensory and autonomic neuropathy in patients with idiopathic slow-transit constipation. Br J Surg 1999;86(1):54–60.
72. Cuthbert JA, Gallagher ND, Turtle JR. Colonic and oesophageal disturbance in a patient with multiple endocrine neoplasia, type 2b. Austr NZ J Med 1978;8(5):518–520.
73. Carney JA, et al. Alimentary-tract ganglioneuromatosis. A major component of the syndrome of multiple endocrine neoplasia, type 2b. N Engl J Med 1976; 295(23):1287–1291.
74. Fuller CE, Williams GT. Gastrointestinal manifestations of type 1 neurofibromatosis (von Recklinghausen's disease). Histopathology 1991;19(1):1–11.
75. Knowles CH, et al. A role for autoantibodies in some cases of acquired nonparaneoplastic gut dysmotility. Scand J Gastroenterology 2002;37(2):166–170.
76. Chinn JS, Schuffler MD. Paraneoplastic visceral neuropathy as a cause of severe gastrointestinal motor dysfunction. Gastroenterology 1988;95(5):1279–1286.
77. Trezza M, et al. Bowel problems in patients with systemic sclerosis. Scand J Gastroenterol 1999;34(4): 409–413.
78. Wegener M, et al. Gastrointestinal transit through esophagus, stomach, small and large intestine in patients with progressive systemic sclerosis. Dig Dis Sci 1994;39(10):2209–2215.
79. Weston S, et al. Clinical and upper gastrointestinal motility features in systemic sclerosis and related disorders. Am J Gastroenterol 1998;93(7):1085–1089.
80. Racanelli V, D'Amore FP. Localized AL amyloidosis of the colon and clinical features of intestinal obstruction. A case report. Ann Ital Med Interna 1999;14(1):58–60.
81. Battle WM, et al. Gastrointestinal-motility dysfunction in amyloidosis. N Engl J Med 1979;301(1):24–25.
82. El Mansoury TM, et al. Screening for amyloid in subcutaneous fat tissue of Egyptian patients with rheumatoid arthritis: clinical and laboratory characteristics. Ann Rheum Dis 2002;61(1):42–47.
83. Tashima K, et al. Gastrointestinal dysfunction in familial amyloidotic polyneuropathy (ATTR Val30Met)—comparison of Swedish and Japanese patients. Amyloid 1999;6(2):124–129.
84. Anan I, et al. Comparison of amyloid deposits and infiltration of enteric nervous system in the upper with those in the lower gastrointestinal tract in patients with familial amyloidotic polyneuropathy. Acta Neuropathol 2001;102(3):227–232.

5

Initial Evaluation of Constipation

J. Marcio N. Jorge

Constipation is a common and subjective symptom that can be related to a multitude of factors, including, dietary, psychological, cultural, anatomic, and functional aspects. In addition, constipation is still surrounded by misconceptions and taboos that hamper an objective evaluation and encourage self-medication that is not always innocuous to the patient.

The definition of constipation varies tremendously among both patients and physicians. When adults not seeking health care were asked to define constipation, their most frequent definitions included "straining" (52%), "hard stools" (44%), "infrequent stools" (32%), as well as terms such as "abdominal discomfort" and "sense of incomplete evacuation."[1] According to Ruben,[2] 62% of the general population believes that a daily bowel movement is a sign of good health; they may report constipation if they fail to achieve a daily bowel movement or even if they fail to achieve a bowel movement at their usual time each day. Definitions used by physicians include (1) unspecific self-reported symptoms,[3] (2) stool frequency of less than three bowel movements per week,[4] and (3) whole gut transit time of more than 68 hours.[5] Ultimately, the Rome criteria have been accepted as a comprehensive standardized definition for constipation[3,6]:

I. The presence of at least two of the following complaints, without the use of laxatives for at least 12 months:
   1. Straining during ≥25% of bowel movements
   2. Sensation of incomplete evacuation with ≥25% of bowel movements
   3. Hard or pellet-like stools with ≥25% of bowel movements
   4. Less than three bowel movements per week

II. Fewer than two stools per week on a regular basis.

These criteria fulfill the definition of constipation, even in the absence of any other symptom.

Constipation is a common symptom in both the general population and in medical practice. In the general population, the prevalence of constipation is reportedly in the range of 2% to 34%, depending on demographic factors, the sampling situation, and the definition used.[3] This symptom accounts for approximately 50% of the patient complaints at specialists' offices.[7,8] Fortunately, the majority of individuals who seek medical care for constipation do not have a life-threatening or disabling disorder, and the primary need is for symptom control.[9]

The prevalence of constipation is three times more common in women, and in most studies shows a marked increase after the age of 65.[1,10] Accordingly, in a longitudinal survey of the self-reported bowel habits of 14,407 adults in the United States, Everhart et al[11] reported that women were more likely than men to report constipation (20.8% vs. 8.0%, respectively) and infrequent defection (9.1% vs. 3.2%, respectively). In addition, older respondents reporting constipation were more likely to use laxatives or stool softeners than younger respondents. In a survey on 10,018 adults, Stewart et al[12] noted an overall prevalence of constipation of 14.7%. When analyzed by subtype, the prevalence was 4.6% for functional constipation, 2.1% for

irritable bowel syndrome, 4.6% for outlet obstruction, and 3.4% for the association of outlet obstruction and irritable bowel syndrome. Outlet obstruction alone or associated with irritable bowel syndrome was the most common subtype among women, with a female-to-male ratio of 2.27 : 1.65.

Constipation is a common and serious problem in women of childbearing age, although the reason for a female preponderance has yet to be explained.[13] It has been suggested that in females, steroid progesterone may decrease the levels of the polypeptide motilin, which may influence progression of food through the bowel.[14,15] Preston et al[16] reported elevated prolactin levels in young constipated women, although this finding has not been reproduced in other studies.[17] In addition, gynecologic surgery, particularly hysterectomy, has been associated with constipation.[18,19] The precise link between slow-transit constipation and hysterectomy remains obscure.[20] Possible factors include hormone variation, postoperative depression, and most probably damage to the pelvic parasympathetic and hypogastric nerves and the pelvic plexus during resection of the ligament of the uterus.[18] In fact, denervation hypersensitivity to the carbachol provocation test in the rectosigmoid has been demonstrated in some patients with severe constipation after hysterectomy, suggesting dysfunction in the autonomic innervation of the hindgut.[21] The association of urinary and sexual dysfunction in patients undergoing pelvic surgery seems to support this theory.[22,23] Other risk factors for constipation include inactivity, low calorie intake, low income, low education level, depression, and sexual abuse.[24–28]

History

To address the broad spectrum of symptoms involving constipation, an extensive questionnaire is recommended. Questioning must be specific and must emphasize the symptom the patient considers most distressing. The main complaint can be infrequent bowel movements, difficult evacuation (straining, hard stools, feeling of incomplete evacuation), symptoms suggesting irritable bowel syndrome (bloating, abdominal pain), or a combination of all these symptoms.

When constipation occurs later in life, the symptom may be of chronic or recent onset. Constipation of recent onset, specifically if less than 2 years, is frequently related to secondary causes, and exclusion of organic colonic and extracolonic disorders, including malignancy, is mandatory.[29] Conversely, this is a lifelong symptom in most patients who have constipation due to congenital disorders such as Hirschsprung's disease or meningocele. Typical clinical manifestations of obstructed evacuation include straining, tenesmus, and the sensation of incomplete evacuation as well as the frequent need for suppositories, enemas, or digitation. It is important to ask the patient which maneuver(s) are used to assist in defecation. Vaginal digitation suggests a rectocele, whereas massage lateral to the anus suggests poor rectal contractility. Patients with cul-de-sac hernias may report leaning forward on the toilet seat, suggesting that the patient is trying to tilt the enterocele forward off the rectum. In fact, patients with a sigmoidocele may report the need to press the lower abdominal quadrant in order to have a bowel movement.[30] One must remember that any organ pressing on the mechanoreceptors adjacent to the rectum may give the patient the perception of impending defecation. These patients frequently have a history of previous treatment for other anorectal conditions associated with straining such as rectocele, descending perineal syndrome, solitary rectal ulcer syndrome, rectoanal intussusception, or prolapse.

The Rome criteria are intended to provide a diagnostic standard of constipation but are not intended for evaluation purposes. Various scoring systems have been developed to uniformly assess the severity of constipation. The Wexner score is based on eight parameters: frequency of bowel movements, difficult or painful evacuation, completeness of evacuation, abdominal pain, time in minutes per attempt for evacuation, type of assistance (laxatives, digitation, or enema), number of unsuccessful attempts for evacuation per 24 hours, and duration (years) of constipation.[31] Based on the questionnaire, scores ranged from 0 to 30, with 0 indicating normal and 30 indicating severe constipation (Table 5.1). According to the authors' experience with 232 patients, the proposed scoring system correlated well with objective physiologic findings. Another proposed instrument consists of 12 items assigned to three subscales of symptoms: stool, rectal, and abdominal. The instrument has been shown to be internally consistent, reproducible, valid, responsive to change, and

Table 5.1. Wexner constipation scoring system (minimum score, 0; maximum score, 30)

Symptom	Score
Frequency of bowel movements	
1–2 times per 1–2 days	0
2 times per week	1
Once per week	2
Less than once per week	3
Less than once per month	4
Difficulty: pain evacuation effort	
Never	0
Rarely	1
Sometimes	2
Usually	3
Always	4
Completeness: feeling incomplete evacuation	
Never	0
Rarely	1
Sometimes	2
Usually	3
Always	4
Pain: abdominal pain	
Never	0
Rarely	1
Sometimes	2
Usually	3
Always	4
Time: minutes in lavatory per attempt	
Less than 5	0
5–10	1
>10–20	2
>20–30	3
>30	4
Assistance: type of assistance	
Without assistance	0
Stimulant laxatives	1
Digital assistance or enema	2
Failure: unsuccessful attempts for evacuation per 24 hours	
Never	0
1–3	1
>3–6	2
>6–9	3
>9	4
History: duration of constipation (yr)	
0	0
1–5	1
>5–10	2
>10–20	3
>20	4

From Agachan et al.[31]

therefore suitable to assess the effectiveness of treatment for constipation.[32] Another symptom scoring questionnaire was validated for chronic constipation by Knowles et al.[33] This questionnaire is composed of 11 questions, and in a study of 71 patients and 20 asymptomatic controls, a strong correlation was found with the Wexner score. Although at present in clinical practice symptom analysis does not adequately differentiate major pathophysiologic subgroups, at least two scoring systems have been developed to uniformly assess the severity of constipation.

In a study comparing symptoms with physiologic findings, Glia et al[34] evaluated 134 patients with symptom registration, anorectal manometry, electromyography, colonic transit time measurement, and defecography. In this study, three symptoms had an independent value for the diagnosis of slow-transit constipation: infrequent evacuation (≤2 stools per week), laxative dependence, and a history of lifelong constipation. Patients with pelvic floor dysfunction, compared to those with normal pelvic floor function, have a higher prevalence of backache and a lower prevalence of normal stool frequency, heartburn, and a history of anorectal surgery. These authors concluded that symptoms are good predictors of transit time but poor predictors of pelvic floor function in patients with constipation.

Koch et al[35] also addressed the issue of whether detailed symptom analysis would help to identify pathophysiologic subgroups in chronic constipation. These authors studied 190 patients with chronic constipation through symptom evaluation, transit time measurement, anorectal manometry, and defecography. They found that infrequent bowel movements alone have a low specificity for slow-transit constipation, and are of little value in the definition of chronic constipation. The symptom "necessity to strain," however, had a good sensitivity (94%) in the definition of chronic constipation. A sensation of obstruction and digital evacuation were relatively specific, but insensitive for disordered defecation. The authors concluded that symptoms of chronically constipated patients are not helpful to differentiate pathophysiologic subgroups of chronic constipation.

In a study of 108 constipated patients, Mertz et al[36] verified the existence of three symptom-based subgroups: slow transit, irritable bowel syndrome, and pelvic floor dysfunction. In addition, they assessed whether these subgroups corresponded to differences in colonic transit studies and anorectal sensorimotor function (anorectal manometry, electromyography, and rectal sensory testing). According to these authors, slow transit and irritable bowel syndrome symptoms correlated well with expected physiology. Conversely, pelvic floor dysfunction

symptoms and physiology did not correlate. These authors, however, did not include defecography in their study, which would probably have affected the final diagnostic rate.

In the assessment of constipation, it is imperative to ask if the patient has already experienced episodes of incontinence to gas or stool. Anal incontinence is frequently an underreported condition, and, in fact, many constipated patients have symptoms related to sphincter and pelvic muscle denervation due to chronic straining. In this situation, the questionnaire should also assess the frequency and type of incontinence and its effect on the patient's quality of life.[37]

Constipation is a major problem in the management of patients with spinal cord injury. The mechanisms involved include lack of a conscious urge to defecate, body immobilization, motor paralysis of abdominal and pelvic muscles, and possible motor alterations at the colon, rectum, and anus.[38,39] The loss of the reflex activity regulation of the anorectum from cerebral input results in fecal impaction and incontinence as the rectum spontaneously evacuates its contents after stimulation by distention.

Physical Examination

Physical examination must be thorough and complement the history in order to exclude systemic etiology. Evidence of systemic illness, including neurologic or muscular deterioration, and endocrine or metabolic disorders, should be sought. In addition, special attention should be directed to the abdominal and anorectal regions.

Abdomen

The abdominal examination may detect excessive stool or gaseous distention and the presence of surgical scars that are evidence of neoplasic or inflammatory bowel diseases. Palpation may reveal a soft mass in patients with a dilated rectosigmoid filled with stool, a tender mass in the left lower quadrant, suggestive of a diverticular disease, or a hard mass that is more characteristic of a neoplasm. Percussion can differentiate gaseous distention from ascites. Finally, auscultation may reveal hyperactive waves in patients with abdominal distention, which can be visualized in the relaxed patient and characteristic of partial bowel obstruction or hypoactive or absent ileal sounds.

Perineum and Anorectum

Both the lateral decubitus and prone jackknife positions are adquate for routine anorectal examination. Although the prone position allegedly provides wider exposure, the left lateral decubitus is a good alternative and better accepted by patients, particularly the elderly or those otherwise incapacitated. Occasionally, however, in order to reveal a rectal prolapse, it may be necessary to place the patient in a squatting position.

The anorectal examination should begin by inspection of the patient's undergarment and perineal skin for evidence of fecal soiling. Soiling may result from overflow incontinence associated with fecal impaction ("overflow or paradoxical fecal incontinence"), especially in elderly patients. This situation must be differentiated from true incontinence due to sphincter dysfunction and "humid anus" or pseudoincontinence, which is caused by hemorrhoidal prolapse, pruritus ani, perianal fistula, rectal mucosal prolapse, and anorectal venereal diseases, and should be excluded. Perineal examination will exclude anatomic causes of constipation such as tumors, stenosis, fissures, or an ectopic anus.

Increased perineal descent can also be estimated during physical examination by observing the perineum during the Valsalva maneuver with the patient in the left lateral position with the buttocks separated. A perineometer, an instrument consisting of a freely moving graduated cylinder within a steel frame positioned on the patient's ischial tuberosities, has also been used. Neither method is physiologically appropriate, as evaluation is undertaken with the patient in the lateral decubitus position and during feigned, rather than actual, expulsion of intrarectal contents.[40] Defecography criteria include perineal descent exceeding 3.0 cm during maximal push effort as compared to that measured at rest (increased dynamic perineal descent) and perineal descent exceeding 4.0 cm at rest (increased fixed perineal descent).[41]

The perineal descent syndrome is considered a component of a vicious cycle involving excessive and repeated straining, protrusion of the anterior rectal wall into the anal canal, a

sensation of incomplete evacuation, weakness of the pelvic floor musculature, more straining, and further pelvic floor weakness.[42] Excessive perineal descent is a physical sign indicative of pelvic floor weakness. However, it may merely represent one facet in a constellation of varied symptoms and findings. Patients with abnormally increased perineal descent may present with rectal prolapse, partial or major incontinence, obstructed evacuation, solitary rectal ulcer syndrome, or vague symptoms of incomplete evacuation or rectal pain. Potential surgical disorders such as large nonemptying rectocele, enterocele, or sigmoidocele may coexist.

During simulated defecation, the anal verge should be observed for any patulous opening or rectal prolapse. Patients with constipation may have signs of anal incontinence during physical examination due to progressive neural injury related to chronic straining or an associated neuromuscular lesion due to childbirth. Occasionally, fecal incontinence is suspected only during physical examination or even during physiologic testing. This may occur due to the patient's embarrassment and unwillingness to seek medical therapy or as a subclinical finding.

Cutaneous sensation around the anus may be absent in patients with neurogenic disorders and may also indicate the level and location of the lesion. An intact bilateral anal reflex, as tested by a light pinprick or scratch, demonstrates that innervation of the external sphincter mechanism is present. Fecal impaction is often noted in children and elderly individuals with symptoms of severe constipation and soiling (paradoxical fecal incontinence). Constipated patients often have hard stool in the rectal vault. Patients with Hirschsprung's disease usually have an empty contracted distal rectum.

The next step is gentle palpation with a well-lubricated gloved index finger to evaluate resting tone. The lower rounded edge of the internal anal sphincter can be palpated on physical examination at approximately 1.2 cm distal to the dentate line. The entire circumference of the anorectum should be palpated by gentle circumanal rotation of the examining finger to assess the integrity of the anorectal ring. This is a strong muscular ring that represents the upper end of the anal sphincter, more precisely the puborectalis, and the upper border of the internal anal sphincter around the anorectal junction. In patients with spine lesions, return of anal resting tone after digital examination is characteristically very slow. The groove between the internal and external anal sphincter (intersphincteric sulcus) can be visualized or easily palpated. Distinction between internal and external anal sphincter hypertonicity can be estimated by inducing relaxation, which can usually be accomplished by prolonging the examination while talking to the patient; hypertonicity is most likely due to striated muscle hyperactivity. Digital examination should include a full 360-degree sweep of the rectum, including the posterior presacral hollow and the pelvic sidewalls.

During dynamic palpation, the examiner should note both the increase in anal canal tone and the mobility of the posterior loop of the puborectal muscle during squeeze. To assess the presence of paradoxical puborectalis syndrome, the patient is asked to strain while the examiner's finger is kept in the rectum. Patients with paradoxical puborectalis syndrome will squeeze and some will have intermittent contractions, rather than the Valsalva maneuver. Although the physical examination may be suggestive of paradoxical puborectalis contraction of the external anal sphincter and puborectalis, the patient's embarrassment may cause a "paradoxical reaction" and the diagnosis is usually reached only after anorectal physiology investigation. Acute localized pain triggered by pulling or compressing the border of the puborectalis muscle is a feature of levator spasm syndrome.

The presence of a rectocele in females can be assessed during physical examination by curving the examining finger and pressing it against the anterior rectal wall until it appears in the vagina, on the other side of the perineal body (Fig. 5.1). This anterior herniation of the rectal wall is much more common than the posterior type, particularly in females in whom the rectovaginal septum is weakened by factors such as multiparity and traumatic vaginal delivery. Rectoceles are found in up to 70% of asymptomatic women; therefore, care must be taken to avoid overtreating this entity, whether found during physical examination or on videodefecography. The clinical history can be highly suspicious when patients describe the need either to press the posterior vaginal wall or to do rectal digitation to assist defecation. Rectoceles can be found in up to 45% of patients with emptying disorders

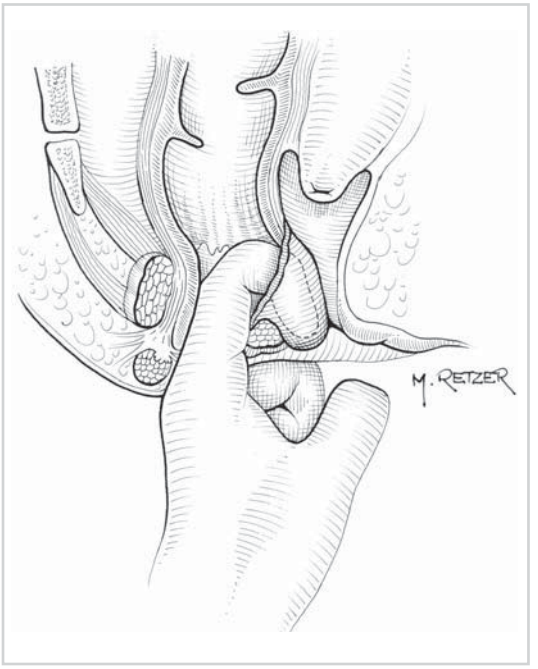


Figure 5.1. Rectocele. From University of Sao Paolo, Sao Paolo, Brazil.

due to nonrelaxing puborectalis syndrome.[43] This type of rectocele usually represents a compensatory mechanism due to the functional closure of the anal canal during attempted defecation and consequent high intrarectal pressure. This finding is of primary importance because, under these circumstances, surgical treatment of a rectocele will fail; instead, biofeedback should be indicated.

Rectal bulging as a result of an internal prolapse may present as a rectocele. Internal prolapse can be palpated by the examining finger as a descending mass during straining on digital examination. Intrarectal and rectoanal intussusception represent initial phases of rectal prolapse: a fold develops in the rectal wall during push, prolapsing into the rectum, and subsequently the intussusception descends to obstruct the anal canal, finally becoming an external prolapse. These findings must be interpreted in light of the patient's clinical history. More advanced degrees of intussusception can cause rectal pain or even lead to solitary rectal ulcer syndrome with elimination of blood or mucus through the rectum.

However, the differential diagnosis can often be made based solely on defecography, which can also determine the size of the rectocele. Moreover, by providing data on rectal emptying, defecography will allow differentiation of a secondary finding from a clinically relevant rectocele. An overt rectal prolapse or procidentia can be diagnosed by conducting the examination while the patient is straining on a commode.

A combined vaginal digital examination can be very helpful; with the patient in a standing position, the examiner's index finger is inserted into the rectum and the thumb is inserted into the vagina. During this examination the patient should be asked to strain. A peritoneal sac containing omentum or a loop of bowel dissecting the rectovaginal septum can be palpable between the thumb and the index finger, indicating the presence of a peritoneocele or enterocele (Fig. 5.2). This examination can be an effective method of distinguishing among enterocele, vaginal vault prolapse, rectocele, or a combination of these weakened conditions. Again, defecography is a crucial method of confirming these findings and evaluating their role in the dynamics of defecation. The cul-de-sac or pouch of Douglas can eventually extend caudally between the rectum and vagina in

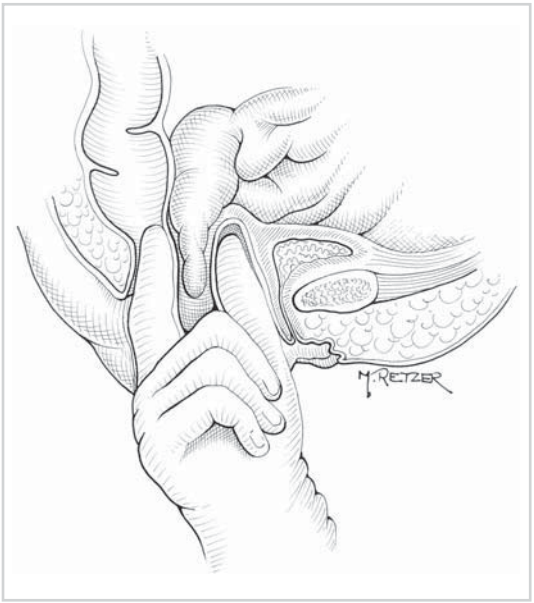


Figure 5.2. Cul-de-sac hernia. From University of Sao Paolo, Sao Paolo, Brazil.

varying degrees even as far as the perineum and become the site of a cul-de-sac or vaginal hernia. The hernia contents can include the omentum, small bowel, and occasionally an elongated loop of sigmoid.[44] Hernias are named according to their location, not their contents. Therefore, strictly speaking, the term *cul-de-sac hernia* is more appropriate than *enterocele* or *sigmoidocele*. However, this latter terminology seems more discriminative and has gained wide acceptance among both colorectal surgeons and gynecologists. Concomitant urogynecologic and colorectal dysfunctions are highly prevalent in a clinical practice. Therefore, it is incumbent upon the colorectal surgeon to develop a working relationship with other clinicians for a comprehensive approach.

Cul-de-sac hernias have been classified as primary when factors such as multiparity, advanced age, general lack of elasticity, obesity, constipation, or increased abdominal pressure are present, and secondary when enteroceles follow previous gynecologic procedures, especially vaginal hysterectomy. The incidence of enterocele at 1 year or more following vaginal hysterectomy ranges from 6% to 25%, although this can be significantly reduced by obliterating the cul-de-sac with suture of the uterosacral ligaments.[45]

Sigmoidocele and enterocele are generally part of a complex entity known as pelvic laxity or pelvic relaxation, which results from weakened supporting tissues of the vagina and pelvic diaphragm. Several defects may coexist including anterior rectocele, rectoanal intussusception or overt rectal prolapse, cystocele, and vaginal or uterine prolapse. Therefore, the clinical relevance of a sigmoidocele or enterocele in this complex syndrome is an important issue to be considered when planning the treatment of these disorders. Consequently, symptoms of pelvic discomfort, sensation of incomplete evacuation, and prolonged straining can be more severe in patients with sigmoidocele. Although more pronounced cul-de-sac hernias can be diagnosed during physical examination as a prolapse of the upper posterior vaginal wall during Valsalva's maneuver, more accurate assessment of this entity, especially sigmoidocele, became possible only after the advent of defecography.

Both anoscopy and proctosigmoidoscopy are useful to exclude anorectal diseases such as neoplasms, rectoanal intussusception, solitary rectal ulcer syndrome, and inflammatory bowel disease. Rigid proctosigmoidoscopy is a more accurate method of measuring the distance from the anal verge, but the average length reached is approximately 20 cm. Flexible sigmoidoscopy has a three to six times higher yield and is more comfortable for the patient. Solitary rectal ulcer syndrome is characterized by the triad of rectal discharge of blood and mucus, a lower anterior benign rectal ulcer, and disordered defecation. The nature of the ulcer is presumably traumatic due to excessive straining, and, in fact, defecography often demonstrates intussusception or paradoxical puborectalis syndrome in these patients.[46]

Rectal Biopsy

Rectal biopsy is required if Hirschsprung's disease is suspected, and less frequently, in the diagnosis of other systemic diseases such as amyloidoses. A full-thickness rectal biopsy confirms the presence or abscense of ganglionic cells in both Meissner's submubosal and Auerbach's myenteric plexi. Based on a recent histologic review of cadaveric disections, the normal distance of aganglionic bowel wall is 2 cm or less from the dentate line. Therefore, it is important that the biopsy be taken 2.5 to 3.0 cm cephalad to the dentate line to avoid the short aganglionic zone.[47]

Differential Diagnosis

Constipation is a disorder and not a disease. It may be secondary to several diseases, including colonic disease (stricture, cancer, anal fissure, proctitis), metabolic and endocrine disturbances (hypercalcemia, hypothyroidism, diabetes mellitus), neurologic disorders (Parkinson's disease, spinal cord lesions), or pharmacologic (antidepressive) (Table 5.2). Therefore, exclusion of both intestinal and systemic organic etiologies is an imperative step prior to referring the patient with functional symptoms to the physiology laboratory. Barium enema or colonoscopy is usually indicated and the primary pathology treated. Additional tests, dictated by the history and physical examination, may be necessary to exclude the above-named diseases.

Table 5.2. Etiology of constipation

- Poor habits
  - Low fiber diet
  - Inadequate fluid intake
  - Inadequate exercise
  - Ignoring call to stool
  - Situational factors (travel, illness)
- Intrinsic bowel disease
  - Mechanical obstruction
    - Neoplasm
    - Inflammation
    - Volvulus
    - Infection
    - Incarceration
    - Intussusception
    - Ischemia
  - Collagen vascular disease
    - Scleroderma
    - Amyloidosis
  - Anorectal disease
    - Anal stenosis
    - Fissure
    - Inflammation
- Pharmacologic agents
  - Antidepressants
    - Amoxapine
    - Bupropion
    - Clomipramine
    - Fluoxetine
    - Maprotiline
    - Mirtazepine
    - Paroxetine
    - Sertraline
    - Venlafaxine
  - Tranquilizers
    - Alprazolam
    - Clozapine
    - Olanzapine
    - Risperidone
  - Neurologic drugs
    - Bromocriptine
    - Felbamate
    - Pergolide
    - Valproic acid
  - Narcotics
    - Burtorphanol
    - Codeine
    - Fentanyl
    - Morphine
  - Nonsteroidal antiinflammatories
    - Diclofenac
    - Indomethacin
    - Nabumetone
    - Naproxen
    - Salicylates
    - Sulindac
  - Muscle relaxants and other analgesics
    - Baclofen
    - Carisoprodol
    - Tizanidine
    - Tramadol
  - Calcium channel blockers
    - Nifedipine
    - Verapamil
  - Antiarrhytmic drugs
    - Amiodarone
    - Flecainide
    - Mexiletine
    - Propafenone
  - Lipid-lowering agents
    - Cholestyramine
    - Colestipol
    - Lovastatin
    - Provachol
  - Antihypertensives
    - Diuretics
    - Acebutolol
    - Clonidine
    - Guanfacine
  - Antiplatelet
    - Anagrelide
  - Hematologic/oncologic drugs
    - Iron therapy
    - Carboplatin
    - Erythropoetin
    - Filgrastim
    - Vinblastine
  - Gastrointestinal drugs
    - Aluminum- and calcium-containing antacids
    - Mesalamine
    - Pancreatin
    - Sandostatin
  - Heavy metal intoxication
    - Arsenic
    - Lead
    - Mercury
    - Phosphorus
  - Miscellaneous agents
    - Barium sulfate
    - Thalidomide
    - Alendronate
    - Interferon-alfa-2b
    - Leuprolide
    - Levofloxacin
    - Ondansetron
    - Pamidronate
- Neurologic disorders
  - Cerebral
    - Parkinson's disease
    - Stroke
    - Tumor
  - Spinal
    - Cauda equina tumor
    - Meningocele
    - Spinal cord injury
    - Tabes dorsalis
    - Multiple sclerosis
    - Paraplegia
  - Peripheral
    - Chagas' disease
    - Hirschsprung's disease
    - Surgical disruption of nervi erigentes
    - Senna toxicity
    - Von Recklinghausen's disease
    - Autonomic plexus neuropathy
    - Multiple endocrine neoplasia II-B
    - Hypoganglionosis
- Endocrine causes
  - Hypothyroidism
  - Hypopituitarism
  - Diabetes mellitus
  - Pheochromocytoma
- Metabolic causes
  - Dehydration
  - Uremia
  - Hypercalcemia
  - Porphyria
  - Pregnancy
  - Hypokalemia

Plain Films

Plain abdominal films can be especially useful in patients complaining of acute abdominal pain and distention. In cases of large-bowel pseudo-obstruction, gaseous colonic distention can be massive, particularly in the cecum.

Barium Enema

Barium enema is generally not useful in the diagnosis of chronic constipation[48] and has been replaced by colonoscopy for the screening and evaluation of many diseases, including diverticular disease and colorectal cancer. However, it

does have the advantage of providing a permanent record for future evaluation regarding the size, length, and anatomic abnormalities of the colon. In this sense, barium enema is probably superior to colonoscopy. High-quality double-contrast technique and inclusion of lateral rectal views are essential in a good study.

A large dilated (megacolon) elongated or redundant (dolichocolon) colon is frequently found in patients with constipation (Figs. 5.3 and 5.4). In fact, based on studies using continuous colonic perfusion and a dye dilution technique, colonic volumes were approximately 50% greater in constipated patiensts, as compared to controls.[49] In clinical practice, however, megacolon and particularly dolichocolon have been found in healthy individuals; thus, these findings are not truly indicative of severity or of the need for surgery. Normal ranges for the width of the colon can vary considerably, but the upper normal limit of the rectosigmoid in a lateral view of the pelvic brim has been considered as 6.5 cm.[50] Therefore, barium or water-soluble enema is essential for the diagnosis of megacolon. Similarly, dolichocolon is somewhat

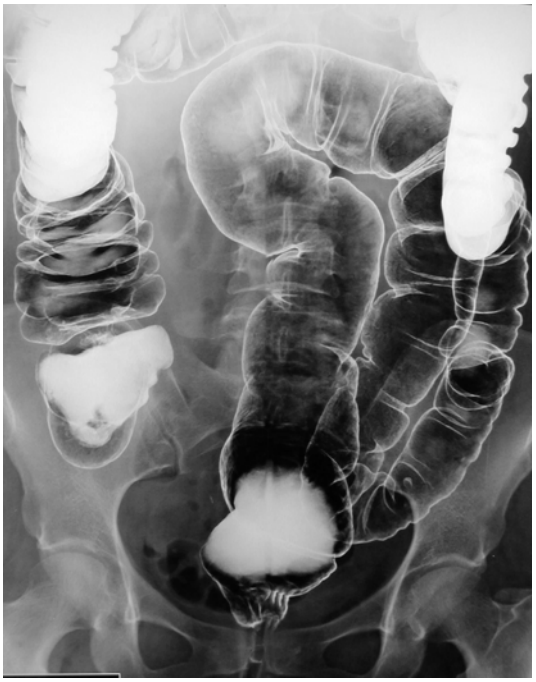


Figure 5.4. Megacolon.

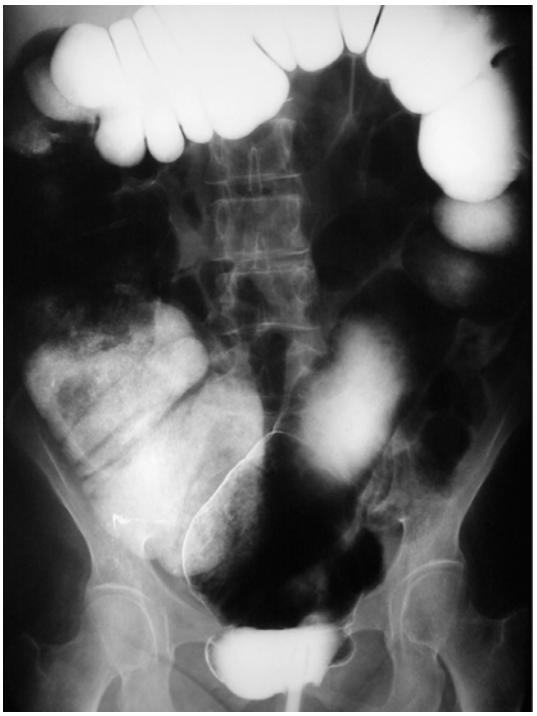


Figure 5.3. Dolichocolon.

poorly defined and has been considered as any case in which the enema-filled pelvic loop rises above a line drawn between the iliac crests.[51] This condition occurs in approximately 50% of patients with a history of constipation exceeding 10 years, compared with 2% in the control group. Patients with a shorter history of constipation fall between these two values.[52] Dolichocolon in constipation can be a reason for an incomplete colonoscopy.

Colonoscopy

Colonoscopy is a complementary study to a barium enema for exclusion of colonic pathology. Compared to barium enema, colonoscopy has a higher risk of complications and is more expensive, although both are probably comparable in the diagnosis of lesions associated with constipation.[53,54] In patients with anthraquinone laxative abuse, the rectal mucosa may present with characteristic aspects of melanosis coli, a brown-black spotty coloration due to deposits of lipofuscin in the lamina propria.

Initial Approach

Because the most common causes of constipation are related to misconceptions of normal bowel function and inadequate dietary habits, the initial approach should include careful assessment, reassurance, and simple guidance. Thus, the initial therapeutic schema should include the following:

1. Evaluation of the patient's expectation and concept of normal bowel frequency in order to understand the complaint and reassure the patient.
2. Dietary assessment (fiber supplementation, increased fluid intake, balanced meals). Meals should be balanced, taken at regular intervals, and contain generous portions of vegetables and fruits. Excessive ingestion of processed carbohydrates should be discouraged. In addition, omission of breakfast may contribute to abnormal bowel function due to inadequacy in elicitation of the gastrocolic reflex. Recommended empirical fiber therapy should include 20 to 40 g of dietary fiber or 10 to 20 g of crude fiber per day.[55,56] The most inexpensive cereal with the highest concentration of crude fiber is bran. Unprocessed bran, particularly coarser preparations, has high hydrophilic properties that soften the stool and increase its volume, stimulating peristalsis. In addition, an increase in daily fluid intake will increase the efficacy of a high-fiber diet.
3. Physical exercise is encouraged; a simple walk in the morning may be effective.
4. Attention to the call to stool. Environmental factors, such as work or school schedules, are often difficult to change, but patients should be advised that to neglect the call to stool will, through the mechanisms of rectal capacity and compliance, lead to fecal stasis.
5. Use of a diary of bowel habits to include frequency and consistency of stool and ease of defecation and association of symptoms. This diary is important because symptoms very often vary with time, and the severity of constipation may be related to associated events in the patient's life.[57]
6. Psychological evaluation, when indicated.[57,58]

This initial trial of empirical therapy is recommended, unless alarming symptoms such as rectal bleeding, abdominal distention, or weight loss are present.[55] These measures facilitate a more thorough evaluation of the severity of symptoms, and patients should be reevaluated through a diary of defecation and symptoms. Furthermore, symptoms may even improve, if they are dietary or psychologically related. If symptoms disappear altogether during this trial, no further evaluation is necessary and treatment should be maintained. If symptoms persist, patients should be referred to the physiology lab for investigation. Thus, patients referred for colorectal physiologic testing generally present with refractory and severe idiopathic symptoms.

Additional Evaluations

Patients with chronic refractory idiopathic constipation must be referred for investigation. The mechanisms responsible for both anal continence and defecation are complex and maintained by the interaction of multiple factors. These factors include stool consistency and delivery of colonic contents to the rectum, rectal capacity and compliance, anorectal sensation, anal sphincter mechanism function, and the pelvic floor muscles and nerves. To adequately evaluate these various aspects, a combination of physiologic studies is usually required, including colonic transit time study, anorectal manometry, defecography, electromyography (EMG), pudendal nerve latency, and small bowel transit study.[59,60] There is no single test that is pathognomonic; thus, final a diagnosis of functional disorders must be based on a collective interpretation of these studies.

According to Rantis et al,[61] the mean cost to investigate chronic constipation in the United States is $2752 (range, $1150 to $4792), including colonoscopy, barium enema, transit time study, defecography, EMG, and rectal biopsy. These authors pointed out that only 23% of patients benefited from this extensive diagnostic evaluation; therefore, the benefits of this assessment are unclear. However, most studies have shown that physiologic testing adds significant information, leading to a specific diagnosis in 50% to 75% of patients.[62–64] Furthermore, physiologic testing permits objective assessment and reliable posttherapeutic follow-up of subjective functional colorectal disorders.

Technical variants have been proposed in an attempt to enhance the diagnostic capability of

defecography, specifically to assist delineation of deep cul-de-sac pouches, enterocele, and sigmoidocele. In addition to the use of video-recording (videoproctography), systematic instillation of air, barium suspension and a substantial amount of barium paste, and oral ingestion of 150 mL of barium contrast 1 to 3 hours prior to the examination may assist in the delineation of pelvic small bowel loops.[65] More recently, intraperitoneal instillation of 50 mL of nonionic contrast has been proposed; despite the potential risk of complications, peritoneography combined with dynamic proctography can provide better assessment of pelvic floor disorders, particularly peritoneocele with or without enterocele.[66] The use of a tampon soaked in iodine contrast medium placed in the posterior fornix of the vagina either as an isolated method or combined with a voiding cystography (colpocystodefecography) also helps to assess the depth of the rectogenital fossa and the eventual interposition of intraabdominal content between the rectum and vagina.[65,67] More recently, by measuring the change in peritoneal–anal distance during evacuation, dynamic anorectal endosonography has been proposed to evaluate enterocele. However, further studies are needed to prove its sensitivity for screening of this disorder.[68] Dynamic pelvic resonance has also been proposed to investigate complex pelvic disorders, particularly in the diagnosis of cul-de-sac hernia and its contents.[69,70] A recent comparison by Matsuoka et al[71] of dynamic pelvic magnetic resonance and videoproctography in patients with constipation revealed that, despite a cost of approximately ten times more for dynamic pelvic resonance imaging than for videoproctography, no clinical changes were made. The routine application of dynamic pelvic resonance imaging is not supported, and further studies are warranted in order to establish its exact role.

The correlation between psychological factors and constipation is a well-known fact, both in clinical practice and in the literature.[57,58,72] Accordingly, the Minnesota Multiphasic Personality Inventory scores for the "neurotic triad" (hypochondria, depression, and hysteria) are significantly higher in patients with constipation when compared to those with anal incontinence and rectal pain.[73] Organic causes of constipation, however, must not be overlooked in psychiatric patients. When a psychiatric disorder is diagnosed in a patient with symptoms of constipation, the patient may have developed both simultaneously; the presence of chronic constipation may have affected the patient's behavior, or the psychiatric disorder precipitated fixation on bowel function symptoms.[74]

References

1. Sandler RS, Drossman DA. Bowel habits in young adults not seeking for health care. Dig Dis Sci 1987;32:841–845.
2. Ruben BD. Public perceptions of digestive health and disease. Survey findings and communications implications. Pract Gastroenterol 1986;10:35–42.
3. Whitehead WE, Chaussade S, Corazziari E, Kumar D. Report of an international workshop on management of constipation. Gastroenterology Int 1991;4:99–113.
4. Connell AM, Hilton C, Irvine G, Lennard-Jones JE, Misiewicz JJ. Variation of bowel habit in two population samples. BMJ 1965;2:1095–1099.
5. Metcalf AM, Phillips SF, Zinsmeister AR, MacCarty RL, Beart RW, Wolff BG. Simplified assessment of segmental colonic transit time. Gastroenterology 1987;92: 40–47.
6. Whitehead WE, Wald A, Diamant NE, Enck P, Pemberton JH, Rao SSC. Functional disorders of the anus and rectum. Gut 1999;45(suppl II):1155–1159.
7. American Gastroenterological Association medical position statement: guidelines on constipation. Gastroenterology 2000;119:1761–1768.
8. Sonnenberg A, Koch TR. Physician visits in the United States for constipation: 1958 to 1986. Dig Dis Sci 1989;34:606–611.
9. Stark ME. Challenging problems presenting as constipation. Am J Gastroenterol 1999;94:567–574.
10. Sonnenberg A, Koch TR. Epidemiology of constipation in the United States. Dis Colon Rectum 1989;32:1–8.
11. Everhart JE, Go VLW, Johanes RS, Fitzsimmons SC, Roth HP, White LR. A longitudinal survey of self-reported bowel habits in the United States. Dig Dis Sci 1989;34:1153–1162.
12. Stewart WF, Liberman, Sandler RS, et al. Epidemiology of constipation (EPOC) Study in the United States: relation of clinical subtypes to socioeconomic features. Am J Gastroenterol 1999;94:3530–3539.
13. Read NW, Timms JM, Barfield LJ, Donnelly TC, Bannister JJ. Impairment of defecation in young women with severe constipation. Gastroenterology 1986;90:53–60.
14. Bannister JJ, Timms JM, Barfield LJ, Donnelly TC, Read NW. Physiological studies in young women with chronic constipation. Int J Colorect Dis 1986;1:175–182.
15. Christofides ND, Ghatei MA, Bloom SR, Borberg C, Gillmer MDG. Decreased plasma motilin concentrations in pregnancy. Br Med J 1982;285:1453–1454.
16. Preston DM, Rees LH, Lennard Jones JE. Gynecological disorders and hyperprolcatinemia in chronic constipation. Gut 1983;24:A480.
17. Watier A, Devroede G, Duranceau A, et al. Constipation with colonic inertia. A manifestation of sistemic disease? Dig Dis Sci 1983;28:1025–1033.
18. Taylor T, Smith AN, Fulton PM. Effect of hysterectomy on bowel function. Br Med J 1989;299:300–301.

19. Roe AM, Bartolo DCC, Mortensen NJMcC. Slow transit constipation. Comparison between patients with or without previous hysterectomy. Dig Dis Sci 1988;33: 1159–1163.
20. Altman D, Zetterström J, López A, Pollack J, Nordenstam J, Mellgren A. Effect of hysterectomy on bowel function. Dis Colon Rectum 2004;47:502–509.
21. Smith NA, Varma JS, Binnie NR, Papachrysostomou M. Disordered colorectal motility in intractable constipation following hysterectomy. Br J Surg 1990;77:1361–1366.
22. Ferghaly AS, Hindmarsh JR, Worth PHL. Post-hysterectomy urethral dysfunction: evaluation and management. Br J Urol 1986;58:299–302.
23. Long DM, Bernstein WC. Sexual dysfunction as a complication of abdomino-perineal resection of the rectum in male: an anatomic and physiologic study. Dis Colon Rectum 1959;2:540–548.
24. Talley NJ, Fleming KC, Evans JM, et al. Constipation in an elderly community: a study of prevalence and potential risk factors. Am J Gastroenterol 1996;91:19–25.
25. Campbell AJ, Busby WJ, Horwarth CC. Factors associated with constipation in an elderly community: a study of prevalence abd potential risk factors. Am J Gastroenterol 1996;91:19–25.
26. Sandler RS, Jordan MC, Shelton BJ. Demographic and dietary determinants of constipation in the US population. Am J Public Health 1990;80:185–189.
27. Whitehead WE, Drinkwater D, CheskinLJ, Heller BR, Schuster MM. Constipation in the elderly living at home. Definition, prevalence, and relationship to lifestyle and health status. J Am Geriatr Soc 1989;37:423–429.
28. Leroi AM, Bernier C, Watier A, et al. Prevalence of sexual abuse among patients with functional disorders of the lower gastrointestinal tract. Int J Colorectal Dis 1995;10:200–206.
29. Kruis W, Thieme C, Weinzierl M, Schussles P, Holl J, Paulus W. A diagnosis score for irritable bowel syndrome. Its value in the exclusion of organic disease. Gastroenterology 1984;87:314.
30. Jorge JMN, Yang Y-K, Wexner SD. Incidence and clinical significance of sigmoidoceles as determined by a new classification system. Dis Colon Rectum 1994;37:1112–1127.
31. Agachan F, Chen T, Pfeifer J, Reissman P, Wexner SD. A constipation scoring system to simplify evaluation and management of constipated patients. Dis Colon Rectum 1996;39:681–685.
32. Frank L, Kleinman L, Farup C, Taylor L, Miner P Jr. Psychometric validation of a constipation symptom assessment questionnaire. Scand J Gastroenterol 1999; 34:870–877.
33. Knowles CH, Eccersley AJ, Scott SM, Walker SM, Reeves B, Luniss PJ. Linear discriminant analysis of symptoms in patients with chronic constipation: validation of a new scoring system (KESS). Dis Colon Rectum 2000; 43:1419–1426.
34. Glia A, Lindberg G, Nilsson LH, Mihocsa L, Åkerlund JE. Clinical value of symptom assessment in patients with constipation. Dis Colon Rectum 1999;42:1401–1410.
35. Koch A, Voderholzer WA, Klauser AG, Müller-Lissner S. Symptoms in chronic constipation. Dis Colon Rectum 1997;40:902–906.
36. Mertz H, Naliboff B, Mayer EA. Symptoms and physiology in severe chronic constipation. Am J Gastroenterol 1999;94:131–138.
37. Jorge JMN, Wexner SD. Etiology and management of fecal incontinence. Dis Colon Rectum 1993;36:77–97.
38. Longo WE, Ballantyne GH, Modlin IM. The colon, anorectum, and spinal cord patient. A review of the functional alterations of the denervated hindgut. Dis Colon Rectum 1989;32:261–267.
39. Menardo G, Bausano G, Corazziari E, et al. Large-bowel transit in praplegic patients. Dis Colon Rectum 1987; 30:924–928.
40. Parks AG, Porter NH, Hardcastle J. The syndrome of the descending perineum. Proc R Soc Med 1966;59:477–482.
41. Jorge JMN, Wexner SD, Ehrenpreis ED, Noqueras JJ, Jagelman DG. Does perineal descent correlate with pudendal neuropathy? Dis Colon Rectum 1993;36: 475–483.
42. Porter NH. A physiological study of the pelvic floor in rectal prolapse. Ann R Coll Surg 1962;31:379–404.
43. Johansson C, Nilsson BY, Holmstrom B, Dolk A, Mellgren A. Association between rectocele and paradoxical sphincter response. Dis Colon Rectum 1992;35: 503–509.
44. Walldén L. Defecation block in cases of deep rectogenital pouch. A surgical, roentgenological and embryological study with special reference to morphological conditions. Acta Chir Scand 1952;165:1–122.
45. Hawksworth W, Roux JP. Vaginal hysterectomy. J Obstet Gynecol 1958;63:214–228.
46. Kerremans R. Radio-cinematographic examination of the rectum and the anal canal in cases of rectal constipation. A radio-cinematographic and physical explanation of dyschezia. Acta Gastroenterol Belg 1968;31: 561–570.
47. Ricciardi R, Counihan TC, Banner BF, Sweeney WB. What is the normal aganglionic segment of anorectum in adults? Dis Colon Rectum 1999;42:380–382.
48. Patriquin H, Martelli H, Devroede G. Barium enema in chronic constipation: is it meaningful? Gastroenterology 1978;75:619–622.
49. Devroede G, Soffié M. Colonic absorption in idopathic constipation. Gastroenterology 1973;64:552–561.
50. Preston DM, Lennard-Jones JE, Thomas BM. Towards a radiological definition of idiopathic megacolon. Gastrointest Radiol 1985;10:167–169.
51. Kantor JL. Anomalies of the colon: their roentgen diagnosis and clinical significance. Radiology 1934;23: 651–662.
52. Brummer P, Seppälä P, Wegelius U. Redundant colon as a cause of constipation. Gut 1962;3:140–141.
53. Beck DE. Initial evaluation in constipation. In: Wexner SD, Bartolo DCC, eds. Constipation: Etiology, Evaluation and Management. Oxford: Butterworth-Heinemann, 1995:31–38.
54. Wexner SD, Jagelman DG. Chronic constipation. Postgrad Adv Colorect Surg 1989;1:1–22.
55. Schiller LR. Review article: the therapy of constipation. Aliment Pharmacol Ther 2001;15:749–763.
56. Devroede G. Constipation. In: Sleisenger MH, Fordtran JS, eds. Gastroeintestinal Disease: Pathophysiology, Diagnosis and Treatment. Philadelphia: WB Saunders, 1989:331–368.
57. Devroede G, Girard G, Bouchoucha M, et al. Idiopathic constipation by colonic dysfunction: relationship with personality and anxiety. Dig Dis Sci 1989;34:1428–1433.

58. Fisher SE, Breckon K, Andrews HÁ, Keighley MRB. Psychiatric screening for patients with faecal incontinence or chronic constipation referred for surgical treatment. Br J Surg 1989;76:352–355.
59. Jorge JMN, Wexner SD. A practical guide to basic anorectal physiology. Contemp Surg 1993;43:214–214.
60. Jorge JMN, Wexner SD. Physiologic evaluation. In: Wexner SD, Vernava AM, eds. Clinical Decision Making in Colorectal Surgery. New York: Igaku-Shoin, 1995: 11–22.
61. Rantis PC Jr, Vernava AM 3rd, Daniel GL, Longo WE. Chronic constipation—is the work-up worth the cost? Dis Colon Rectum 1997;40:280–286.
62. Halverson AL, Orkin BA. Which physiologic tests are useful in patients with constipation? Dis Colon Rectum 1998;41:735–739.
63. Glia A, Lindberg G, Nilsson LH, Minocsa L, Åkerlund JE. Constipation assessed on the basis of colorectal physiology. Scand J Gastroenterol 1998;33:1273–1279.
64. Wexner SD, Jorge JMN. Colorectal physiological tests: use or abuse of technology? Eur J Surg 1994;160: 167–174.
65. Finlay IG, Bartolo DCC, Bartram CI, et al. Symposium: proctography. Int J Colorectal Dis 1988;3:67–89.
66. Bremmer S, Ahlbäck S-O, Udén R, Mellgren A. Simultaneous defecography and peritoneography in defecation disorders. Dis Colon Rectum 1995;38:969–973.
67. Hock D, Lombard R, Jehaes C, et al. Colpocystodefecography. Dis Colon Rectum 1993;36:1015–1021.
68. Karaus M, Neuhaus P, Wiedenmann B. Diagnosis of enteroceles by dynamic anorectal endosonography. Dis Colon Rectum 2000;43:1683–1688.
69. Lienemann A, Anthuber C, Baron A, Reiser M. Diagnosing enteroceles using dynamic magnetic resonance imaging. Dis Colon Rectum 2000;43:205–213.
70. Rentsch M, Paetzel Ch, Lenhart M, Feuerbach S, Jauch KW, Fürst A. Dynamic magnetic resonance imaging defecography: a diagnostic alternative in the assessment of pelvic disorders in proctology. Dis Colon Rectum 2001;44:999–1007.
71. Matsuoka H, Wexner SD, Desai MB, et al. A comparison between dynamic pelvic resonance imaging and videoproctography in patients with constipation. Dis Colon Rectum 2001;44:571–576.
72. Kamm MA. Role of surgical treatment in patients with severe constipation. Ann Med 1990;22:435–444.
73. Heymen S, Wexner SD, Gulledge AD. MMPI assessment of patients with functional bowel disorders. Dis Colon Rectum 1993;36:593–596.
74. Creed F, Guthrie E. Psychological factors in the irritable bowel syndrome. Gut 1987;28:1307–1318.

6

Constipation-Predominant Irritable Bowel Syndrome

Eli D. Ehrenpreis

Diagnosis and Definition

Irritable bowel syndrome (IBS) is a common chronic intestinal disorder characterized by abdominal discomfort and altered bowel habits. These symptoms occur in the absence of "structural or biochemical abnormalities."[1] It is estimated that up to 20% of the population of the United States has symptoms suggestive of IBS.[2] Multiple comorbidities, the high cost of medical utilization, and diminished productivity and quality of life all may be found in association with IBS.[3] Despite extensive research, there is no specific test that can diagnose this condition. In clinical practice, a diagnosis of IBS is accomplished after performing a careful medical history, including a system assessment using established diagnostic criteria, a complete physical examination, and limited laboratory testing.[4] A flexible sigmoidoscopy or colonoscopy is often suggested; the choice of these evaluations depends on the age and risk factors of the individual patient. The clinician must carefully assess the patient for any signs and symptoms of organic disease. So-called red flags or findings suggestive of an alternative diagnosis include the presence of fever, anemia, age greater than 50 years at symptom onset, severe diarrhea associated with dehydration, rectal bleeding, symptoms that awaken the patient, and a family history of colon cancer or inflammatory bowel disease. Laboratory findings including anemia, elevated C-reactive protein, thyroid-stimulating hormone (TSH) abnormalities, electrolyte disturbances, or hypoalbuminemia should prompt other evaluations, as they are not features of IBS.[3,4] Once organic disorders have been eliminated from the differential diagnosis, established diagnostic criteria assist with the diagnosis of IBS. The most recent of these parameters, the Rome II criteria (Table 6.1), resulted from the consensus of an expert working team in 1998.[1] When used in clinical practice, diagnostic criteria for IBS have been determined to be accurate and reproducible in these patients. The use of diagnostic criteria for IBS accomplishes several important goals. Accurate diagnosis assists in limiting the excessive use of testing and even abdominal surgery, to which these patients are often subjected.[4] A secure diagnosis of IBS is beneficial to the physician–patient relationship by providing patients with reassurance that potentially life-threatening organic disorders are not the cause of their symptoms.

These criteria may also help the clinician, working with the patient, to establish appropriate parameters to evaluate the effects of various treatments. Finally, the consistent use of diagnostic criteria such as Rome II is required for evidence-based clinical trials designed to investigate the epidemiology, pathophysiology, and treatments of IBS.[2–4]

Clinicians and researchers have also found it useful to subclassify patients with IBS. The major subclasses of IBS are the constipation-predominant, diarrhea-predominant, and alternating diarrhea and constipation forms of the condition.[1] Although some authors have questioned the usefulness and durability of this subclassification system since many patients will ultimately have alternating symptoms[5], management strategies for the various subgroups are quite different. The Rome II group has also established diagnostic criteria for functional constipation, including the passage of fewer than three stools per week, frequent straining, incomplete evacuation,

Table 6.1. Rome II criteria for irritable bowel syndrome (IBS) diagnosis*

Abdominal discomfort or pain for 12 weeks or more (consecutive or nonconsecutive) with at least two of these features:
- Relieved with defecation
- Onset associated with a change of stool frequency
- Onset associated with a change in stool form

* In the absence of structural or metabolic abnormalities to explain the symptoms.

passage of hard or lumpy stools, symptoms resembling anorectal blockage, and the use of manual maneuvers to assist with evacuation.[1] When these defining factors for functional constipation are combined with Rome II criteria for IBS, specific criteria for constipation predominant IBS are also established (Table 6.2).

Data related to the epidemiology, pathophysiology, and comorbidities of IBS are best discussed in general terms, as is the approach in the following discussion. This chapter focuses specifically on constipation-predominant IBS. A description of pharmacotherapy for IBS will be restricted to the specific subgroup of patients with constipation-predominant IBS.

Epidemiology and Health Care Costs

Although approximately one in six residents of the United States has symptoms suggestive of IBS, the majority of these symptomatic individuals do not seek medical attention.[6] Furthermore, in the United States, IBS occurs twice as often in women than in men. However, four times as many American females with symptoms of IBS consult a physician for medical care.[7] The converse appears to be true in countries such as India and Sri Lanka, where less than one third of patients with IBS are female.[3]

Of additional interest, one in eight visits to family practitioners involves management of IBS, and IBS patients comprise up to 50% of consultations to specialty gastroenterology practices.[8] The overall prevalence of IBS appears to be similar in Caucasian and African-Americans, but U.S. residents of Hispanic background are less likely to consult physicians for symptoms of IBS than are their Caucasian counterparts.[9] Familial aggregation has also been described in IBS.[10] Patients with IBS, particularly those with severe symptoms of the condition, are frequent seekers of medical care, creating a large burden on the medical system. For example, patients with IBS symptoms have an increased number of other health complaints, compared to patients without IBS. These complaints result in increased overall health care utilization and more physician visits for IBS patients. When translated into actual terms, an estimated 3.5 million physician visits per year in the United States occur for symptoms of IBS, and more than 2 million drug prescriptions are written annually for this condition.[4]

Irritable bowel syndrome patients have more than 10 times as many overall physician visits for gastrointestinal complaints compared to the general population and more than twice the overall number of visits to physicians for nongastrointestinal complaints. It has been estimated that the annual health care costs (including both direct and indirect costs) attributed to IBS in the United States amount to more than $20 billion per year. Patients with IBS in health maintenance organizations are responsible for $1000 more in health care costs annually when compared to other patients.[2,4]

Patients with IBS are frequently off from work; one study reported 13.4 days compared to the average 4.9 days per year.[6] Additionally, IBS is a cause of discontinuing work in a significant number of patients, particularly those with severe symptoms. Quality-of-life studies have been performed comparing patients with IBS to patients with organic diseases such as diabetes and psychiatric disorders, including major depression. These studies have demonstrated that scores for physical functioning in patients with IBS closely resemble diminished scores

Table 6.2. Rome II criteria for functional constipation*

At least 12 weeks (consecutive or nonconsecutive) in the preceding 12 months of two or more of the following:
- Straining for more than 25% of defecations
- Lumpy or hard stools for more than 25% of defecations
- Sensation of incomplete evacuations in more than 25% of defecations
- Sensation of anorectal blockage or blockage in more than 25% of defecations
- Manual maneuvers to facilitate more than 25% of defections (including digital evacuation, support of the pelvic floor, etc).
- Fewer than three defections per week

* In the absolute definition of functional constipation, no loose stools are present and the patient has insufficient criteria for IBS.

seen in patients with chronic medical disorders.[11,12] However, lower quality-of-life scores for social and mental function are consistently seen in IBS, resembling patients with decreased quality-of-life scores reported by individuals suffering from depression.[13]

Pathophysiology

Since its description more than 150 years ago, clinicians and scientists have been puzzled over the cause(s) of IBS. Current basic and clinical research studies have suggested that this syndrome is a disorder associated with physiologic alterations of several organ systems including the gut, spinal cord, and brain;[14] altered signaling among these systems fuels and perpetuates the condition. Just as the gastrointestinal tract sends signals to the brain in response to a variety of local stimuli, sensory input to the brain affects the function of the gut. Integrated signaling occurs between the gut and brain; these connected activities are influenced by a variety of factors. Increased intestinal motility and mucosal hyperemia induced by stressful or painful experiences is an example of alteration of gut function induced by the brain and spinal cord.[15] Examples of altered central nervous system functioning as a response to gastrointestinal stimuli seen in IBS include changes in the processing of painful and noxious gut stimuli in the brain, as described below.

Psychological disturbances and past experiences of physical or sexual abuse are risk factors for IBS.[1–3] Abnormal integration of the intestinal sensory, motor, and autonomic systems, coupled with the appropriate psychological milieu, ultimately may produce functional-type gut disorders. Neural connections from the brain to the gut allow extrinsic information (including visual, olfactory, and auditory stimulation) and cognitive stimuli such as emotional responses, to subsequently interact with the intestinal nervous system. Neurotransmitters are involved in all of the aforementioned neuronal activities.

When aberrant actions are present in these systems, patients develop symptomatic gut dysfunction as shown in Figure 6.1. The most consistently demonstrated abnormality in patients with IBS is the presence of visceral hyperalgesia. Patients with IBS exhibit a markedly decreased threshold for the sensation of painful stimuli in the gut when compared to controls.[16]

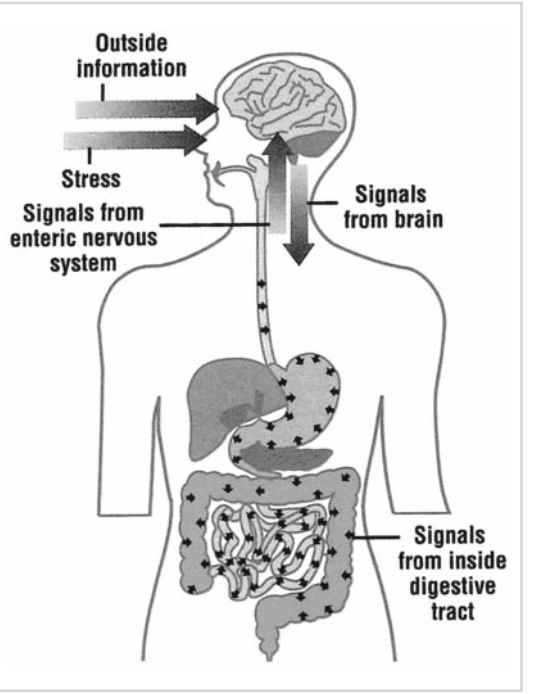


Figure 6.1. The brain–gut connection. Ehrenpreis ED, Burns EA, Hoffman C. *The AFP guide to diagnosis and treatment of the irritable bowel syndrome.* Copyrighted and published by Family Practice Education Network, Illinois Academy of Family Physicians, Lisle, Illinois, 2003.

The most commonly utilized method for demonstrating intestinal hypersensitivity involves the analysis of symptoms produced by the inflation of balloons within the rectosigmoid colon. Multiple research trials have demonstrated that patients with IBS experience discomfort after inflation of smaller volumes of fluid or air into the rectosigmoid colon than do controls.[16,17] In fact, the threshold for the initial sensation of discomfort seen at low volumes as well as the development of rectosigmoid pain with larger balloon volumes are both much lower in individuals with IBS compared to normal controls. These types of studies appear to establish the presence of a specific defect of the sensory portion of the enteric nervous system in patients with IBS.[4,17,18] Further studies have demonstrated that this rectosigmoid hypersensitivity may also reflect abnormalities in specific portions of the brain that are involved in the regulation of painful stimuli. For example, studies comparing normal individuals with IBS patients using rectosigmoid balloon inflation performed with simultaneous positron emission tomography (PET) scanning have shown that the

anterior cingulate gyrus, a portion of the brain normally involved in the downregulation of noxious stimuli, has decreased activity in IBS patients.[19] Of interest, repeated distention of the rectosigmoid colon results in stimulation of prefrontal cortex in IBS patients but not in normal volunteers. The prefrontal cortex is responsible for anticipation of unpleasant stimuli.[3,19] These data suggest that IBS patients have altered brain function, characterized by enhanced anticipation of unpleasant gastrointestinal stimuli coupled with an inability to downregulate unpleasant sensations produced by these stimuli. These findings validate the concept that complex alterations in the brain–gut axis play an important role in symptoms experienced by patients with IBS.[2–4]

Several studies have demonstrated that IBS may occur as a late consequence of gastrointestinal infection, including traveler's diarrhea and acute bacterial gastroenteritis.[20–24] One study has shown that the likelihood of developing IBS after an intestinal bacterial infection was approximately 10 times higher than that of the general population.[20] Histologic changes, such as the heightened presence of chronic inflammatory cells in the lamina propria, have been demonstrated after a colonic bacterial infection.[22] Alteration of local immune function of the gastrointestinal tract following bacterial infections have also been demonstrated.[23,24]

Gut dysfunction, including rectosigmoid hypersensitivity and increased intestinal motility, occur for at least 6 months in all individuals after a bacterial gastroenteritis.[22] However, only a small percentage (for example, 5% of individuals having a salmonella gastroenteritis) will develop the chronic symptoms of IBS by actually experiencing the sensation of altered gut function.[21] The appropriate psychological milieu, including anxiety or stress, or a history of childhood trauma, appears to be characteristic of developing IBS.

Psychosocial factors are clearly important in the development of IBS. One study has demonstrated that approximately 50% of individuals with IBS meet the criteria for psychiatric diagnoses,[25] compared to less than 20% of patients without IBS. Anxiety, depression, and somatization disorders are the most common psychiatric diagnoses in individuals with IBS. Patients who have symptoms of IBS and psychosocial disturbances are more likely to complain of abdominal pain and to seek medical therapy.[4] Unfortunately, increased seemingly unnecessary abdominal surgeries are also seen in these patients. Insightful studies by Drossman et al[26] have demonstrated that a significant number of women with functional gut disorders report a history of physical or sexual abuse.

Clinical experience suggests that mild-to-moderate gut dysfunction in IBS occurs primarily from disturbances in both gut and brain biology, while psychosocial abnormalities predominate in patients with the most severe forms of IBS.[4]

Serotonin and the Gastrointestinal Tract

Serotonin (5-hydroxytryptamine, 5-HT) functions as both a neurotransmitter as well as a paracrine chemical in the bowel. Serotonin is found throughout the gastrointestinal tract and resides within enterochromafin cells. It is also found within nerve fibers in the enteric nervous system. Enterochromafin cells within the gut are responsible for the production of more than 95% of the body stores of serotonin.[27] The remainder of serotonin is located within the brain and spinal cord. There are three subtypes of serotonin receptors found within the gastrointestinal tract: 5-HT1, 5-HT3, and 5-HT4. Increased serotonin concentration in the serum and mucosa has been demonstrated in women with diarrhea-predominant IBS.[28] The direct affect of the application of serotonin to the intestine increases intestinal motility and secretion; therefore, this neurotransmitter has attracted a great deal of attention as a putative mediator of the symptoms of IBS. Additionally, laboratory studies and clinical trials have shown that alteration of serotonin receptors with various pharmacologic agents have a direct effect on visceral sensation.[3] It is with this background that modulators of intestinal serotonin receptors have been employed for the development of new treatments for IBS. Additional research is being directed toward the development of medications that will affect peripheral nerve terminal receptors of visceral afferent neurons, such as opioid receptors, ion channels, neuroreceptors within the spinal cord such as opioid, glutamate, calcitonin gene–related peptide, and natural killer cell 1 (NK-1), as well as receptors within the brainstem and prefrontal cortex, including dopamine, acetylcholine, and epinephrine.[29]

Management

As previously mentioned, a large number of patients with symptoms of IBS do not report these symptoms to their physicians. Moreover, some symptomatic patients who visit a physician do not require specific therapy but rather derive a great deal of benefit from explanation of their diagnoses and factors that worsen IBS, including stress and possibly dietary factors. A stepwise approach, beginning with the establishment of a trusting physician–patient relationship is required for effective management of IBS.[3] A summary of this approach is shown in Table 6.3.

The health care provider should reassure patients with IBS that their condition will not degenerate into other life-threatening disorders, that it most likely represents a physiologic abnormality involving the intestinal motor and sensory system, and that IBS can correlate with psychosocial disorders that require treatment when present. At this point, determining the severity of the condition may help with planning future therapeutic regimens. For example, the majority of patients with severe excruciating abdominal pain and symptoms that adversely affect the overall quality of life should be investigated for a history of physical or sexual abuse or the presence of the aforementioned psychiatric disorders.[4] Early involvement in psychological or psychiatric care may be highly beneficial in these patients. If a physiologic disturbance of the gastrointestinal tract appears to predominate, utilization of pharmacotherapy is justified and may be highly beneficial.

After the diagnosis of IBS has been made, symptomatic improvement may be achieved using dietary modification. One study has shown that 48% of patients with IBS benefit from the elimination diet, with the gradual reintroduction of foods that do not cause additional symptoms.[30]

Table 6.3. Stepwise approach for the treatment of patients with IBS

Establish physician–patient relationship
Reassurance
Education
Lifestyle modifications
Stress management
Dietary changes
Healthy habits, exercise
Pharmacotherapy
Psychological/behavioral therapy

Elimination of lactose is recommended, as up to 60% of the population in the United States has lactose intolerance and these symptoms can mimic IBS.[31] Both caffeinated and decaffeinated coffee have been demonstrated to stimulate motor activity of the rectosigmoid colon in normal volunteers.[32] Sorbitol, a sugar alcohol that is a common ingredient of sugar-free candies, medicines, and antacids, may produce bloating, diarrhea, and gas, mimicking IBS. Establishment of exercise and stress management routines is often also recommended. A method for determining whether life stresses, dietary components, and other psychosocial factors exacerbate IBS symptoms involves the use of a symptom diary for 2 to 6 weeks. This may be used to determine if dietary factors and stressful events are associated with worsening of IBS symptoms. These journal entries may then be used for recommending dietary exclusions, stress management, and psychological counseling.[2,3]

Additional therapy for IBS is warranted when patients and their physicians have determined that the condition has adversely affected the patient's quality of life. Initial treatment for patients with constipation-predominant IBS usually involves increasing dietary fiber intake and the addition of commercial bulking agents. Fiber decreases total gut transit time and may lessen colonic contractility.[33] Fiber supplementation has been demonstrated to be beneficial in several studies of patients with constipation-predominant IBS.[3] A variety of fiber supplements are available commercially and include synthetic fibers containing calcium polycarbophil (Fibercon® Wyeth Pharmaceuticals, Madison, NJ; Equalactin Newmark Laboratories, Edison, NJ). Soluble fibers occur naturally in a number of fruits and grains, including apples, oranges, apricots, prunes, and oat bran. Psyllium, the active component in Metamucil® and Konsyl® (Proctor and Gamble, Mason, OH) is also a soluble fiber. Methylcellulose, the active ingredient of Citrucel®, is an insoluble fiber that theoretically may produce less gas and bloating than soluble fibers in some patients. Over-the-counter laxatives may help some patients with constipation-predominant IBS. Osmotic laxatives, including milk of magnesia and mineral oil, and stool softeners such as docusate sodium, may be safely and effectively administered in some patients. Polyethylene glycol in a balanced electrolyte solution (Miralax™, Braintree Laboratories, Braintree, MA) is a prescription medication that

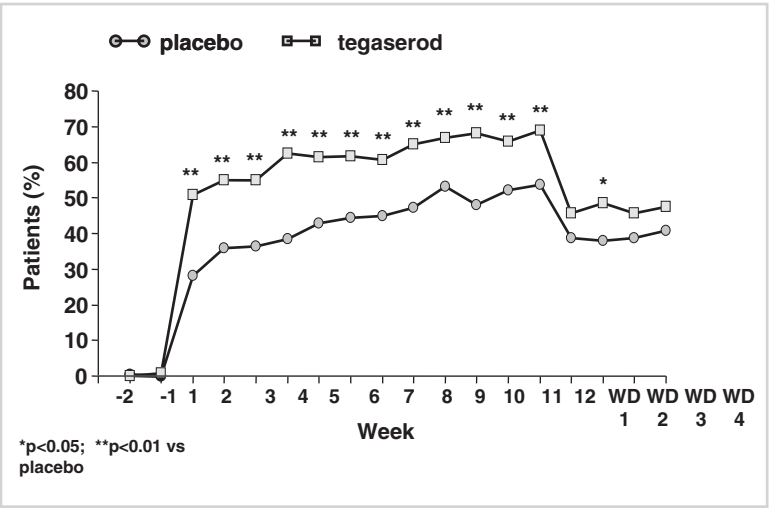


Figure 6.2. Subject Global Assessment of Relief. The data demonstrate the weekly percent of study patients who had complete or considerable relief or were somewhat relieved with tegaserod 6 mg b.i.d. and placebo. $*p < .05$, $**p < .01$ vs. placebo (39). Ehrenpreis ED, Burns EA, Hoffman C. *The AFP guide to diagnosis and treatment of the irritable bowel syndrome.* Copyrighted and published by Family Practice Education Network, Illinois Academy of Family Physicians, Lisle, Illinois, 2003.

is very similar to a colonoscopy preparation solution. This is administered as a 16-g dose in 8 oz of fluid once or twice a day. This agent has proven to be effective in patients with refractory constipation.[34] Furthermore, antispasmodic therapy including anticholinergic agents may be beneficial for pain relief.[3] Due to the fact that these are constipating agents, antispasmodics have a more limited role in constipation-predominant IBS. Antidepressants have been utilized for the treatment of IBS and other functional bowel disorders, and their effectiveness appears to occur primarily due to central nervous system activity.[3,33] Tricyclic antidepressants, which have anticholinergic properties, have been demonstrated to improve abdominal pain and diarrhea in patients with IBS.[4] These drugs often produce constipation and should be used carefully in patients with constipation-predominant IBS. Selective serotonin reuptake inhibitors (SSRIs) may cause either diarrhea or constipation and have been utilized as clinical treatment for IBS and other functional bowel disorders. Evidence-based studies proving the beneficial effects of most of these treatments of IBS are lacking at this time.

Recently, the 5-HT4 receptor agonist tegaserod (Zelnorm®; Novartis Pharmaceuticals, East Hanover, NJ) has been approved by the Food and Drug Administration (FDA) for the treatment of constipation-predominant IBS. This drug, which binds the 5-HT4 receptors in the gastrointestinal tract with high efficiency, has been shown in laboratory studies to stimulate intestinal peristalsis and secretion and to reduce visceral sensitivity.[35] Tegaserod also stimulates the release of other neurotransmitters including calcitonin gene–related peptide, which may contribute to its effects on gastrointestinal function.[35,36] Physiologic studies have demonstrated that tegaserod enhances basal motor activity and corrects intestinal motility in patients with constipation-predominant IBS. Three randomized, placebo-controlled double-blind clinical trials involving 2471 female patients with constipation-predominant IBS who ingested either tegaserod (6 mg b.i.d.) or placebo for 12 weeks were performed prior to approval of this drug.[3,4] These studies demonstrated that tegaserod therapy results in the overall relief of discomfort and other symptomatology in female patients with constipation-predominant IBS (Fig. 6.2).[37] Additionally, patients on tegaserod experienced more frequent bowel movements, decreased abdominal pain, and improvement in stool consistency.[3,4,37] The most common self-limiting adverse reaction experienced in subjects consuming tegaserod was diarrhea. Future therapies for constipation-predominant IBS include the development of additional 5-HT4 agonists such as prucalopride and renzapride.[38] Other gut-directed therapies being investigated for IBS include 5-HT1 receptor agonists, kappa opioid receptor agonists,

somatostatin analogues, as well as antagonists of neurokinin and tachykinin.[39]

References

1. Drossman DA, Corazziari E, Talley NJ, et al. Rome II: a multinational consensus document on functional gastrointestinal disorders. Gut 1999;45:1–81.
2. Ehrenpreis ED, Burns EA, Hofmann C. The AFP Guide to Diagnosis and Management of the Irritable Bowel Syndrome. Lisle, IL: Illinois Academy of Family Physicians Press, 2003.
3. Evidence-based position statement on the management of irritable bowel syndrome in North America. Am J Gastroenterol 2002;97(11 suppl):S1–5.
4. Drossman DA, Camilleri M, Mayer EA, Whitehead WE. AGA technical review on irritable syndrome. Gastroenterology 2002;123(6):2108–2131.
5. Mearin F, Balboa A, Badia X, et al. Irritable bowel syndrome subtypes according to bowel habit: revisiting the alternating subtype. Eur J Gastroenterol Hepatol 2003;15:165–172.
6. Drossman D, Li Z, Andruzzi E, et al. US householder survey of functional gastrointestinal disorders. Prevalence, sociodemography, and health impact. Dig Dis Sci 1993;38:1569–1580.
7. Coulie B, Camilleri M. Irritable bowel syndrome. Clin Perspect Gastroenterol 1999;2:329–338.
8. Camilleri M, Williams DE. Economic burden of irritable bowel syndrome reappraised with strategies to control expenditures. Pharmacoeconomic 2000;4:331–338.
9. Zuckerman M, Guerra L, Drossman D, Foland J, Gregory G. Health-care-seeking behaviors related to bowel complaints: Hispanics versus non-Hispanic whites. Dig Dis Sci 1996;41:77–82.
10. Kalantar JS, Locke GR, Zinsmeister AR, Beighley CM, Talley NJ. Familial aggregation of irritable bowel syndrome: a prospective study. Gut 2003;52(12):1703–1707.
11. El-Serag HB, Olden K, Bjorkman D. Health related quality of life among persons with irritable bowel syndrome: a systematic review. Aliment Pharmacol Ther 2002;16(6):1171–1185.
12. Halder SL, Locke GR, Talley NJ, Fett SL, Zinmeister AR, Melton LJ. Impact of functional gastrointestinal disorders on health-related quality of life: a population-based case-control study. Aliment Pharmacol Ther 2004;19(2):233–242.
13. Gralnek I, Hays R, Kilbourne A, Naliboff, B, Mayer E. The impact of irritable bowel syndrome on health-related quality of life. Gastroenterology 2000;119:654–660.
14. Aziz Q, Thompson D. Brain-gut axis in health and disease. Gastroenterology 1998;114:559–578.
15. Thompson W, Longsreth G, Drossman D, et al. Irritable bowel syndrome. In: Drossman D, ed. The Functional Gastrointestinal Disorders. McLean, VA: Degnon Associates, 2000.
16. Rao S. Visceral hyperalgia: the key for unraveling functional gastrointestinal disorders. Dig Dis 1996;14:271–275.
17. Mertz H, Naliboff B, Munakata J, Niazi N. Altered rectal perception is a biological marker of patients with irritable bowel syndrome. Gastroenterology 1995;109:40–52.
18. Kellow J, Eckersley C, Jones M. Enhanced perception of physiological motility in the irritable bowel syndrome. Gastroenterology 1991;101:1621–1627.
19. Silverman D, Munakata J, Ennes H, et al. Regional cerebral activity in normal and pathological perception of visceral pain. Gastroenterology 1997;112:64–72.
20. Garcia-Rodriguez l, Ruigomez A. Increased risk of irritable bowel syndrome after bacterial gastroenteritis: cohort study. BMJ 1999;318:565–566.
21. McKendrick M, Read N. Irritable bowel syndrome post Salmonella infection. J Infect 1994;29:1–3.
22. Neal K, Hebdon J, Spiller R. Prevalence of gastrointestinal symptoms six months after bacterial gastroenteritis and risk factors for development of the irritable bowel syndrome. Br J Med 1997;314:779–782.
23. Gwee K, Collins S, Read N, et al. Increased rectal mucosal expression of interleukin-1 beta in recently acquired post-infectious irritable bowel syndrome. Gut 2003;52:523–526.
24. Barbara G, Stanghellini V, DeGiorgio R, et al. Activated mast cells in proximity to colonic nerves correlate with abdominal pain in irritable bowel syndrome. Gastroenterology 2004;126(3):693–702.
25. AGA Patient Care Committee. Irritable bowel syndrome: a technical review for practice guideline development. Gastroenterology 1997;112:2120–2137.
26. Drossman D, Leserman J, Nachman, LiZ. Sexual and physical abuse in women with functional or organic gastrointestinal illnesses. Ann Intern Med 1990;113:828–833.
27. Shen B, Soffer E. The challenge of irritable bowel syndrome: creating an alliance between patient and physician. Cleve Clin J Med 2001;68:229–233.
28. Bearcroft C, Perrett D, Farthing M. Postprandial plasma 5-hydroxytryptamine in diarrhea predominant irritable bowel syndrome: a pilot study. Gut 1998;42:42–46.
29. Ahn J, Ehrenpreis ED. Emerging treatments for irritable bowel syndrome. Expert Opin Pharmacother 2001;3(1):9–21.
30. Nanda R, James R, Smith H, Dudley C, Jewell D. Food intolerance and the irritable bowel syndrome. Gut 1989;30:1099–1104.
31. Ehrenpreis E. Lactose intolerance: definition, clinical features, and treatment. Practical Gastroenterol 1999;23:15–19.
32. Brown S, Cann P, Read NW. Effects of coffee on distal colon function. Gut 1990;31:450–453.
33. Camillari M. Review article: clinical evidence to support current therapies of irritable bowel syndrome. Aliment Pharmacol Ther 1999;13:48–53.
34. DiPalma JA, DeRidder PH, Orlando RC, Kolts BE, Cleveland MB. A randomized, placebo-controlled, multicenter study of the safety and efficacy of a new polyethylene glycol laxative. Am J Gastroenterol 2000;95(2):446–450.
35. Camilleri M. Review article: tegaserod. Aliment Pharmacol Ther 2001;15:277–289.
36. Grider J, Fox-Orenstein A, Jin J. 5-Hydroxytryptamine receptor agonists initiate the peristaltic reflex in human, rat and guinea pig intestine. Gastroenterology 1998;115:370–380.
37. Tegaserod maleate (Zelnorm) for IBS with constipation. Med Lett Drugs Ther 2002;44(1139):79–80.

38. Otten M, Schneider H, Wurzer H, et al. A double-blind, placebo-controlled evaluation of safety and efficacy of 12 week, twice-daily treatment with prucalopride in patients with chronic constipation. Gastroenterology 1999;116:A1043.

39. Novick J, Miner P, Krause R, et al. A randomized, double-controlled trial of tegaserod in female patients suffering from irritable bowel syndrome with constipation. Aliment Pharmacol Ther 2002;16:1877–1888.

7

Methods to Measure Small-Bowel and Colonic Transit

Hack Jae Kim and Michael Camilleri

This chapter reviews the methods currently used in clinical practice and research laboratories to measure small-bowel and colonic transit. The advantages and disadvantages of each method are discussed. Examples of the recent application of novel approaches illustrate the potential of these methods both in research and in clinical practice.

Historical Perspective

A number of approaches have been used in the past to assess gut transit. These methods include radiologic techniques (bismuth subnitrate, barium sulfate) as well as the use of insoluble colored powders (e.g., carmine or charcoal) or markers that can be chemically measured (chromium sesquioxide, copper thiocyanate, or sodium chromate).[1–7]

In 1924, investigators at the Mayo Clinic used colored glass beads to study transit times.[8] This method, however, required liquefaction of stools for recovery of markers by sieving.

Clearly, none of these techniques meets current guidelines on acceptable radiation exposure for healthy subjects or patients. Most are also inconvenient due to the laborious stool analytical procedures involved. Nevertheless, these approaches provide interesting landmarks in this field and illustrate the concept that assessment of gut transit has been deemed an important goal for the clinician.

Indications for Measuring Transit

The indications for small-bowel and colon transit measurements are summarized in Table 7.1. Symptoms such as nausea, vomiting, pain, and alterations in bowel movements occur in both functional gastrointestinal diseases and organic motility disorders.[9] Moreover, the severity of symptoms is subjective, often unrelated to the degree of altered function. The diagnosis of regional or generalized motor disturbances cannot be based solely on the assessment of symptoms. The severity of motor dysfunction is quantifiable by transit measurements and may be an important variable; it affects the choice of therapy and long-term prognosis. In clinical practice, an objective and reliable means to identify impaired motility[10] is useful; it may facilitate the selection of patients for further invasive testing, treatment with prokinetic agents, or a change in the method chosen for supplementation of nutrients. Rarely, surgery is a viable option for localized motility disorders such as megaduodenum or colonic inertia. In the latter patients, transit tests are also useful to exclude more generalized motor disturbances that might preclude a surgical approach.

Manometric evaluation has contributed to a better understanding of gastroduodenal motor dysfunctions.[10] However, this requires intubation, which may be difficult in ill patients. Moreover, manometry does not really assess the result of the pressure profile, that is, the transit of chyme. Measurement of transit represents a summary of the overall propagation of chyme over time and thus reflects the net result of gastrointestinal motor activity.

In patients with prolonged orocecal transit, differentiation between delayed gastric emptying and slow small-bowel transit is important since it identifies those in whom enteral nutrition via a jejunal tube may bypass a dysfunctional stomach and thereby avoid total parenteral nutrition. Colonic transit data can be used to assess the severity of constipation or colonic inertia; in the past, prolonged whole-gut (oroanal) transit time had been assumed to

Table 7.1. Indications for measurement of small-bowel and colonic transit

Initial evaluation of suspected small-intestine dysmotility, such as pseudo-obstruction or postvagotomy diarrhea
Differentiation of gastric emptying delay from small-bowel transit delay in patients with prolonged orocecal transit
Differentiation of neuropathic and myopathic small-bowel dysmotility
Assessment of severity of constipation or colonic inertia
Assessment of therapeutic response

From von der Ohe M, Camilleri M. Measurement of small bowel and colonic transit: indications and methods. Mayo Clin Proc 1992;67:1169–1172.

reflect predominantly colonic transit. However, many patients with colonic inertia have a generalized disturbance of gut motility with considerable retardation in small-bowel transit. Thus, oroanal transit times do not merely reflect colonic transit; selective assessment of colonic transit is important, as it may lead to appropriate treatments to correct this disturbance. The results of the transit study may be pivotal in the decision to perform a colectomy for constipation. Finally, transit measurements remain a useful tool for physiologic studies and help provide objective information on the responses to treatment in clinical practice and research.

The Ideal Transit Test

Ideally, a gastrointestinal transit test would quantitatively and reliably measure the transit of chyme through different regions, using the same marker at all levels in a single study. Because the gastric emptying kinetics for solids, liquids, and nondigestible solids of different sizes vary considerably,[11] delivery of chyme into the duodenum depends on the substrate used. A digestible solid is digested as a solid in the stomach, but once it is triturated and reaches the duodenum, it is digested as a liquid. In an ideal test, the same solid particle size should be assessed at all levels of the alimentary tract. Thus, preference is given to a nondigestible solid particle that retains its size and shape despite changes in the pH and chemical milieu during its transit through the entire gastrointestinal tract.

In the ideal colonic transit test, markers should be delivered directly into the right colon to avoid their dispersion during gastric emptying and passage through the small bowel. Finally, the ideal test for small-bowel and colonic transit should be easy to perform, repeatable, noninvasive, and inexpensive.

Currently Available Tests

Measurement of Small-Bowel Transit

A comparison of methods for evaluation of small-bowel transit is shown in Table 7.2.

Determination of Breath Hydrogen Concentration

Probably the most widely used small-bowel transit test is the determination of breath hydrogen concentration. It measures the time required for the appearance of hydrogen in the breath after ingestion of a substrate metabolized by colonic bacteria.[12] Such substrates include lactulose[12] and baked beans.[13] Lactulose is metabolized by lactobacilli, which in healthy subjects are located in the colon. The test assesses the arrival of the first portion or head of the "meal" in the ascending colon; it thus represents overall orocecal transit. To assess small-bowel transit exclusively, lactulose has to be infused into the duodenum by intubation.

Although its simplicity and low cost make the breath hydrogen test attractive, a number of disadvantages render it less useful in pathologic states. Depending on the substrate being used (lactulose or baked beans), this method measures the transit of either liquids or solids. Moreover, results may be greatly influenced by noncolonic bacterial flora in the upper gastrointestinal tract, such as bacteria in the oral cavity,[14] as well as small-intestine bacterial overgrowth. However, oral bacteria can be significantly reduced by the use of a mouthwash prior to the test.[14] Breath hydrogen may also be altered by smoking or exercise, and by the technique of breath expiration.[14] Small-bowel bacterial overgrowth is commonly encountered in patients with motility disorders associated with delayed transit. Since the most proximal bacterial flora that reside in the digestive tract determine the time of the first breath hydrogen peak, bacterial overgrowth in the small bowel may lead to an underestimation of the time taken for the substrate to reach the colon. In some individuals, it may be difficult to identify the true first peak of breath hydrogen,[15] necessitating

Table 7.2. Comparison of methods for evaluation of small-bowel transit

Method	Advantages	Disadvantages	Precautions
Breath H_2 concentration	Simple, inexpensive	Orocecal transit of head of column Influenced by bacterial overgrowth Difficulty identifying "peak"	Mouthwash Avoid cigarettes and exercise Standardize substrate in each laboratory (e.g., liquid lactulose or solid baked beans
Plasma sulfapyridine concentration after oral salicylazosulfapyridine	Simple	Multiple blood samples (300 mL) Orocecal transit unless duodenum intubated Probably reflects liquid transit Influenced by bacterial overgrowth	Avoid in those allergic to sulfonamides
Scintigraphy	Not influenced by bacterial overgrowth Same radiation with more scans	Requires gamma camera	Radiation exposure
^{99m}Tc mashed potato	Relatively simple	Probably measures liquid transit	Radiation exposure acceptable for clinical and research studies
^{131}I fiber	Measures gastric and small bowel transit of nondigestible solids	Very laborious preparation Long half-life of ^{131}I	Excessive radiation No longer used
^{111}In-labeled food or inert particles, e.g., charcoal	Measures gastric and small bowel transit of digestible or nondigestible solids Easy preparation		Radiation exposure acceptable for clinical and research studies Pellets require laborious regulatory oversight

Adapted from von der Ohe M, Camilleri M. Measurement of small bowel and colonic transit; indications and methods. Mayo Clin Proc 1992;67:1169–1179.

approximations or curve fitting of the plotted data (Fig. 7.1). For all of these reasons, this strategy is not used to measure transit in clinical practice at the Mayo Clinic.

Plasma Sulfapyridine After Oral Salicylazosulfapyridine

Another method that depends on bacterial metabolism of a substrate uses the detection of a metabolite in the plasma; oral administration of salicylazosulfapyridine is followed by drawing of multiple blood samples to detect sulfapyridine in plasma.[16] However, this test requires approximately 300 mL of blood and has the same limitations as the breath hydrogen test in that it provides an overall assessment or orocecal transit unless substrate is administered directly into the duodenum, and its results are greatly influenced by small-bowel bacterial overgrowth.

Small-Intestine Scintigraphy

Several radioisotopes such as technetium-99m,[13,17] iodine 131,[18,19] and indium 111[20] have been used as markers to evaluate small-bowel transit. In general, this methodology requires gamma camera equipment and adequate precautions (a pregnancy test in women of childbearing potential) owing to the exposure to radiation. The exposure should be restricted according to guidelines for clinical and research practice. It is important to note that radiation exposure does not increase as more images are obtained by the gamma camera in research studies. Typical radiation exposures are shown in Table 7.3. Radiolabeled polystyrene ion-exchange pellets were extensively used at the Mayo Clinic because they remained nondigestible and unaltered in size at the range of pH found in the stomach and small intestine; hence, the same marker evaluated gastric emptying and small-bowel transit.

Small-bowel transit is calculated by subtracting the time taken for a certain amount of the marker (10% or 50% of ingested radioisotope) to empty from the stomach, from the time taken for the same amount of radioisotope to reach the colon. Radioisotope marker studies are not influenced by small-intestine bacterial overgrowth. Complicated deconvolution analyses are rarely used in research or clinical practice.[18]

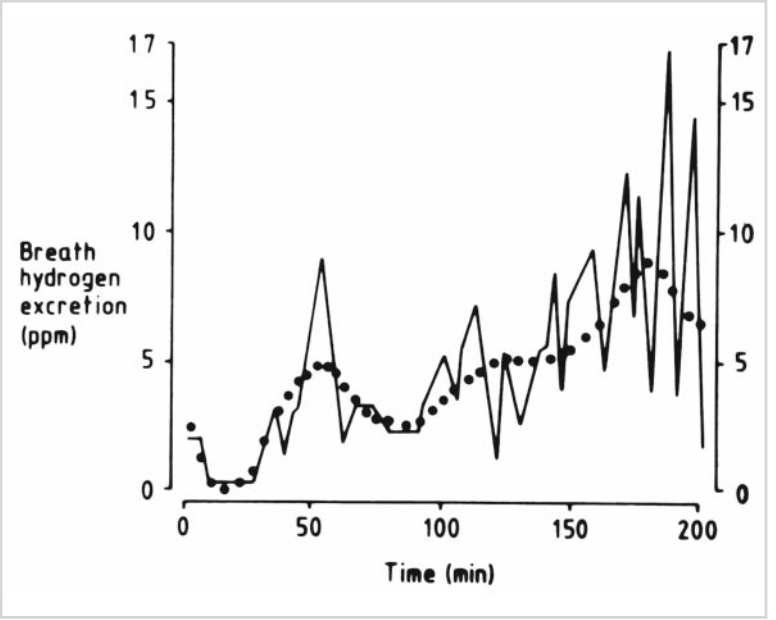


Figure 7.1. Example of repeated peaks of hydrogen in breath; investigators applied a ninth-order polynomial to identify the hydrogen peak.

Different phases of a meal can be labeled with radioisotopes. A mashed potato meal can be labeled easily with ^{99m}Tc sulfur colloid or diethylenetriaminepentaacetic acid (DTPA)[13]; it measures the gastric transit of triturated solids and does not exhibit the lag time customarily seen with digestible or non-digestible solid markers.[13] This is not ideal in the evaluation of gastric emptying in disease states that are known to alter the lag period, such as in gastroparesis.[21] However, the small-bowel transit times of solids and liquids are similar in health[18] and in disease states[19]; hence, ^{99m}Tc sulfur colloid might be suitable to assess small-bowel transit time, but appears to have not advantage over the use of a liquid meal labeled with ^{99m}Tc pertechnetate.[17]

Fiber labeled with ^{131}I is ingested with a standardized mixed meal and measures gastric emptying and small-bowel transit of nondigestible solids.[18] Using ^{131}I-labeled cellulose fiber strands (<2 mm size), the prolonged mouth-to-cecum transit times observed in patients with gastroparesis or antral hypomotility and intestinal pseudo-obstruction or dysmotility were shown to result from selective delays in the transit of radiolabeled solids in the stomach or small bowel.[21] Radiolabeled fiber is no longer used in Mayo Clinic research studies because this method requires very laborious preparation and is associated with relatively high radiation exposure owing to the long half-life of ^{131}I.

Ion-exchange polystyrene pellets labeled with ^{99m}Tc or ^{111}In have been used to evaluate the gastric emptying and small-bowel transit of the solid phase of a meal[20] (Fig. 7.2). Scintigraphy also identifies focal accumulation and persistence of isotope in abnormal, hypomotile segments of small bowel (Fig. 7.3). The emptying of the distal ileum into the colon does not occur linearly in healthy individuals (Fig. 7.4), but is

Table 7.3. Radiation exposure organ dose (cGy) per exposure

			Intestine							
Isotope form	Dose (mCi)	Stomach	Small	Upper large	Lower large	Ovary	Testis	Total body	Bone marrow	H_E
^{111}In	0.1	0.1	0.2	0.45	0.75	0.15	0.01	0.03	0.04	0.03
^{99m}Tc	1.0	0.24	0.24	0.40	0.28	0.08	—	0.02	0.14	0.10

H_E, effective dose equivalent.
Adapted from von der Ohe M, Camilleri M. Measurement of small bowel and colonic transit; indications and methods. Mayo Clin Proc 1992;67:1169–1179.

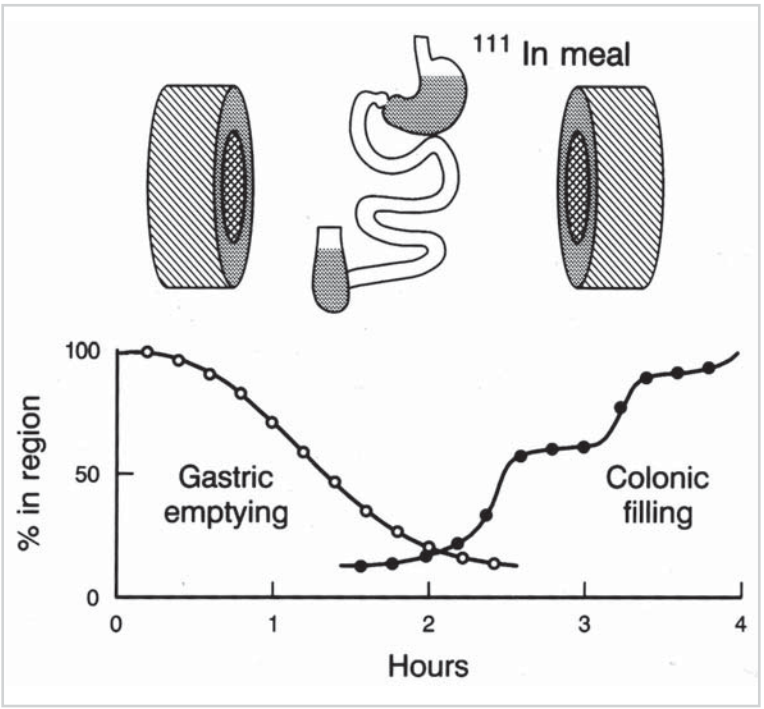


Figure 7.2. Dual gamma camera measurement of gastric and small-bowel transit; profiles of transit are shown in the lower half of the figure. Note the normal pattern of intermittent filling of solid radiolabel in boluses separated by periods during which no residue enters the colon.

associated with a series of bolus transfers.[20] The size and frequency of bolus transfers are significantly impaired in disease processes that affect the smooth muscle of the small bowel, such as progressive systemic sclerosis.[22]

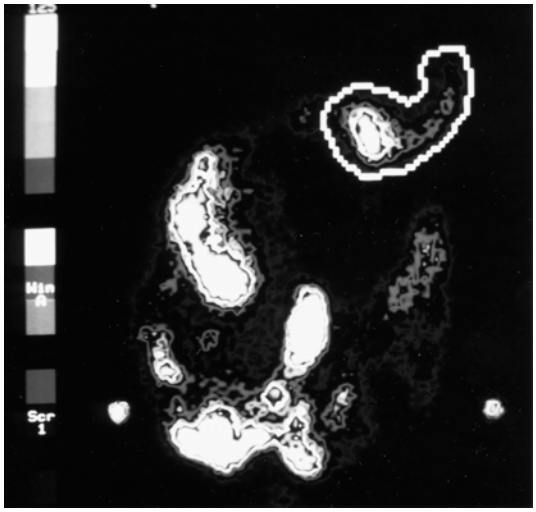


Figure 7.3. Delayed gastric emptying and focal accumulation of isotope in dilated small-bowel loops.

Because of laborious regulatory oversight, most centers simply radiolabel digestible solid or liquid and follow its transit through both stomach and small bowel, using a region of interest program to evaluate stomach emptying and colonic filling. Scintigraphic small-bowel transit is associated with a large interindividual[23] and intraindividual[24] variation. Hence its diagnostic validity in clinical practice is limited.

Newer Methods

Small-Bowel Magnetic Resonance Imaging

A magnetic resonance image (MRI)-based method to determine the small-intestine transit time has been described in the literature in a small number of healthy individuals.[25,26]

Different contrast agents, gadolinium and perfluorononane, have been used to track the flow of these agents through the gastrointestinal (GI) tract noninvasively. Gadolinium is a highly stable nontoxic aqueous-phase marker, and the safety of the agent following oral administration

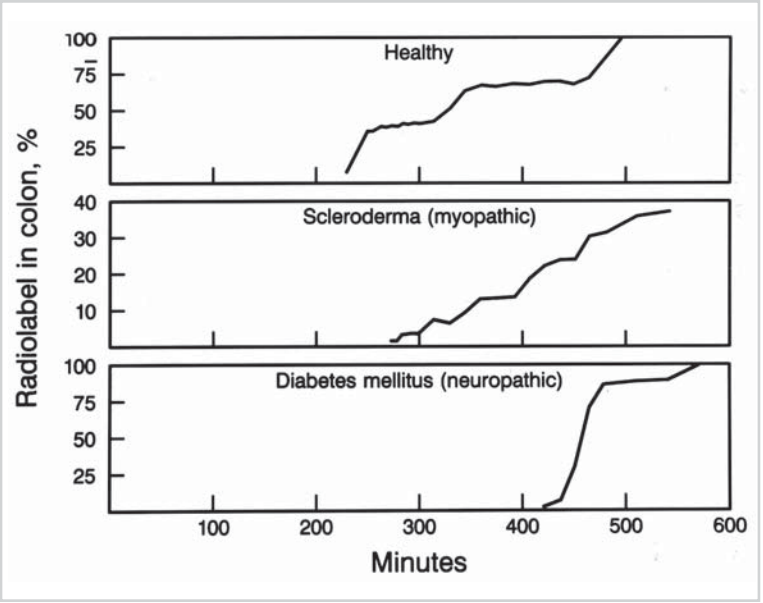


Figure 7.4. Patterns of colonic filling in health and disease. Note the delayed but normal bolus transfer in a neuropathic disorder; in contrast, the patient with systemic sclerosis transfers small amounts of radiolabel from ileum to colon over several hours.

has been documented extensively in gastric emptying studies.[7,27]

Magnetic resonance imaging is performed immediately before and for up to 96 hours after oral contrast ingestion. Each imaging session lasts about 5 minutes, and contrast is easily followed. The three-dimensional (3D) images using this method ensure sufficient image quality to permit delineation of individual bowel loops and to characterize any particular small- or large-bowel segment.

This method seems attractive in that there is no ionizing radiation, images can be collected as often as necessary, and other disease processes such as neoplasia can be detected; however, cost may represent a major limitation. Furthermore, the clinical utility of the proposed method remains to be proven with large number of subjects. This method has not been either standardized or validated for research and clinical practice.

Magnetic Telemetry

A method using a special magnetic marker to measure gastrointestinal transit in healthy subjects has been documented.[28] This method requires continuous monitoring of an ingested, magnetically marked capsule with biomagnetic equipment. After ingestion of a magnetic capsule, its magnetic field distribution over the abdomen is recorded with a magnetometer. Using the magnetic field distribution, the position of the capsule within the gastrointestinal tract is calculated.

This is an attractive, noninvasive method to measure gastrointestinal transit without the risk of radiation exposure. However, it requires a stable magnetic environment, and any heavy metal can disturb the magnetic field. This method requires presence in the lab for the entire duration of the test, and any movement, even breathing, of the subject can interfere with the trajectory of the magnet and cause artifacts. This method is at a preliminary stage and has not been standardized or validated.

Stable Isotope, [^{13}C] Ureide, Breath Test

The stable isotope, [^{13}C] ureide, breath test is an indirect method to measure orocecal transit time of solids or liquids that produces results that are comparable with those of radioscintigraphy.[29] This test measures the changes in the expired air of the ^{13}C to ^{12}C ratio measured by mass spectrometry. Breath samples are collected over 10 hours after administration of a stable isotope (^{13}C)-labeled test substrate, lactose-ureide. The orocecal transit time is then determined semiquantitatively from the kinetics of

the breath $^{13}CO_2$ excretion. Lactose-ureide is not absorbed in the human small intestine, but colonic bacteria readily metabolize lactose-ureide, producing ^{13}C-labeled CO_2. The time at which $^{13}CO_2$ appears in the breath corresponds to the orocecal transit time. Breath samples can be mailed to the analytic laboratory and can be stored for months without a change in their isotopic enrichment.

The advantages of the breath test are that it is noninvasive, there is no use of ionizing radiation, and it is convenient. The limitations are the lack of information on the possible influence of noncolonic bacterial flora in the upper GI tract, such as in the oral cavity and small intestine. Furthermore, the test does not provide information about gastric emptying or large-bowel transit studies that are possible with scintigraphic technique.

Measurement of Colonic Transit

Radiopaque Marker Techniques

The most frequently used test for measurement of colonic transit involves radiopaque markers ingested in a medication capsule. In the original design of this method, a defined number of radiopaque markers were given orally at one time and excretion in the feces was monitored,[30] thus providing an estimate of mouth-to-anus transit time. This approach is generally accepted as an inexpensive and suitable evaluation of total colonic transit, since the latter accounts for the major (but undefined) proportion of overall mouth-to-anus transit time.

This widely used method to quantify colonic transit has been modified by several groups,[31–34] and the modifications are summarized in Table 7.4. An estimate of regional or segmental colonic transit is also obtained.[34] For these purposes, radiopaque markers are given on several consecutive days in order to reach steady-state conditions, and abdominal radiographs are taken 4 days after the start of marker ingestion. In practice, a 7-day radiograph is also taken. The distribution of the markers in the right and left colon and rectosigmoid region provides some information about regional function. However, it must be emphasized that a disturbance in mechanics of defecation would also delay transit through one or more regions, irrespective of the method chosen. Hence, colonic transit data need to be interpreted with due consideration of other information, as discussed elsewhere in this book.

Table 7.4. Comparison of different radiopaque marker methods

Series	*n*	Types of markers	Size range (mm)	X-ray	Transit time calculated	Transit normal (h) (mean ± SD)
Hinton et al 1969[30]	25	3	2.7–4.5 × 3	Stools, serially	Mouth to anus 1st marker in stool 80% markers in stool	95 percentile <66 95 percentile <114
Cummings and Wiggins 1976[31]	15	4	1.1 × 4.5	Stool, day 4	Mouth to anus Single stool transit (3-marker analysis)	60.3 ± 3.6
Read et al 1980[13]	14	1	2 × 4	Stools, serially	Mouth to anus 1st marker in stool 50% markers in stool All markers in stool	48.5 ± 10.1 78.6 ± 15.1 100.3 ± 25.4
Arhan et al 1981[32]	37	1	3 × 6	Abdomen, serially (days 1–7)	Colon Right colon Left colon Rectosigmoid	39 ± 5 13 15 11
Chaussade et al 1986[33]	22	3	3 × 3 to 1 × 10	Abdomen, serially (days 4, 7, 10)	Colon Right colon Left colon Rectosigmoid	34.4 ± 16.2 6.9 ± 7.8 9.1 ± 10.3 18.4 ± 12.5
Metcalf et al 1987[34]	49	3	1 × 6 to 6 × 6	Abdomen, day 4	Mouth to anus Colon Right colon Left colon Rectosigmoid	53.3 ± 3.7 35.0 ± 2.1 11.3 ± 1.1 11.4 ± 1.4 12.4 ± 1.1
Bouchoucha et al 1992[41]	174	Several	Various	Abdomen, single and multiple	Total	20.7 ± 1.9

Counting the number of markers found in three segments of the large bowel (Fig. 7.5) has been useful in clinical practice to differentiate patients with constipation-predominant irritable bowel syndrome from those with colonic inertia or pseudo-obstruction who might benefit from subtotal colectomy with ileorectostomy.[35–38] These methods are fairly reproducible in carefully selected patients (Fig. 7.6).

Using this method, investigators showed an association between colonic transit and stool consistency—hard stools were correlated with slow transit and loose stools with fast transit through the colon,[39] suggesting a complementary role or utility of stool form scale (Bristol stool form scale) as a possible simple method of assessing intestinal transit rate.[40]

A simple approach is to ingest 20 markers on day 1 and take a radiograph on day 3. The presence of greater than eight markers remaining in the colon implies delayed colonic transit.[41] Although one plain abdominal radiograph could sufficiently measure colonic transit at an acceptable radiation exposure, this technique would not be applicable in motor disturbances associated with accelerated colonic transit. To identify and quantitate accelerated transit, earlier,

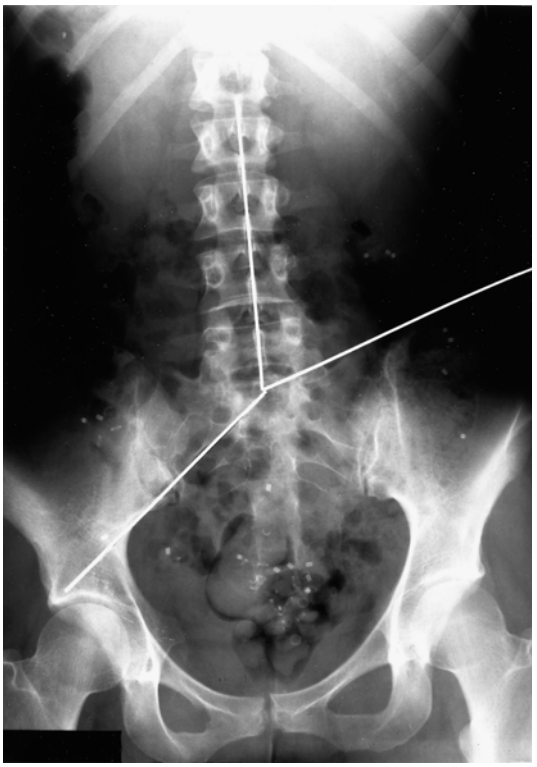


Figure 7.5. Abdominal radiograph showing radiopaque markers in three segments of colon: right, left, and rectosigmoid.

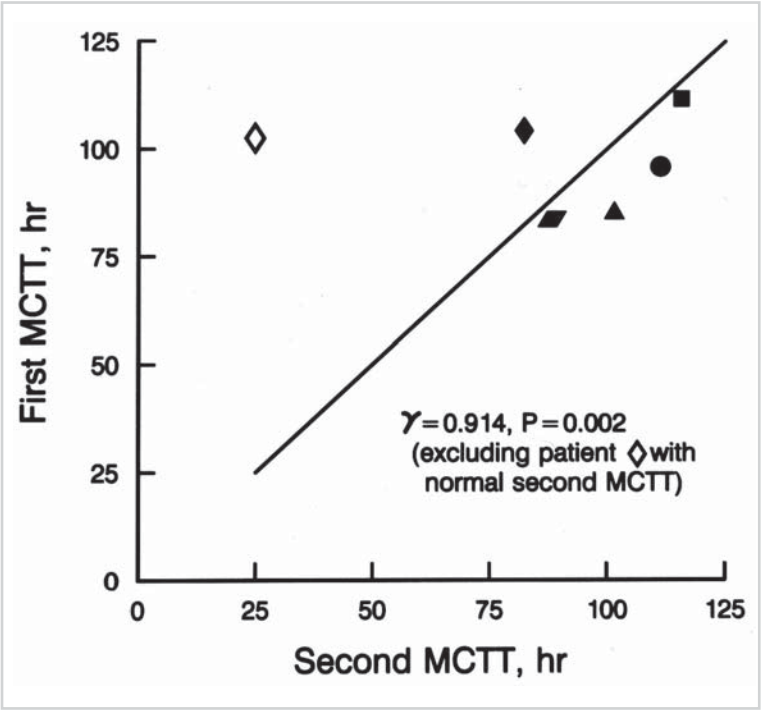


Figure 7.6. Reproducibility of radiopaque marker method in patients with severe idiopathic constipation. Note that one patient has a great discrepancy in measured colonic transit time (MCTT) on two occasions, approximately 1 year apart.

Table 7.5. Comparison of methods for measurement of colonic transit

Method	Advantages	Disadvantages	Precautions
Radiopaque markers	Simple, inexpensive, and reproducible	Day 4 x-ray may miss transit profile	Supplement diet with 10 g fiber
Scintigraphy	No increased radiation exposure with increased number of scans	Needs gamma camera	Radiation exposure acceptable
^{111}In-DTPA liquid transit	Simple Follow emptying of liquid throughout gut	Needs gamma camera	Radiation exposure acceptable
Delayed-release capsule	Noninvasive Identifies onset of colonic transit Labels solid phase No preparation needed Applicable for fast or slow transit	5% failure of capsule dissolution 1 hour preparation of materials	Requires use of ^{111}In to measure prolonged transit in constipation

Adapted from von der Ohe M, Camilleri M. Measurement of small bowel and colonic transit; indications and methods. Mayo Clin Proc 1992;67:1169–1179.

repeated radiographs would be necessary, thereby increasing the radiation exposure. This simple test is easy to follow; thus, patients can easily be given instructions to perform the test at home and mail the radiographs to a referral center during follow-up. Table 7.5 compares the advantages and disadvantages of both radiopaque marker and scintigraphic tests.

Colonic Scintigraphy

More recently, radioscintigraphy has been used to provide a more detailed assessment of overall and regional colonic transit with an acceptable radiation exposure. Two approaches have been used.

Orocecal Intubation

To avoid dispersion of radiolabel during its passage through the stomach and small bowel, orocecal intubation was utilized to instill liquid radioisotopes, such as ^{111}In-DTPA, directly into the large bowel.[42] This method has been adapted by simply following an ^{111}In-liquid meal emptied from the stomach.[43] Thus, there is a definite starting time for colonic transit, and liquid transit through the different colonic regions could be assessed. Using this method, Krevsky et al[42] suggested that the ascending colon empties content rapidly, in an exponential manner; in contrast, the transverse colon was the major site of colonic storage. This method was a significant advance that allowed for a more detailed and dynamic assessment of colonic transit, previously impossible using radiopaque markers; because the radiation exposure does not increase with the number of gamma camera scans taken, multiple images can be taken at defined time intervals. However, the need for orocecal intubation renders such a method much less applicable in clinical practice. An alternative approach involves cecal intubation via colonoscopy; however, the latter requires emptying of the colon and, hence, transit tests obtained after colonoscopic intubation may not mimic physiologic conditions.

Delayed-Release Capsule

In an attempt to avoid orocecal intubation, a new technique has been developed that exploits the pH gradient in the small intestine (mean duodenal pH, 6.5; ileal pH, 7.4; cecal pH, 6.8.[44–46] The distal ileum empties solid residue in boluses, and this ensures that isotope in the distal ileum is transferred to the colon as a bolus.[20] Radiolabeled polystyrene pellets (^{99m}Tc or ^{111}In) or activated charcoal was placed in a medication capsule covered with a single coating of the pH-sensitive polymer, methacrylate (Fig. 7.7). In vitro studies showed that this capsule dissolved at a pH of between 7.2 and 7.4 within approximately 1 hour of exposure, which was the average residence time of radiolabeled pellets in the distal small bowel,[20] where the intraluminal pH is typically alkaline. However, if the pH was

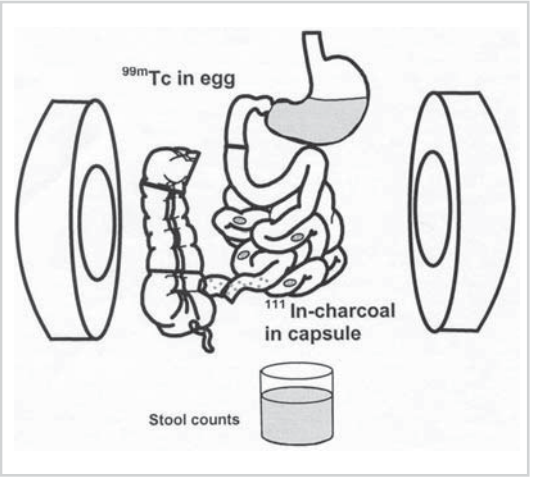


Figure 7.7. Scintigraphic method for combined gastric, small-bowel, and colonic transit measurement. Note the use of different isotopes to label solids or activated charcoal that are incorporated in the meal and the methacrylate-coated capsule. Adapted from Burton DD, Camillieri M, Mullan BP et al. Colonic transit scintigraphy labeled activated charcoal compared with ion exchange pellets. J. Nucl. Med. 1997;38:1807–1810. Reprinted by permission of the Royal Society of Nuclear Medicine.

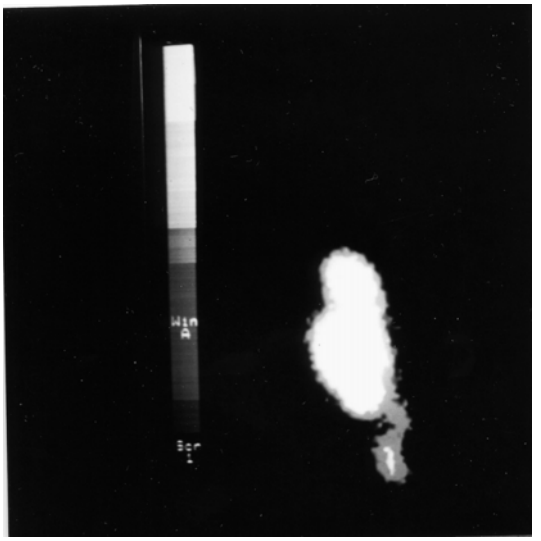


Figure 7.8. Entry of ^{111}In pellets from distal ileum into ascending colon following release from a methacrylate-coated capsule.

below 7, dissolution of the polymer did not occur for several hours.[47] Thus by using the natural pH gradient in the small bowel, radiolabeled solid pellets can be reliably delivered directly into the right colon (Fig. 7.8), permitting noninvasive evaluation of colonic transit.[47] Application of this novel technique to the unprepared GI tract showed the ascending colon to be a reservoir for solid residue (Fig. 7.9). Emptying of the ascending colon occurs in two phases: an initial lag phase, followed by an emptying phase, which is often linear.[47] By simultaneous study of the transit of radiolabeled solid particles with liquid delivered into the cecum by means of an orocecal tube, it was found that, in healthy subjects, a small volume of liquid isotope traverses the ascending colon with the solid pellets. This finding suggested that there is no discrimination between solid and liquid transit in the ascending colon.[48] Instead of polystyrene pellets, the ^{111}In can be adsorbed on activated charcoal.[49]

Colonic Magnetic Resonance Imaging

The colonic transit measurements using MRI has been described in a small number of healthy subjects in a feasibility study.[25,26] This uses the same method and contrast agents as described in the small-bowel MRI section, above. This method provides a fast and easy method for quantifying GI transit; however, the clinical utility of this method remains to be proven.

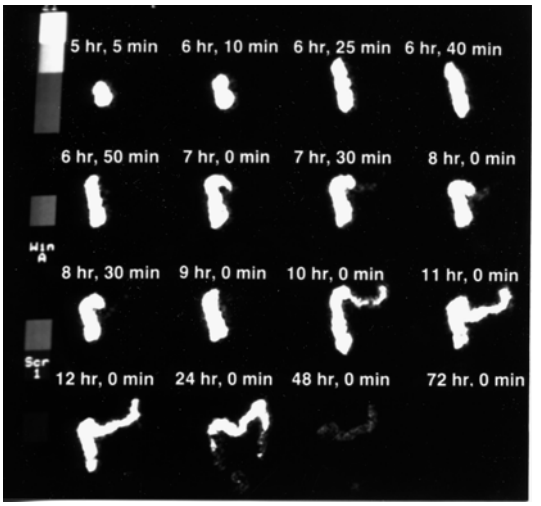


Figure 7.9. Colonic scans at sequential time points in a healthy subject. Note the prolonged residence of isotope in ascending and transverse regions of colon.

Combined Measurement of Gastrointestinal and Colonic Transit

The noninvasive techniques that evaluate transit of solid particles of the same size through the stomach, small bowel, and colon provide reliable assessments in the majority of patients with common GI symptoms such as nausea, vomiting, abdominal pain, diarrhea, and constipation. There is likely to be a significant growth in the application of these methodologies in the near future. The combination of transit measurements within one study limits radiation exposure, and by optimal use of personnel and equipment, leads to improved efficacy and reduction in costs.

The procedure to measure whole-gut transit in the unprepared state requires simultaneous use of two different radioisotopes.[50,51] A methacrylate-coated capsule containing polystyrene pellets or activated charcoal labeled with ^{111}In is ingested by the patient after an overnight fast. With a half-life of approximately 68 hours, ^{111}In is preferred to ^{99m}Tc, which has a half-life of approximately 6 hours. Thus ^{111}In is a superior marker for colonic transit because patients with colonic inertia may have very prolonged transit. Gastric emptying of the capsule is monitored by following its position relative to external radioactive markers placed over the patient's xiphisternum and both anterior superior iliac spines. After the capsule empties from the stomach, a standard 1260-kJ (300-kcal) breakfast meal consisting of scrambled eggs, whole wheat bread, and skimmed milk or apple juice is given. Polystyrene pellets labeled with ^{99m}Tc are mixed with the egg, which is cooked to a firm consistency. For lunch and dinner, standardized meals are given 4 hours and 8 hours after the breakfast meal. Ordinary physical activity is allowed during the test. Anterior and posterior gamma camera images (2-minute acquisitions) are acquired with patients in an erect position.

In research studies, these images are obtained at regular intervals for 12 hours, and a final image is obtained 24 hours after ingestion of the radiolabeled breakfast. Using a variable region-of-interest program, ^{99m}Tc is measured in the stomach and large bowel and ^{111}In is measured in four regions in the colon (ascending, transverse, descending, and rectosigmoid). Corrections are performed for isotope decay and Compton scatter from the ^{111}In to the ^{99m}Tc window. Gastric emptying is summarized by calculating the duration of the lag phase and the slope of postlag emptying.[21] Small-bowel transit time is estimated by subtracting the time for a proportion (10% or 50%) of isotope to empty from the stomach from the time taken for the same proportion to enter the colon.[20] Overall colonic transit is evaluated by the geometric center, that is, the weighted average of the proportions of counts in each colonic region at 4 hours, 12 hours, and 24 hours.[50,51] For this analysis, each colonic region (ascending, transverse, descending rectosigmoid, stool) is given a number from 1 to 5 as a weighting factor. The proportion in each region is multiplied by the weighting factor, and the sum for the five regions calculated. Thus, a low geometric center implies that most radiolabel is closer to the cecum, whereas a high geometric center implies most radiolabel is closer to the stool. The proximal colonic emptying rate can also be plotted as an activity-time curve, since the start time of colonic transit is easily defined by this method. This approach has provided interesting observations in health and disease states, particularly regarding the importance of altered proximal colonic transit in severe constipation and in irritable bowel syndrome with diarrhea (Fig. 7.10).

Simultaneous colonic transit measurements have also been compared in idiopathic constipation patients using a radiopaque marker method simultaneously with scintigraphy.[34,47] The mean transit times through the ascending and transverse colon for radiopaque markers (6 mm average size) were significantly faster than the time for 50% of radiolabeled pellets (1 mm average size) to empty from these combined colonic regions.[47]

In clinical practice, the sequence of measurements and calculations used in research is far too laborious. Hence, a simplified routine has been validated in the authors' laboratory. Selected scintigraphic observations made within the first 6 hours after ingestion of the ^{99m}Tc-labeled solid meal were compared with the results of more detailed analyses requiring multiple scans. The data showed that in patients with neuropathic and myopathic motility disorders, the proportion of radioisotope retained in the stomach at 2 hours, 4 hours, and 6 hours could differentiate health from neuropathic and myopathic motility disorders at a sensitivity greater than 90%, with a specificity of 78%. These accuracy figures are

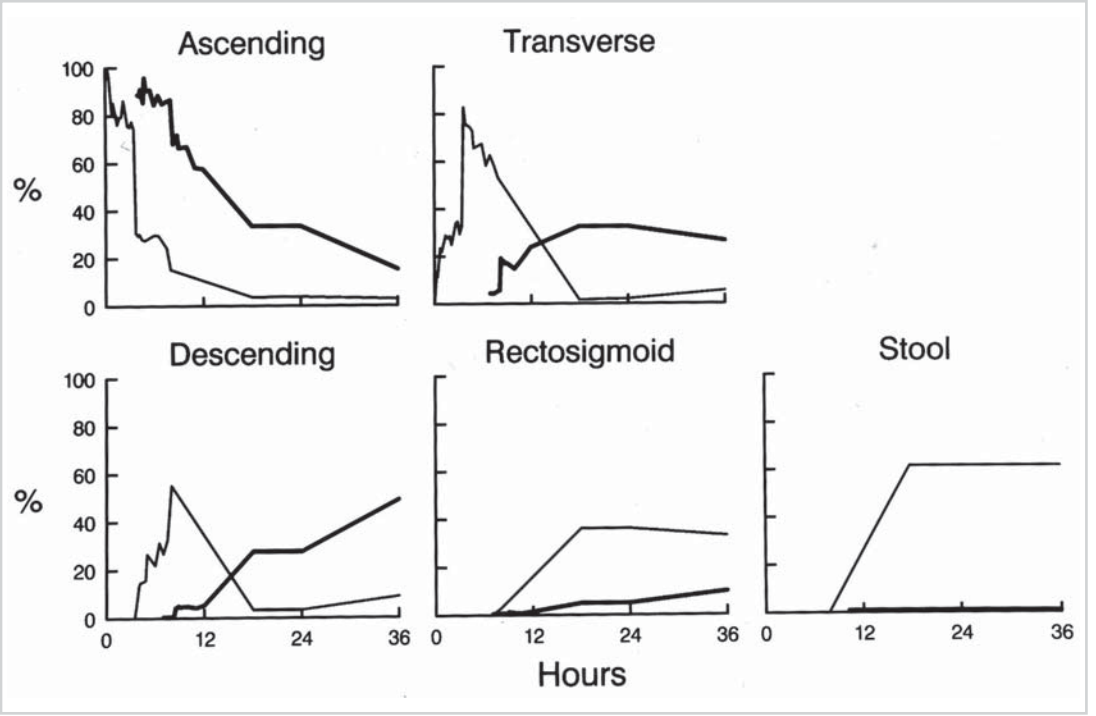


Figure 7.10. Regional colonic transit in health (thick line) and diarrhea-predominant irritable bowel syndrome (thin line). Note the accelerated transit of isotope in all regions.

comparable to those of more detailed analyses.[52] A similar approach has been developed for colonic transit measurements, and recently, the validity of this method relative to clinical results has been shown in several clinical trials using alosetron, a 5-hydroxytryptamine (5-HT_3) antagonist,[53] and tegaserod, a 5-HT_4 agonist.[54,55]

The scintigraphic measurements at 4 hours, 12 hours, and 24 hours after ingestion of the delayed release capsule (Fig. 7.11) discriminate

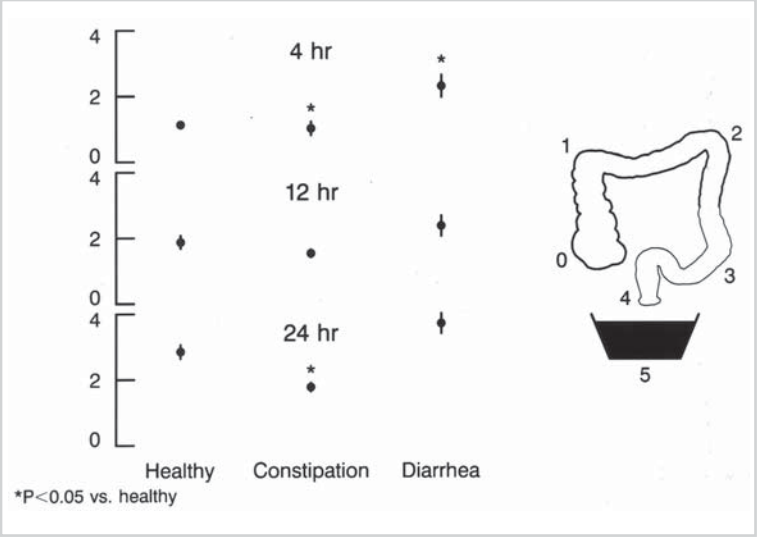


Figure 7.11. Geometric center of colonic isotope after 4 hours, 12 hours, and 24 hours in disorders of colonic transit.

health from disease states associated with accelerated or delayed colonic transit.[52] These data appear to justify the authors' preference for the scintigraphic approach over the more widely used radiopaque marker methods in conditions associated with rapid colonic transit, since radiopaque markers may have already passed through part or all of the colon at the time the abdominal radiograph is taken (day 4). A more accurate evaluation of rapid colonic transit could certainly be achieved using radiopaque markers by increasing the frequency of abdominal radiographs, but this would require an unacceptable increment in radiation exposure. These scintigraphic measurements involve limited radiation exposure (Table 7.3), permitting repeated evaluation to monitor the progress or efficacy of treatment.

Conclusion

Radiopaque markers provide a robust, inexpensive, and practical measurement of colonic transit. Scintigraphy has been simplified and provides information about transit throughout the gut.

The stable isotope breath test is a promising, noninvasive, and reliable way to measure orocecal transit time. Because test materials and breath samples can be easily and safely mailed to a central laboratory, tests can also be performed at home, in clinics, or in hospitals without facilities for mass spectrometry. Applications to larger groups of patients in clinical practice can be realistically envisaged in the future. In the future, the role of newer techniques involving magnetism or magnetic resonance imaging will be clarified.

References

1. Hurst AF. Constipation and Allied Intestinal Disorders, 2nd ed. London: Frowde, 1919.
2. Wallace RP, Ehrenfeld I, Cowett MP, et al. Motility of the gastrointestinal tract. AJR 1938;39:64–66.
3. Lonnerblad L. Transit time through the small intestine. A roentgenologic study on normal variability. Acta Radiol Suppl (Stockh) 1951;88:1–85.
4. Whitby LG, Lang D. Experience with the chromic oxide method of fecal marking in metabolic balance investigations on humans. J Clin Invest 1960;39:854–863.
5. Hansky J, Connell AM. Measurement of gastrointestinal transit using radioactive chromium. Gut 1962;3:187–188.
6. Manousos ON, Truelove SC, Lemsden K. Transit times of food in patients with diverticulosis or irritable colon syndrome and normal subjects. Br Med J 1967;3:760–762.
7. Dick M. Use of cuprous thiocyanate as a short-term continuous marker for faeces. Gut 1969;10:408–412.
8. Alvarez WC, Freedlander BL. The rate of progress of food residues through the bowel. JAMA 1924;83:576–580.
9. Malagelada J-R, Stanghellini V. Manometric evaluation of functional upper gut symptoms. Gastroenterology 1985;88:1223–1231.
10. Malagelada J-R, Camilleri M, Stanghellini V. Manometric Diagnosis of Gastrointestinal Motility Disorders. New York: Thieme, 1986.
11. Kelly KA. Gastric emptying of liquids and solids: roles of proximal and distal stomach. Am J Physiol 1980;239: G76–76.
12. Levitt MD. Production and excretion of hydrogen gas in man. N Engl J Med 1969;281:122–127.
13. Read NW, Miles CA, Fisher D, et al. Transit of a meal through the stomach, small intestine and colon in normal subjects and its role in the pathogenesis of diarrhea. Gastroenterology 1980;79:1276–1282.
14. Thompson DG, Biufield P, Debelder A, et al. Extra-intestinal influences on exhaled breath hydrogen measurements during the investigation of gastrointestinal disease. Gut 1985;26:1349–1352.
15. Howard PJ, Lazarus C, Maisey MN, et al. Interpretation of postprandial breath hydrogen excretion in relation to small bowel transit and ileocecal flow patterns of a radiolabeled solid meal in man. J Gastrointest Motil 1990;2:194–201.
16. Kellow JE, Borody TJ, Phillips SF, et al. Sulfapyridine appearance in plasma after salicylazosulfapyridine. Another simple measure of intestinal transit. Gastroenterology 1986;91:396–400.
17. Caride VJ, Prokop EK, Troncale FJ, et al. Scintigraphic determination of small intestinal transit time: comparison with the hydrogen breath technique. Gastroenterology 1984;86:714–720.
18. Malagelada J-R, Robertson JS, Brown ML, et al. Intestinal transit of solid and liquid components of a meal in health. Gastroenterology 1984;87:1255–1263.
19. Camilleri M, Brown ML, Malagelada J-R. Impaired transit of chyme in chronic intestinal pseudo-obstruction: correction by cisapride. Gastroenterology 1986;91:619–626.
20. Camilleri M, Colemont LJ, Phillips SF, et al. Human gastric emptying and colonic filling of solids characterized by a new method. Am J Physiol 1989;257:G284–290.
21. Camilleri M, Brown ML, Malagelada J-R. Relationship between impaired gastric emptying and abnormal gastrointestinal motility. Gastroenterology 1986;91:94–99.
22. Greydanus MP, Camilleri M, Colemont LJ, et al. Ileocolonic transfer of solid chyme in small intestinal neuropathies and myopathies. Gastroenterology 1990; 99:158–164.
23. Argenyi EE, Soffer EE, Madsen MT, et al. Scintigraphic evaluation of small bowel transit in healthy subjects: inter- and intra-subject variability. Am J Gastroenterol 1995;90:938–942.

24. Cremonini F, Mullan BP, Camilleri M, et al. Performance characteristics of scintigraphic transit measurements for studies of experimental therapies. Aliment Pharmacol Ther 2002;16:1781–1790.
25. Patak MA, Weishaupt D, Frohlich JM, et al. Sequential fast 3D MRI following oral ingestion of Gd-DOTA: a new means to assess intestinal transit time. J Magn Reson Imaging 1999;10:474–476.
26. Schwarz R, Kaspar A, Seelig J, et al. Gastrointestinal transit times in mice and humans measured with ^{27}Al and ^{19}F nuclear magnetic resonance. Magn Reson Med 2002;48:255–261.
27. Kunz P, Crelier GR, Schwizer W, et al. Gastric emptying and motility: assessment with MR imaging—preliminary observations. Radiology 1998;207:33–40.
28. Weitschies W, Kotitz R, Cordini D, et al. High-resolution monitoring of the gastrointestinal transit of a magnetically marked capsule. J Pharm Sci 1997;86:1218–1222.
29. Geypens B, Bennink R, Peeters M, et al. Validation of the lactose-[13C]ureide breath test for determination of orocecal transit time by scintigraphy. J Nucl Med 1999;40:1451–1455.
30. Hinton JM, Lennard-Jones JE, Young AC. A new method for studying gut transit times using radio-opaque markers. Gut 1969;10:842–847.
31. Cummings JH, Wiggins HS. Transit through the gut measured by analysis of a single stool. Gut 1976;17:219–223.
32. Arhan P, Devroede G, Jehannin B, et al. Segmental colonic transit time. Dis Colon Rectum 1981;24:625–629.
33. Chaussade S, Roche H, Khyari A, et al. Mesure du temps de transit colique (TTC): description et validation d'une nouvelle technique. Gastroenterol Clin Biol 1986;10:385–389.
34. Metcalf AM, Phillips SF, Zinsmeister AR, et al. Simplified assessment of segmental colonic transit. Gastroenterology 1987;92:40–47.
35. Pemberton JH, Rath DM, Ilstrup DM. Evaluation and surgical treatment of severe chronic constipation. Ann Surg 1991;214:403–413.
36. Wexner SD, Daniel W, Jagelman DG. Colectomy for constipation: physiologic investigation is the key to success. Dis Colon Rectum 1991;34:851–856.
37. Wexner SD, Jagelman DG. Constipation. Postgrad Adv Colorect Surg 1989;51:1–22.
38. Beck DE. Colectomy for constipation. Semin Colon Rect Surg 1992;63:151.
39. Degen LP, Phillips SF. How well does stool form reflect colonic transit? Gut 1996;39:109–113.
40. Lewis SJ, Heaton KW. Stool form scale as a useful guide to intestinal transit time. Scand J Gastroenterol 1997;32:920–924.
41. Bouchoucha M, Devroede G, Arhan P, et al. What is the meaning of colorectal transit time measurement? Dis Colon Rectum 1992;35:773–782.
42. Krevsky B, Malmud LS, D'Ercole F, et al. Colonic transit scintigraphy. A physiologic approach to the quantitative measurement of colonic transit in humans. Gastroenterology 1986;91:1102–1112.
43. Bonapace ES, Maurer AH, Davidoff S, et al. Whole gut transit scintigraphy in the clinical evaluation of patients with upper and lower gastrointestinal symptoms. Am J Gastroenterol 2000;95:2838–2847.
44. Fordtran JS, Locklear TW. Ionic constituents and osmolality of gastric and small intestinal fluids after eating. Am J Dig Dis 1966;11:503–521.
45. Sladen GE. PH profile of gut as measured by radiotelemetry capsule. Br Med J 1972;2:104–106.
46. Evans DF, Pye G, Bramley R, et al. Measurement of gastrointestinal pH profile in normal ambulant human subjects. Gut 1988;29:1035–1041.
47. Proano M, Camilleri M, Phillips SF, et al. Transit of solids through the human colon: regional quantification in the unprepared bowel. Am J Physiol 1990;258:G856–862.
48. Proano M, Camilleri M, Phillips SF, et al. The unprepared human colon does not discriminate between solids and liquids. Am J Physiol 1991;260: G13–16.
49. Burton DD, Camilleri M, Mullan BP, et al. Colonic transit scintigraphy labeled activated charcoal compared with ion exchange pellets. J Nucl Med 1997;38: 1807–1810.
50. Stivland T, Camilleri M, Vassallo M, et al. Scintigraphic measurement of regional gut transit in idiopathic constipation. Gastroenterology 1991;101:107–115.
51. Vassallo M, Camilleri M, Phillips SF, et al. Transit through the proximal colon influences stool weight in irritable bowel syndrome with diarrhea. Gastroenterology 1992;102:102–108.
52. Camilleri M, Zinsmeister AR. Towards a relatively inexpensive, noninvasive, accurate test for colonic motility disorders. Gastroenterology 1992;103:36–42.
53. Viramontes BE, Camilleri M, McKinzie S, et al. Gender-related differences in slowing colonic transit by a 5-HT_3 antagonist in subjects with diarrhea-predominant irritable bowel syndrome. Am J Gastroenterol 2001;96: 2671–2676.
54. Prather CM, Camilleri M, Zinsmeister AR, et al. Tegaserod accelerates orocecal transit in patients with constipation-predominant irritable bowel syndrome. Gastroenterology 2000;118:463–468.
55. Degen L, Matzinger D, Merz M, et al. Tegaserod, a 5-HT_4 receptor partial agonist, accelerates gastric emptying and gastrointestinal transit in healthy male subjects. Aliment Pharmacol Ther 2001;15:1745–1751.

8

Anorectal Manometry and the Rectoanal Inhibitory Reflex

Johann Pfeifer and Lucia Oliveira

Anorectal sphincter assessment through physiologic testing has been in use for more than 120 years. The first studies of anorectal manometry were done in 1877 by Gowers,[1] who measured anal canal resting tone and was reportedly the first to explore the rectoanal inhibitory reflex. A comprehensive physiologic evaluation of the anorectal sphincter function includes assessment of the shape and function of the rectum, the sphincter muscles, the pelvic floor, and the anal canal. Anorectal manometry is one way of evaluating the pressures in the rectum and anal canal as well as the compliance of the rectum and the basic reflex and sensory mechanisms.

Methods of Performing Anorectal Manometry

Anorectal manometry is an investigation used to assess the pressures in the rectum and anal canal; in other words, it is a measurement of the resistance of the anal sphincter complex involuntary evacuation. This evaluation is performed by placing a specially designed catheter or balloon into the lower rectum and anal canal. This pressure-sensitive device is connected to a transducer, which converts mechanical into electronic signals that are then recorded and displayed on a computer monitor. The aim is to record reproducible measurements and a quantitative assessment of the anal sphincter complex. However, the procedure as well as the equipment used during anal manometry are not yet standardized; therefore, comparing results among various centers is difficult. Thus, follow-up investigations comparing results should be performed with the identical technique in the same anorectal manometry unit. General parameters evaluated by anal manometry include (1) internal and external anal sphincter pressures, (2) anal and rectal pressure response during straining, (3) anal sphincter length, (4) anal and rectal motility, (5) rectal sensation, (6) rectal capacity and compliance, and (7) anal sphincter muscle reflexes.

Fluid-Filled and Air-Filled Balloon Systems

One of the most common methods of measuring anorectal pressure utilizes a closed balloon system. The pressure result obtained with balloon recording is an average of all pressures acting into the balloon; radial asymmetry cannot be detected. However, larger balloons are unphysiologic as the probe itself may cause reflex contractions but the results obtained are more representative of a greater area of the sphincter. It is of tremendous importance to understand that a compliance hysteresis phenomenon exists in the anal canal, wherein both pressure-radial curves (distention/deflation) are not superimposable, and the level of pressure is lower on return, for similar levels of distention due to compliance adaptation processes. Thus, probes with a larger diameter generate greater pressures in the same patient than do smaller balloons.[2] Furthermore, more rapid distention records higher pressures. Air is compressible; therefore the use of water for the balloon filling may be more reproducible.[3]

Air-Filled Balloon Technique (Schuster)

In the 1960s, Schuster[4] invented a simple method for measuring anorectal pressure changes. The device consisted of a metal cylinder around which double-molded latex balloons are tied forming two compartments (Fig. 8.1). These balloons were connected with separate catheters through a hole in the cylinder to either inflate air or to record pressure changes, when appropriate. The inner balloon has a doughnut shape when inflated with 7 to 10 ml of air; the outer balloon has a pear-shaped structure. Through the metal cylinder, further balloons (rectal and/or colonic) can be inserted. Thus, rectal pressures can be measured or the rectoanal inhibitory reflex can be elicited.

This device is inserted into the anus and positioned where the inner balloon lies attached to the internal anal sphincter and the pear-shaped balloon to the outer bundle of the external anal sphincter. Thus, theoretically, the pressures of the internal and external sphincter can be independently measured; however, the overlap of these two portions is too wide to allow adequate differentiation. Normally, recording is performed with an aneroid manometer. The advantage is that recording is done from a larger surface reflecting overall pressures of a large area of the sphincters. Furthermore, the technique is simple and cost-effective, and the balloon stays fixed in place, thereby requiring only one operator. The disadvantage is that larger balloons create more artifacts during recording; therefore, this method is better for evaluating pressure changes than for evaluating actual pressures. Balloons and cylinders are available in three sizes: infant, pediatric, and adult. Although the device is not widely used for diagnostic evaluation, it may have a therapeutic role as a biofeedback catheter.[4,5]

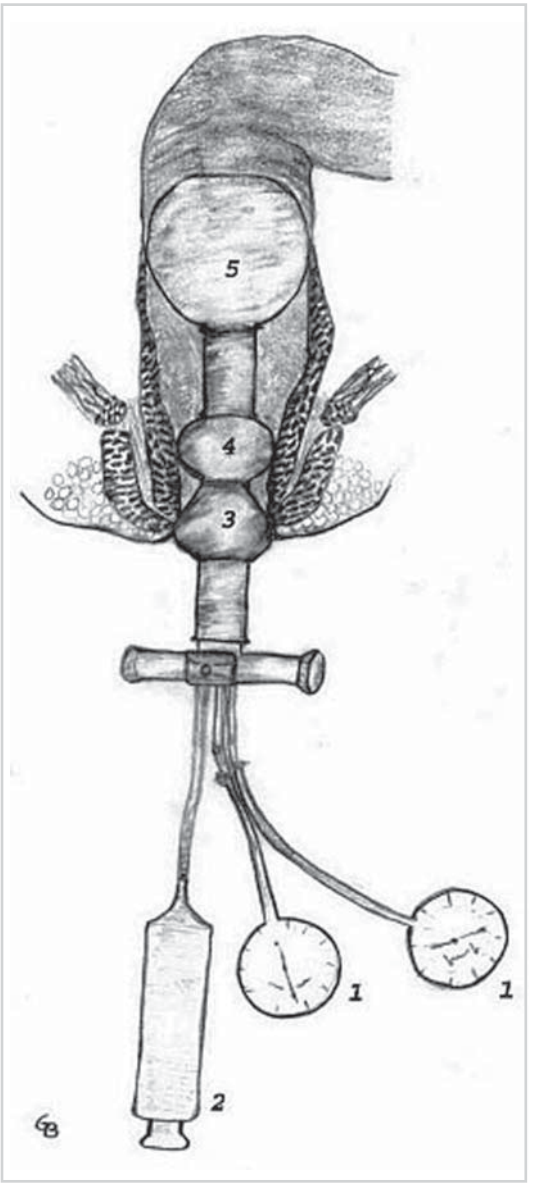


Figure 8.1. Air-filled balloon of Schuster. 1, aneroid manometer; 2, syringe for air insufflations; 3, pear-shaped balloon (for the external anal sphincter); 4, doughnut-shaped balloon (for the internal anal sphincter); 5, rectal balloon for eliciting the rectoanal inhibitory reflex.

Small Balloon Tube Technique

Another form of measuring anorectal pressures is with small tubes. The advantage of this technique is that only minor changes and irritation of the sphincters by the device itself are obtained.[6] Standardization is very important in order to obtain reliable and reproducible results; a three-balloon system is generally used. While the water-filled microballoons (diameter 5–7 mm) are placed in the upper and lower anal canal, the third balloon on top of the catheter is distended by air to elicit the rectoanal inhibitory reflex in the distal rectum (Fig. 8.2).

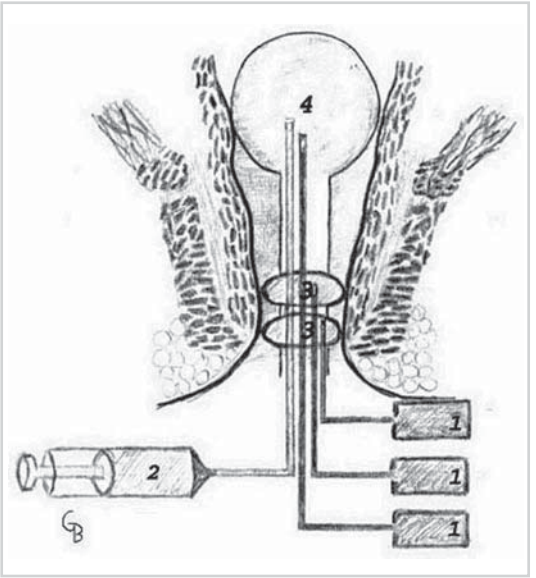


Figure 8.2. Small balloon tube technique. 1, transducer; 2, syringe for air insufflations; 3, microballoons (5–7 mm); 4, rectal balloon.

Microtransducer

The microtip pressure transducer technique was introduced to provide a simplified method for performing anorectal manometry.[7] As the name implies, the microtips are small electronic devices used to decrease artifacts; the 2-mm diameter of the microtip is mounted on a solid-state catheter (Fig. 8.3). The advantage of this technique is that, compared with balloons or larger catheters, the recordings are more physiologic due to diminished stretch artifacts of the sphincter complex.[8] Furthermore, these devices are easy to handle, stable against temperature changes, sensitive to pressure changes, and well tolerated by the patient. In the ambulatory setting, microtransducer catheters are more useful than plastic catheters.[9] The disadvantages are that the recording area is very small, pressures are measured in only one direction and not circumferentially, and these catheters are more expensive.[10] However, follow-up studies have shown no significant differences in the positioning of the microtip catheter.[11] Electronic catheters are more fragile and expensive than catheters made from plastic. Microtip pressure transducers are connected directly to a computer for recording and displaying the results.

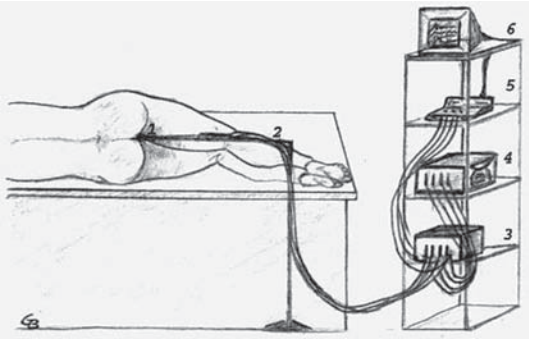


Figure 8.3. Microtransducer (3).

Water-Perfused Systems

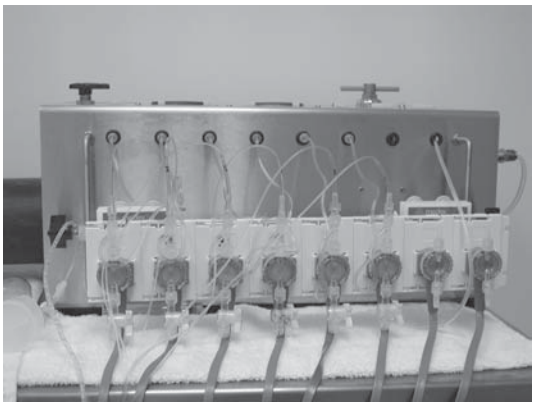
The most widely used anal manometry system is water perfused; pressures recorded are not "true sphincter pressures" but resistance pressures to a flow of water out of the catheter. At the onset of water perfusion, an artificial cavity is created, filled with the perfused fluid surrounded by the sphincter muscles. If the amount of fluid increases, a limited capacity is reached. Overfilling does not increase the artificial capacity or increase pressures, but overflow runs into the distal rectum or out of the anus. This pressure is often referred to as "yield pressure."[12] The yield pressure is reached faster with a faster perfusion rate. However, the artifacts created by the water-perfused fluid have been criticized.[13]

The advantages of the water-perfused system are its wide availability, the specific measurements, the longitudinal or radial positioning, and the relatively low costs.[14,15] This system includes a water pump, pressure polygraph, computer, and water-perfused catheters (Fig. 8.4).

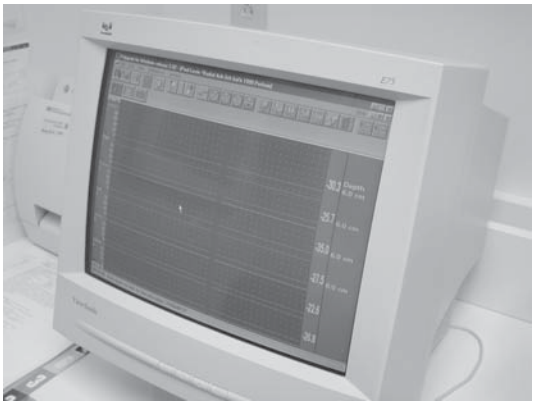
Manometry Catheters

Water-Perfused Catheters

In principle, smaller catheters are superior to larger ones and flexible are preferred over rigid. The latter have the advantage of easy insertion but are associated with patient discomfort and are often refused. Flexible catheters are more comfortable for the patient but tend to twist in the anal canal. The outside diameter should not



a



b

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Figure 8.4. Water-perfused system (a) with computer screen (b) and polygraph (c).

exceed more than 8 mm in order to diminish artifacts.[16–18] There is a huge array of various types of catheters available, most of which are made of soft plastic. The most commonly used catheters are open-end or side-open catheters, with two to eight lumina (Fig. 8.5). Arrangement of the lumina depends on the operator. Radial catheters are most useful in recording longitudinal pressures in the anal canal. Up to eight channels are used to give a precise pressure description of the different sections of the sphincter muscle during rest, squeeze, or push at a specific height. The catheters are normally marked in 1-cm intervals for vertical orientation (Fig. 8.6). Furthermore, for radial orientation into the anal canal, an additional mark should be made on the catheter. However, assessing sphincteric defects with anorectal manometry is limited.[19,20] We use a water-perfused system with four radial ports for routine evaluation and eight ports for scientific research studies. While the radial lumina are usually 5 cm apart from the catheters end in adults, the radial ports are more proximal in children. If rectal pressures are measured, an open-end catheter is preferred. Spiral catheters are useful for investigating the rectoanal inhibitory reflex. In this catheter, eight ports are set at 45-degree intervals, 5 to 8 mm apart on the longitudinal axis. A balloon at the very end of the catheter is used for rapid inflation to elicit the reflex. Sleeve catheters are rarely used in anal manometry, as with these catheters only global pressures can be recorded.

Solid-State Catheters

Konigsberg catheters are solid-state/microtip catheters for pressure measurement. They require no water perfusion setup and are therefore easy to use and give reliable, accurate

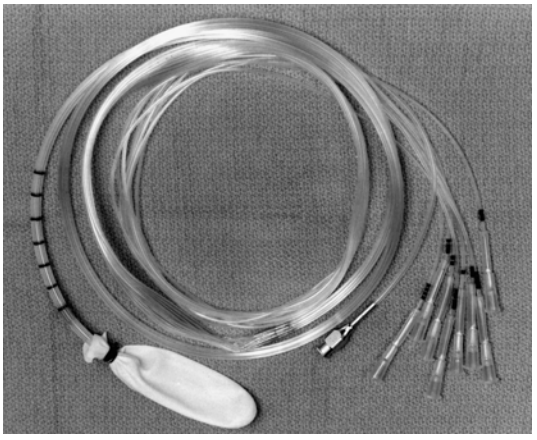

Figure 8.5. Water-perfused catheter.

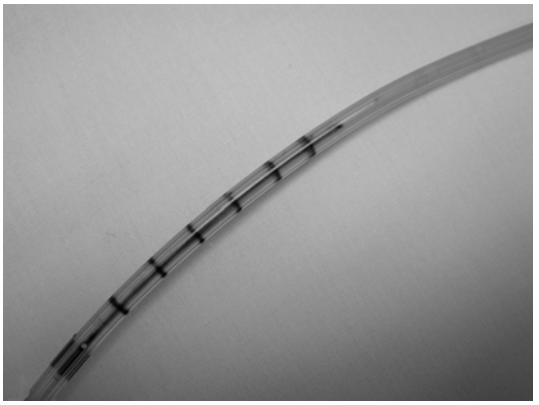

Figure 8.6. Water-perfused radial catheters with 1-cm intervals.

results. The catheters are available in a variety of configurations and come with attached probe adapters. The advantage is that these catheters can also be used in the ambulatory setting and allow evaluation in various positions.

Technique of Manometry

There are several methods to perform anal manometry. Every technique is associated with inherent pros and cons. We prefer a water-perfused stationary pull-through technique or a water-perfused automatic continuous pull-through technique. With the former method, pressures can be more accurately measured, while the latter technique has the advantage of a more exact definition of the high pressure zone. For the automatic continuous pull-through technique, a mechanical puller is utilized (Fig. 8.7). Furthermore, due to a standardized pull-through technique with a puller, a three-dimensional sphincter model can be calculated by means of a computer (Fig. 8.8).

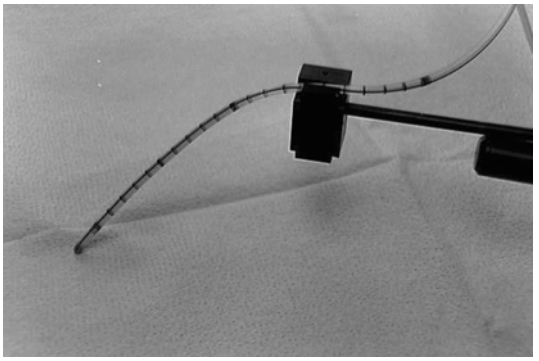

Figure 8.7. Water-perfused catheter with mechanical arm.

Definitions of Various Manonetry Techniques

1. *Stationary technique:* the catheter is left in one position during recording.
2. *Stationary pull-through:* the catheter is replaced within the anal canal, and static measurements are taken at set intervals.
3. *Continuous pull-through technique:* the catheter is moved through the lower rectum and the anal canal at a constant speed (often 1 cm/second), and the pressures are simultaneously recorded; this evaluation is done with a specially designed puller, as manual pull-through is imprecise.

Preparation and Performance of Manometry

Prior to undergoing anorectal manometry, patients are well informed regarding the need for this evaluation and are given an explanation of the technique. It is very important to let patients know that the investigation is relatively painless and that active participation is necessary to achieve accurate results. The test can usually be performed within 30 to 45 minutes. Patients are instructed to take one to two sodium phosphate enemas 2 hours prior to the evaluation.[21] This cleansing is especially important in constipated patients, as the presence of large amounts of fecal content in the rectum impairs adequate positioning of the catheters.

Digital examination can jeopardize accurate pressure measurements; therefore, it should not be performed prior to anorectal manometry.[22] The patient is placed in the left lateral decubitus position with knees and hips flexed. The manometry equipment is calibrated and the lubricated catheter inserted to the 6-cm marker. After equilibration of the system, the stationary manual pull-through technique is applied. At 1-cm intervals, resting, squeeze, and push pressures are recorded for 30 seconds. Furthermore, pressures during coughing are noted to assess the reflex activity of the external anal sphincter. An automatic continuous pull-through technique is then applied. The rectoanal inhibitory

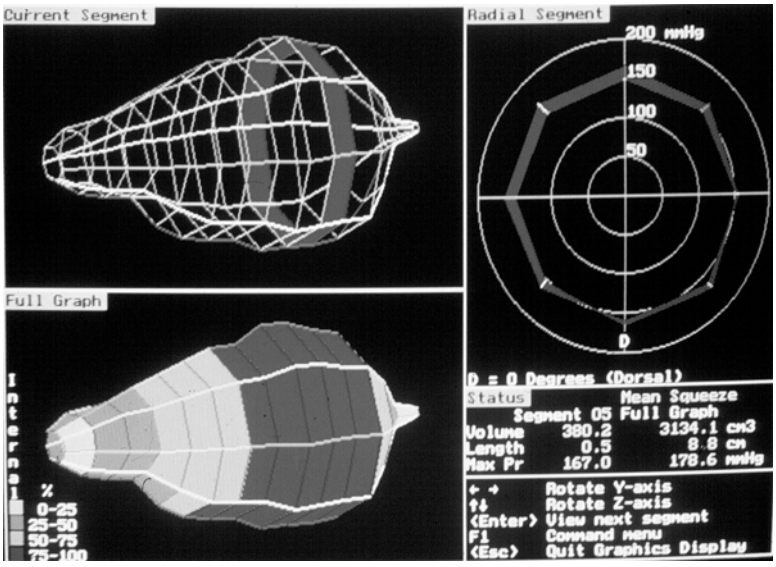

Figure 8.8. Volume vectography.

reflex is elicited by rapid inflation of a rectal balloon while the catheter is placed in the high pressure zone (Fig. 8.9).

Sensibility, urge, and rectal volume testing by inflating the rectal balloon with water are the next steps. Finally, compliance can be calculated by comparing the pressure rise with the volume of fluid used.

Potential Pitfalls and Tips

Technical problems can occur with the catheters. Electronic catheters are fragile, and water-perfused catheters can give altered results if air bubbles are in the system. Occasionally, a channel records high pressures incorrectly due to either blockage by close apposition of the

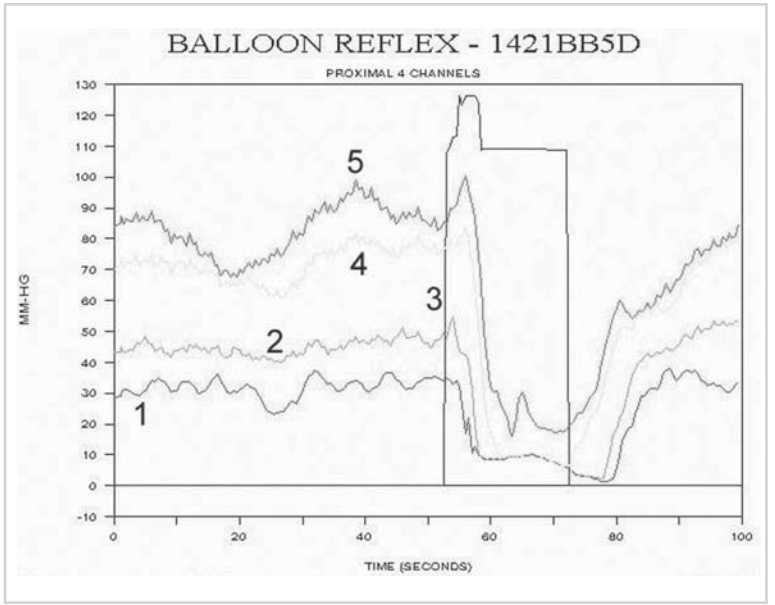

Figure 8.9. Rectoanal inhibitory reflex. 1, channel 1; 2, channel 2; 3, balloon; 4, channel 4.

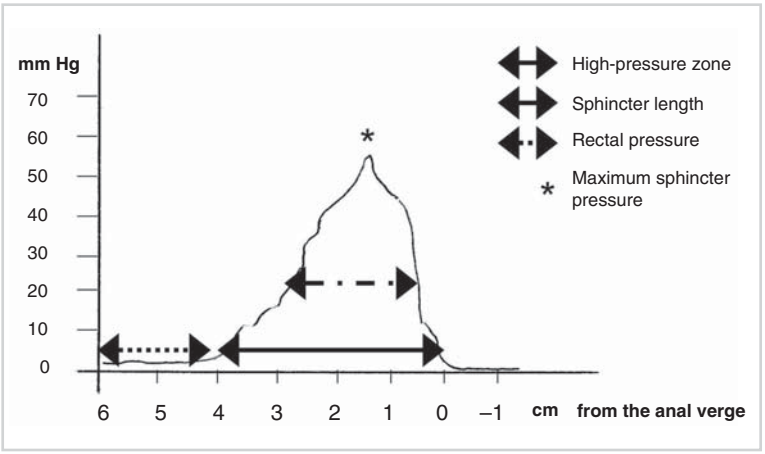

Figure 8.10. High-pressure zone. Typical longitudinal sphincter profile of a normal anal sphincter generated by a continuous pull-through technique. The high-pressure zone is defined by increase in pressure of 50% while the catheter is pulled out.

catheter to the anal wall or by stool particles. Often, a slight adjustment of the catheter will solve this problem. A lengthy investigation can modify pressures by the accumulation of water in the rectum. Eliciting the rectonal inhibitory reflex is sometimes difficult or impossible due to the rapid distention of the rectal wall, such as in patients with megarectum. Instead of eliciting the reflex, the too slow inflation will lead to repetitive relaxation of the internal anal sphincter.

Patient-dependent problems can occur during the squeeze phase. Often patients squeeze the buttocks rather than the anal sphincters, leading to erroneous results and catheter displacement. Furthermore, maximal squeeze pressures are strongly dependent on the patient's cooperation and effort.

Calculation of Manometry Data

Pressure analysis during manometry can be performed using various methods. With the stationary pull-through technique, the following parameters are evaluated:

1. Mean resting pressure (MRP): the mean of all resting pressures calculated in the high pressure zone
2. Maximal resting pressure (MaxRP): the highest pressure in the resting status in the high pressure zone
3. Mean squeeze pressure (MSP): the mean of all squeeze pressures calculated in the high pressure zone
4. Maximal squeeze pressure (MaxSP): the highest pressure achieved during squeezing in the high pressure zone
5. High pressure zone (HPZ): an increase in pressure of 50% while retracting the catheter. In the stationary pull-through technique, the HPZ can be roughly estimated. For exact determination, a continuous pull-through technique is preferable (Fig. 8.10).

Pressure Analysis

Pressure analysis should be performed in each patient in association with the clinical history. Manometry allows the therapist a good impression of the functional status of the anal sphincter complex. For pressure calculations, a few points must be considered: normal values and ranges vary among institutions. Therefore, follow-up studies should be undertaken in the same laboratory.

Females tend to have lower pressures than males.[16] While the anal canal pressures show a steady but slow decrease in female, in males pressures generally remain constant until age 60, after which there is a steep decrease, so that at age 80 in both genders the same low pressures are present. Anal pressures are dependent on the daily cycle as well as the position.[23] During daytime, pressures are higher than during nighttime.[24] Furthermore, the hydrostatic pressure must be considered, leading to higher pressures in the upright compared to the prone or supine position.[25–28] Normal manometric pressures are listed in Table 8.1.

Table 8.1. Normal manometric values (vary by age*)

Resting pressure	40–70 mm Hg
Squeeze pressure	100–180 mm Hg
High-pressure zone length**	2–3 cm (female) 2.5–3.5 cm (male)
Rectoanal inhibitory reflex	Present
Sensory threshold	10–30 cc
Rectal capacity	100–250 cc
Compliance†	3–15 cc H_2O/mm Hg

* Normal must always be considered in light of the clinical presentation and the technique used.
** High-pressure zone is defined as that point where the resting pressure decreases in at least 50% of the measured gradients by at least 20 mm Hg.
† The velocity of infusion and position and type of balloon affect compliance.

Volumetric Parameters

After evaluation of anal sphincter pressures, volumetric manometry parameters can be obtained by filling the rectal balloon with various volumes. Balloon distention is used to detect the threshold (the smallest volume of rectal distention) for three common sensations. The first detectable sensation refers to the rectal sensory threshold, the second sensation is of urgency to defecate, and the third is the sensation of pain, which is defined as the maximum tolerable volume. Rectal sensation can be assessed either by the intermittent or rapid rectal distention method. Alterations in rectal compliance may result in decreased or increased rectal capacity, impaired ability to perceive rectal distention, and altered threshold parameters.

Rectal capacity correlates well with the frequency of evacuation. Rectal compliance is the capacity of the rectum to accommodate different volumes without great alteration in rectal pressures. Therefore, rectal compliance is responsible for the degree of urgency for evacuation.

Constipated patients usually have altered sensory thresholds due to a distended rectum. A vicious cycle is created as the presence of fecal contents in the rectum distends the rectal wall and impairs the patient's perception of the need to evacuate. Rectal capacity is increased and the rectum is usually very compliant.[3]

Anorectal Pressure Response During Straining

In the constipated patient, another tool that can be utilized during anal manometry is the response of the striated muscles during straining. This evaluation can be particularly useful in patients with a history of excessive straining during defecation, the use of digitations or suppositories to evacuate, where a paradoxical contraction of the puborectalis muscle or anismus is suspected, or when other, more specific tests such as electromyography or cindefecography are unavailable. After resting and squeeze pressures are obtained, patients are asked to strain as they would during a bowel movement. The normal response is a relaxation in the pressure recordings and thus a decrease is seen in the monitor curve. In patients with anismus, this test demonstrates an opposite response: an increase in the pressure curve and a nonrelaxation of the striated muscles.[29] This test has some limitations, as the patients are usually examined in a unphysiologic position and the embarrassment created could cause a reflex contraction of the voluntary muscles. However, in a well-informed patient in an adequate ambient setting, this simple evaluation can be utilized and subsequently complemented by electromyography and/or cinedefecography.

Motility

Despite increased awareness of motility disorders and advances in the availability of instruments, colonic motility may be less well understood than in any other area of the gastrointestinal tract. One of the main reasons is the relative inaccessibility of the colon. Furthermore, recordings of colonic motility are complicated by several technical factors: colonic contents in the nonprepared colon; the influence of colonic preparation, stress, exercise, menstruation, and the use of antidepressants; and the variety of protocols used among institutions.

The investigation of colonic motility involves the study of myoelectric activity and phasic and contractile activity and movement of the intraluminal contents. For this purpose, manometric or colonic transit studies can be used. Although colonic transit studies are more common and ideal for functional analysis, colonic manometry is becoming more popular, allowing evaluation of contractile activity over prolonged periods.

In general, colonic manometry recordings of motor and myoelectrical activity in animal models have identified three contractile events: (1) short duration waves of less than 15 seconds, (2) long-duration waves of 40 to 60 seconds, and

(3) high-amplitude propagating contractions (HAPCs). In humans, reproduction of these motility patterns are more difficult to demonstrate, and reports in the literature have yielded varying results. In general, the most common recognizable events are the high-amplitude propagating contraction, which are associated with either the conscious sensation of urgency or the passage of flatus. Moreover, the absence of HAPCs may serve as a marker of colonic motor dysfunction. The frequency of these contractions varies among individuals and is more common in young children. The contractions usually start in the cecum or ascending colon and are propagated into the sigmoid colon at a rate of 1 cm/minute.

Investigation of colonic motility has increased over the last several years, and interesting findings have been reported to explain the pathophysiology of patients with slow-transit constipation. In a study of 18 patients who underwent 24-hour colonic manometry (eight patients with slow-transit constipation versus 10 controls), Hagger et al[30] observed that the frequency of HAPC was reduced in chronic idiopathic constipation, leading to a reduction in the propulsion of intraluminal contents.

In another study, Leroi et al[31] evaluated 21 patients with 24-hour colonic manometry: seven patients with constipation secondary to antidepressant use, seven constipated patients, and seven controls. The number of HAPC was lower in the two groups of constipated patients.

Colonic motility evaluation by 24-hour manometry can also be helpful in other conditions such as diverticular disease, irritable bowel syndrome, Parkinson's disease, and defecatory disorders in children.

Anorectal motility can be measured by evaluating the activity of the internal anal sphincter. This smooth muscle is responsible for the maintenance of a resting tonus through electrical and mechanical activity, which has a frequency of between 15 and 35 cycles per minute. This activity results in three wave patterns known as slow, intermediate, and ultraslow waves (Fig. 8.11).

The slow waves are the most frequent, from nine to 20 cycles per minute. The intermediate waves have frequencies varying from four to eight cycles per minute and has been noted in patients with neurogenic incontinence and after ileal pouch-anal anastomosis. The ultraslow waves are the second most frequent, with frequencies varying from five to 15 cycles per minute and were associated with the presence of hemorrhoid disease and anal fissures. In addition, the ultraslow waves have been seen in patients with high resting pressures related to chronic constipation (Fig. 8.12).

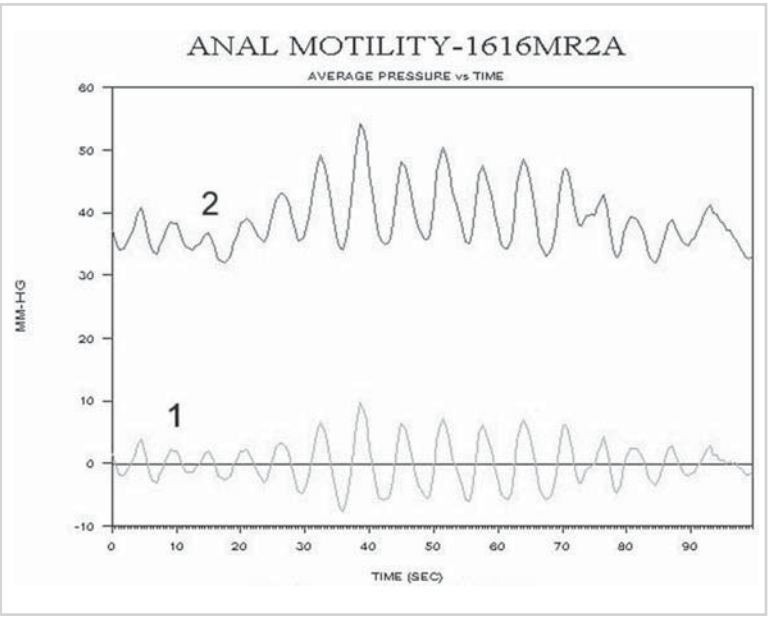

Figure 8.11. Slow, intermediate, and ultraslow wave patterns of the internal anal sphincter. 1, average pressure; 2, reduced average.

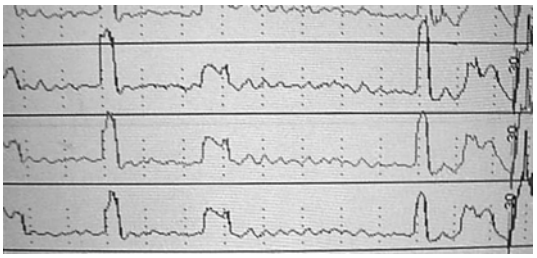

Figure 8.12. Ultraslow waves in patients with high resting pressures related to chronic constipation.

Rectoanal Inhibitory Reflex

The rectoanal inhibitory reflex (RAIR) was initially described by Gowers[1] in 1877. This reflex is a normal response to rectal distention by 10 to 30 cc of air; the external sphincter transiently contracts and there is a relaxation of the internal anal sphincter, enabling rectal contents to be "sampled" by the sensory area of the anal canal. Thus, the RAIR is generally a common finding during anal manometry. In the constipated patient, the RAIR represents an important marker for Hirschsprung's disease, as the aganglionic segment impairs the relaxation of the internal sphincter secondary to rectal distention (Fig. 8.13). Additionally, in patients with megarectum, regardless of the cause of the rectal distention, the RAIR is not always seen; the large rectum requires larger volumes to elucidate the sphincteric response. Therefore, while testing for the RAIR in constipated patients, larger volumes of air should be utilized, usually greater than 50 to 80 cc. When the RAIR cannot be demonstrated utilizing much larger volumes of air, it is advisable to change the radial catheter to a spiral manometry catheter in order to demonstrate a positive reflex in a more proximal situation.

Although demonstration of a sphincteric relaxation is the anticipated response when testing for the RAIR, recent concepts on the amplitude of relaxation and duration have been associated with constipation (J. Netinho, personal communication, 2002).

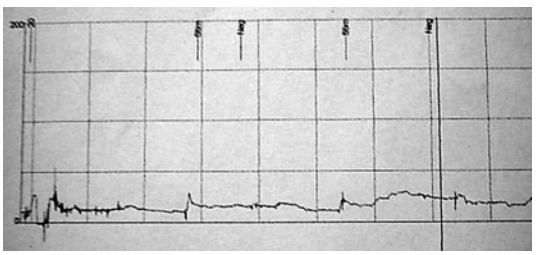

Figure 8.13. Rectoanal inhibitory reflex. Impairment of the relaxation of the internal anal sphincter, suggesting congenital megacolon.

Clinical Application of Anal Manometry

Anal manometry is an objective means of evaluating the sphincteric muscles. Differences in manometric parameters exist between males and females; sphincteric pressures and the high pressuzure zone are higher in males (Table 8.1). Similarly, differences in sphincteric profiles vary according to age.

Abnormalities in the sphincteric mechanisms can occur in a variety of conditions, including constipation. In this particular situation, anal manometry can evaluate a hypertonic sphincter, an uncoordinated pelvic floor, a nonrelaxing puborectalis, or an absent or altered rectoanal inhibitory reflex. Therefore, anal manometry can be utilized in a constipated patient to assess sphincter tonus, both at rest and during squeeze, the presence or absence of the RAIR, a nonrelaxing pelvic floor, and abnormalities in rectal sensation and the capacity to function as a reservoir.

Anal manometry is a painless and simple method of evaluation; therefore, it can be performed in both adults and children. In the pediatric population, manometry can precisely identify patients with aganglionosis or encopresis.

Manometry in Disease States

Anorectal manometry is an ideal tool for the evaluation of patients with a variety of pelvic floor disorders and is indicated for the investigation of conditions including fecal incontinence and constipation. A number of scenarios where constipation is the main symptom can be evaluated by anal manometry including encopresis, Hirschsprung's disease, neuronal intestinal dysplasia (NID) anismus, anal fissure and hypertonic sphincter, and irritable bowel syndrome (IBS).[32]

Encopresis

Various terms have been used to describe this problem, including functional encopresis,

primary nonretentive encopresis, and stool toileting refusal. Encopresis affects 1% to 3% of children, with higher rate in boys than in girls. It is characterized by the passage of large feces at intervals of less than twice per week and deferring bowel movements by contracting the pelvic floor muscles. The history usually varies from other types of constipation in children, such as aganglionosis, and no additional diagnostic testing is necessary. However, further diagnostic investigation using anal manometry is reserved for use in children who fail conservative therapy or whose history and physical examination suggest an organic etiology. In addition, manometry can detect disturbances, chiefly in the activity of the external anal sphincter, and can be a useful indicator for biofeedback therapy in these patients.[33,34]

Hirschsprung's Disease

Hirschsprung's disease is a rare congenital abnormality with an incidence of 1 in 5000 births, resulting in distal obstruction. The inadequate motility is due to aganglionosis, resulting in megacolon. Anorectal manometry is an important test in these situations, as the evaluation of the rectoanal reflex is simple and easily obtained. In these patients, the normal internal sphincter relaxation is not present in response to rectal distention, which strongly indicates Hirschsprung's disease.[35,36]

Neuronal Intestinal Dysplasia

Neuronal intestinal dysplasia (NID) is characterized by a reduced motility of the large intestine due to abnormalities of the enteric nerves. The unusually slow passage of waste through the large intestine leads to chronic problems, such as constipation and uncontrollable soiling. Neuronal intestinal dysplasia can be diagnosed soon after birth and may mimic or coincide with Hirschsprung's disease. Therefore, in well-selected patients, anal manometry, specifically through anal reflex evaluation, could be of value in the differentiation of these cases.

Anismus

Paradoxical contraction of the puborectalis is a functional disorder of the pelvic floor with some controversial aspects: the nonrelaxation of the puborectalis during straining can be observed in normal or asymptomatic patients.[37] However, the characteristic history of prolonged periods of straining, necessitating the use of suppositories or enemas, and tenesmus in females, is an indication of such functional outlet obstruction. Together with a clinical history, electromyography, and cinedefecography, anorectal manometry can aid in the selection of patients for more specific evaluations and biofeedback treatment.[38] In addition, patients in whom a nonrelaxation of the striated muscles can be easily demonstrated during anal manometry, biofeedback therapy can be utilized. In a long-term study on the effects of visual biofeedback and muscle retraining as a therapeutic modality in anismus, Battaglia el al[39] demonstrated in 24 patients the likelihood of continued benefit from biofeedback retraining during the time course.

Anal Fissure and Hypertonic Sphincter

Hypertonic internal anal sphincter have been associated with chronic anal fissures. Although the mechanism of development of hypertonia in these cases is controversial, the literature suggests that an increase in resting pressures may cause ischemia of the anal lining, with resultant pain and poor healing of the fissure. In some patients, a phenomenon known as overshoot is demonstrated when a reflex contraction of the hypertonic internal sphincter is observed in patients with chronic fissure.

Irritable Bowel Syndrome

The role of anal manometry for patients with IBS is debatable. Certainly, this evaluation should not be utilized for all patients with symptoms related to IBS. However, recent evaluation on colonic motility in patients with IBS has demonstrated that in select patients this test may be utilized for the evaluation of hypertonic sphincter and altered sensory thresholds.

Manometry for Biofeedback

Manometry can be utilized for the performance of biofeedback techniques in the treatment of fecal incontinence and constipation. The most

widely utilized method is the microballoon or water-perfused system. The patients are instructed to squeeze and relax the muscles while the physician observes the changes in the curves reproduced on the computer monitor. In the constipated patient, the focus is on obtaining relaxation of the striated muscles during straining. This technique is time-consuming and demands a well-motivated patient and physician/therapist. Before beginning the sessions, the patients should receive information regarding the mechanism of defecation, the normal actions of the pelvic muscles, and the goals of the treatment.

Despite the lack of objective data favoring biofeedback therapy for the treatment of defecation disorders, the clinical improvement and impact on the quality of life obtained by more than 60% of the patients justify its use. In addition, this method is safe and may be performed as self-training with a special home equipment apparatus. The experience of Gilliland et al[38] with selected constipated patients and a medium of four sessions of biofeedback using anal manometry demonstrated a clinical improvement in these patients. As previously demonstrated in the literature,[38,39] the number of sessions completed is the only predictable factor for the success of biofeedback therapy.

References

1. Gowers WR. The autonomic action of the sphincter ani. Proc R Soc Med (Lond) 1877;26:77–84.
2. Devroede G, Hemond M. Anorectal manometry: small balloon tube. In: Smith LE, ed. Practical Guide to Anorectal Testing. Tokyo: Igaku-Shoin Medical Publishers, 1990:55–64.
3. Jorge JMN, Wexner SD. Anorectal manometry: techniques and clinical applications. South Med J 1993; 86:924–931.
4. Schuster MM. Biofeedback treatment of gastrointestinal disorders. Med Clin North Am 1977;61:907–912.
5. Heyman S, Jones KR, Scarlett Y, Whitehead WE. Biofeedback treatment in constipation: a critical review. Dis Colon Rectum 2003;46:1208–1217.
6. Orrom WJ, Wong WD, Rothenberger DA, Jensen LL. Evaluation of an air-filled microballoon and minitransducer in the clinical practice of anorectal manometry: preliminary communication. Dis Colon Rectum 1990;33:594–597.
7. Vela AR, Rosenberg AJ. Anorectal manometry: a new simplified technique. Am J Gastroenterol 1982;77:486–490.
8. Varma JS, Smith AN. Anorectal profilmetry with the microtransducer. Br J Surg 1984;71:867–869.
9. Ronholt C, Rasmussen OO, Christiansen J. Ambulatory manometric recording of anorectal activity. Dis Colon Rectum 1999;42:1551–1559.
10. Miller R, Bartolo DCC, Roe AM, Mortensen NJMcC. Assessment of microtransducers in anorectal manometry. Br J Surg 1988;75:40–43.
11. Sundblad M, Hallböök O, Sjöhdahl R. Anorectal manometry with microtransducer. Eur J Surg 1993; 159:365–370.
12. Harris LP, Winans CS, Pope CE II. Determination of yield pressures: a method for measuring anal sphincter competence. Gastroenterology 1966;50:754–760.
13. Hancock BD. Measurement of anal pressure and motility. Gut 1976;17:645–651.
14. Dalley AF II. The riddle of the sphincters: the morphophysiology of the anorectal mechanism reviewed. Am Surg 1987;53:298–306.
15. Lestar B, Penninckx F, Kerremans R. The composition of anal basal pressure. An in vivo and in vitro study in man. Int J Colorect Dis 1989;4:118–122.
16. Pfeifer J, Oliveira L, Park UC, Gonzales A, Nogueras JJ, Wexner SD. The relation of normal manometry to age and gender. Tech Coloproctol 1996;4:10–13.
17. Coller JA. Clinical application of anorectal manometry. Gastroenterol Clin North Am 1987;16:17–33.
18. MacHugh SM, Daimant NE. Effect of age, gender and parity on anal canal pressures. Dig Dis Sci 1987; 32:726–736.
19. Jorge JMN, Wexner SD. A practical guide to anorectal physiology. Contemp Surg 1993;443:214–224.
20. Rao SS, Hartfield R, Soffer E, Rao S, Beaty J, Conklin JL. Manometric tests of anorectal function in healthy adults. Am J Gastroenterol 1999;94:773–783.
21. Azpiroz F, Enck P, Whitehead WE. Anorectal functional testing: review of collective experience. Am J Gastroenterol 2002;97:232–240.
22. Hardcastle JD, Mann CV. Study of large bowel peristalsis. Gut 1968;9:512–520.
23. Kumar D, Williams NS, Waldron D, Wingate DL. Prolonged manometric recording of anorectal motor activity in ambulant human subjects: evidence of periodic activity. Gut 1989;30:1007–1011.
24. Enck P, Eggers E, Koletzko S, Erckenbrecht JF. Spontaneous variation of anal "resting" pressure in healthy humans. Am J Physiol 1991;261:G823–G826.
25. Johnson GP, Pemberton JH, Ness J, Samson M, Zinsmeister AR. Transducer manometry and the effect of body position on anal canal pressures. Dis Colon Rectum 1990;33:469–475.
26. Harris LD, Pope CE II. "Squeeze" vs. resistance: an evaluation of the mechanism of sphincter competence. J Clin Invest 1964;43:2272–2278.
27. Taylor BM, Beart RW, Philips SF. Longitudinal and radial variation of pressure in the human anal sphincter. Gastroenterology 1984;86:693–697.
28. Morgado PJ Jr, Wexner SD, Jorge JMN. Discrepancies in anal manometric pressure measurement: important or inconsequential? Dis Colon Rectum 1994;37:820–823.
29. Park UC, Choi SK, Piccirillo MF, Verzaro R, Wexner SD. Patterns of anismus and the relation to biofeedback therapy. Dis Colon Rectum 1996;39:768–773.
30. Hagger R, Kumar D, Benson M, Grundy A. Colonic motor ativity in slow-transit idiopathic constipation as identified by 24-h pancolonic ambulatory manometry. Neurogastroenterol Motil 2003;15:515–522.

31. Leroi AM, Lalaude O, Antonietti M, et al. Prolonged stationary colonic motility recording in seven patients with severe constipation secondary to antidepressants. Neurogastroenterol Motil 2000;12:149–154.
32. Drug VL, Bradatan B, Tarasi I, et al. The importance of ano-rectal manometry in irritable bowel syndrome. Rev Med Chir Soc Med Nat Iasi 2000;104:43–50.
33. Pensabene L, Youseef NN, Griffiths JM, Di Lorenzo C. Colonic manometry in children with defecatory disorders: role in diagnosis and management. Am J Gastroenterol 2003;98:949–950.
34. Blesa Sierra MfM, Nunez R, Blesa Sanchez E, Vargas I, Cabrera Garcia R. Utility of anorectal manometry in the diagnosis and treament of encopresis. Ann Pediatr 2004;60:310–315.
35. Kara S, Istek D, Okandan M. Low-cost instrumentation for the diagnosis of Hirschsprung's disease. J Med Syst 2003;27:157–162.
36. Loening-Baucke VA. Anorectal manometry: experience with strain gauge pressure transducers for the diagnosis of Hirschsprung's disease. J Pediatr Surg 1983; 18:595–600.
37. Schouten WR, Briel JW, Auwerda JJ, et al. Anismus: fact or fiction? Dis Colon Rectum 1997;40:1033–1041.
38. Gilliland R, Heymen S, Altomare D, Park UC, Vickers D, Wexner SD. Outcome and predictors of success of biofeedback for constipation. Dis Colon Rectum 1997;84:1123–1126.
39. Battaglia E, Serra AM, Buonafede G, et al. Long term study on the effects of visual biofeedback and muscle training as a therapeutic modality in pelvic floor dyssynergia and slow-transit constipation. Dis Colon Rectum 2004;47:90–95.

9

Defecography: Technique, Interpretation, and Current Use

Arden M. Morris and Susan C. Parker

Defecography, or evacuation proctography, is the dynamic study of expulsion of radiopaque material from the rectum, in order to assess changing anatomic relationships of the pelvic floor and associated organs during evacuation. In 1952, Wallden[1] first described enteroceles, sigmoidoceles, and rectoceles, using roentgenogram techniques developed to evaluate patients with symptoms of obstructed defecation. He postulated that such outlet obstruction was due to an abnormally deep rectogenital pouch and could be corrected surgically. However, performing these static studies using rectal, vaginal, and small bowel contrast was a cumbersome, expensive, and embarrassing process for the patient. Recognizing the limitations of these studies, subsequent authors streamlined the procedure over the ensuing three decades.

Broden and Snellman[2] proposed the use of cineradiographic methods and a physiologic position, which contributed enormously to the simultaneous study of function and anatomy. Several centers built radiolucent commodes with air and water chamber modifications to optimize image density.[3] To more closely replicate stool consistency, investigators varied the texture of barium contrast with materials such as oatmeal and potato starch. Technological advancements in videography and manufacturing have enhanced sophistication, efficiency, and patient comfort during the test.

Today, defecography can provide an invaluable aid in the diagnosis and treatment planning for patients with constipation and rectal outlet obstruction issues. This chapter explores the current use of defecography, with a special focus on technique, interpretation, and implications for specific patient populations.

Indications for Testing

Constipation

Defecography was initially developed to assess patients with complaints of constipation and a sensation of rectal outlet obstruction. The diagnostic armamentarium has expanded to include anal manometry, electromyography, and colonic transit time studies, all of which are crucial for distinguishing end-organ versus total organ etiologies. Therefore, although the major indication for performing defecography continues to be constipation, other complaints may occasionally warrant defecographic evaluation. Table 9.1 demonstrates the primary indications and their proportionate prevalence among our referred patients. There is considerable overlap in many of these symptoms and diagnoses.

Suspected Enterocele or Rectocele (Obstructed Defecation)

Patients with symptoms of enterocele or rectocele describe prolonged straining at defecation, with a sensation of partial or complete blockage (frequently a "closed trapdoor" preventing passage of stool). Defecography can demonstrate the presence of a rectocele or enterocele, suggest the presence of a peritoneocele, and clarify contributing disorders such as a nonrelaxing pelvic

Table 9.1. Indication for defecography among patients referred to the Minnesota Center for Pelvic Floor Disorders seen over a 12-month period

Indication for defecography	% ($n = 954$)
Constipation	33
Suspected enterocele or rectocele (obstructed defecation)	11.3
Incomplete emptying	6.3
Rectal intussusception or prolapse	11.3
Fecal incontinence	31.3
Pain with defecation	3.7
Urinary incontinence or uterovaginal prolapse	2.5
Postoperative evaluation	0.6

floor, rectal intussusception or prolapse, and potentially uterovaginal prolapse.

Incomplete Emptying

Incomplete emptying refers to a sensation of stool retained in the rectum after defecation, coupled with an immediate need to empty again or a need for digital manipulation in order to attempt complete evacuation. Incomplete emptying is closely related to obstructed defecation and is generally caused by rectal intussusception, rectocele, or enterocele.

Rectal Intussusception or Prolapse

Internal prolapse or intussusception may be difficult or impossible to diagnose without defecography. As intussusception progresses toward overt prolapse, patients may complain of rectal bleeding and a sensation of fullness. Physical exam reveals a patulous anus with decreased sphincter tone. Anoscopy or rigid proctoscopy may demonstrate associated conditions, such as erythema or a solitary rectal ulcer, thought to be caused by sheer stress on the anterior rectal wall.

Fecal Incontinence

Defecography plays a limited role in evaluation of fecal incontinence, and is most useful among those patients with attendant obstructive symptoms. Defecography can aid in the diagnosis of overflow fecal incontinence, demonstrating retention of stool due to a nonrelaxing puborectalis muscle or retained stool within a large rectocele.

Pain with Defecation

Ill-defined low pelvic pain and painful straining at defecation (tenesmus) are frequently difficult to explain and even more difficult to treat. After evaluating for obvious sources, such as fissure, hemorrhoids, or ulcer, defecography may help to establish or exclude an anatomic etiology. For example, paradoxical contraction of pelvic muscles may explain anismus and cramping or spastic pain. Extensive perineal descent may result in stretching of the pudendal nerve that can cause a dull, aching sensation after defecation.

Urinary Incontinence and Uterovaginal Prolapse

Up to 41% of patients with urogynecologic pelvic floor disorders also have fecal incontinence; therefore, Kelvin et al[4] and others have recommended a complete pelvic floor evaluation prior to extensive operative intervention. Alternatively, repair of an anterior enterocele or rectocele may uncover previously occult urinary incontinence. Clearly, a careful history and thorough evaluation are necessary prior to planning an intervention for patients at risk for both urogynecologic and anorectal disorders (generally postmenopausal multiparous women).

Postoperative Evaluation

Follow-up evaluation of postoperative patients is a little-discussed but important indication for defecography. Patients who experience difficult evacuation after an ileal pouch–anal anastomosis may have a long spout, kinking of the pouch or spout, a strictured anastomosis, or another mechanical reason for obstruction. Defecography may be helpful for the evaluation of new-onset evacuation difficulties after a sphincteroplasty, prolapse repair, or colon resection. Alternatively, it may help to assess patients with unrelieved symptoms of incontinence after a repair, or to ascertain continence prior to stoma closure.

Technique

Dynamic defecography, as originally described by Broden and Snellman[2] in 1968, used rectal, small bowel, and vaginal contrast. Since that

initial description, the technique has been further refined, but a consensus still does not exist regarding the optimal examination technique. Practitioners may vary the number of cavities or organs that are opacified (small bowel, vagina, bladder, peritoneum), the method of opacification (ingested or injected contrast, contrast applied to a sponge or tampon), and even the type of contrast used for each anatomic site (liquid, paste, or prepared mixtures).

Contrast

Options for rectal contrast preparations include barium suspension, mixtures of barium and starch (oatmeal, potato flakes), and commercial products formulated specifically for defecography.

Ikenberry and colleagues[5] compared three types of contrast (thin barium liquid, commercial paste, and thick prepared contrast paste) in normal subjects and found that contrast materials and consistency altered their pathologic findings. Increased viscosity resulted in a significantly increased anorectal angle measurement. Using thin barium decreased evacuation time and increased the prevalence of intussusception. The authors found little benefit to the use of elaborate heated mixtures of barium and starch but advised against the use of liquid alone or with other contrasts, particularly when diagnosing intussusception.

Mahieu et al[6] also found thin contrast inferior; among other issues, its rapid passage led to missed pathologic results. Additionally, evacuation of thin barium requires less pelvic floor relaxation than do more viscous substances. However, use of thinner contrast would be appropriate among patients who normally pass liquid stool, such as some individuals who have undergone proctocolectomy and ileoanal pouch procedure.

Pelvic Structures

Instillation of radiodense contrast into adjacent organs or cavities can provide useful information about abnormal changes in pelvic anatomy during defecation. For example, placement of a barium-soaked tampon or gauze sponge, gel, or thin barium in the vagina allows visualization of vaginal wall motion, possible anterior pelvic prolapse, and potential widening of the rectovaginal space, which may indicate an enterocele. Some authors discourage tampon use, arguing that it stents the vagina, thereby obscuring rectoceles, enteroceles, and prolapse.[7,8] We recommend opacification of the vagina with 5 to 10 cc of thick barium paste (barium sulfate esophageal cream, 60% w/w, E-Z-EM, Westbury, NY) inserted using a rounded flexi-tip applicator. Contrast is slowly injected as the applicator is withdrawn to coat the entire length of the vagina.

The use of bladder contrast is less common and requires sterile bladder catheterization and the instillation of 150 to 200 cc of water-soluble contrast. Bladder opacification is advocated for patients with bladder symptoms or a large vaginal eversion, and can help to differentiate a cystocele from an enterocele or rectocele.[9]

Peritoneal Cavity

The small intestine may be highlighted by ingestion of an oral barium meal given 45 minutes to 1.5 hours before the defecography study, to allow transit to the distal loops of bowel most likely to lie in the pelvis. Although a wide space between the rectum and vagina filled with air lucency may indicate an enterocele, the diagnosis is made easily if contrast-filled loops of bowel occupy that space. However, a deep pouch of Douglas may not fill with small bowel on all occasions, resulting in an underinterpretation of enteroceles.

Peritoneography allows visualization of the potential enterocele space by outlining the peritoneum with a liquid, water-soluble contrast.[10] As originally described by Gullmo,[11] 60 cc of contrast in inserted via injection into the peritoneal cavity in the left lower quadrant or infraumbilically. Other than highlighting the rectovaginal space, peritoneography reveals the presence (or absence) of in-dwelling organs.

Filming and Position

Once contrast is inserted, spot films may be taken either with the patient lying in the lateral decubitis position or sitting on a special radiolucent commode. The pelvis and opacified rectum are filmed while the patient is instructed

to rest, squeeze, strain, and cough. The films permit measurement of perineal descent with straining, changes in the anorectal angle, and changes in anal canal length.

Lateral radiographs of the pelvis produce glare in the area of the anal canal, due to the difference in radiolucency between air and the pelvis.[12] Commodes used for defecography are designed to reduce the variation by employing a filtration device to absorb radiation below the seat and buttocks. Options include metal strips (usually copper) attached to the side of the commode or water-filled bottles or a doughnut below the seat. Commodes can be constructed of horizontally grained pine wood with steps up to a raised seat for ease of filming in a normal sitting position. Alternatively, a commode can be clamped to a horizontal x-ray table beneath a patient in the lateral decubitis position. With vertical movement of the table, the patient ends up sitting on the commode. This design allows filming of the patient during the movement from the supine to the sitting position, a distinct advantage among patients with fecal incontinence or significant genital prolapse, for example, who quickly lose contrast in an upright position. Of course, the lateral decutibus position is not in any way physiologic as compared to the seated upright position. Moreover, prospective patient evaluation revealed statistically significant differences between the two positions relative to anorectal angle, perineal descent, and puborectalis length.[13] Because of these differences, the same technique should be used in each incidence in the same center. Whether the left lateral decubitus or upright position is selected, the same position should always be used.

Risks

Perforation

Potential abrasion of the rectum during catheter insertion is a minor risk. Perforation of the rectum during defecography is more a theoretical than a real risk. After 3000 defecographies, our center has yet to experienced such an event, and there are no reports of it in the literature. However, perforation of the small bowel during peritoneography contrast injection has been reported. Our center has a 3% rate of complications including small-bowel perforation, pain, fever, and bleeding during peritoneography. All complications were treated conservatively, with no adverse sequelae.[14]

Radiation Dose

The radiation dose from fluoroscopy can vary widely but is generally low. The radiation dose from a barium enema is two to three times that of defecography.[15] Goei and Kemerink[16] estimated the mean effective dose at 4.9 mSv for females and 0.6 mSv for males; the difference is due to the higher gonadal dose among females compared to males. In contrast to the uterus and ovaries, which are always within the primary beam, the testes are only exposed to scattered radiation. The authors found a wide range of effective doses due to individual variations in speed of evacuation. For comparison, the effective dose due to background radiation is 3 mSv/year. Assuming that 10 mSv carries an increased risk of fatal cancer of 0.04%, the risk increase for females is 0.08% and the risk increase for males is 0.008% above the normal lifetime fatal cancer risk of 20%.

Measurement Parameters and Interpretation

Normal Defecation

Familiarity with the basic steps of evacuation is essential for accurate interpretation of cinedefecography. As shown in Figure 9.1, the process begins with migration of stool into the rectum. The increased rectal volume leads to stimulation of pressure receptors located on the puborectalis muscle and in the pelvic floor muscles, which in turn stimulate the rectoanal inhibitory reflex (RAIR). The RAIR consists of external anal sphincter contraction and internal anal sphincter relaxation, allowing sampling of anal canal contents. When the anal canal is deemed to have solid contents and a decision is made to evacuate, the glottis closes, pelvic floor muscles contract, and the diaphragm and abdominal wall muscles contract—all of which increase abdominal pressure. The puborectalis muscle relaxes, resulting in straightening of the anorectal angle, and the pelvic floor descends slightly. The external anal sphincter relaxes and anal canal

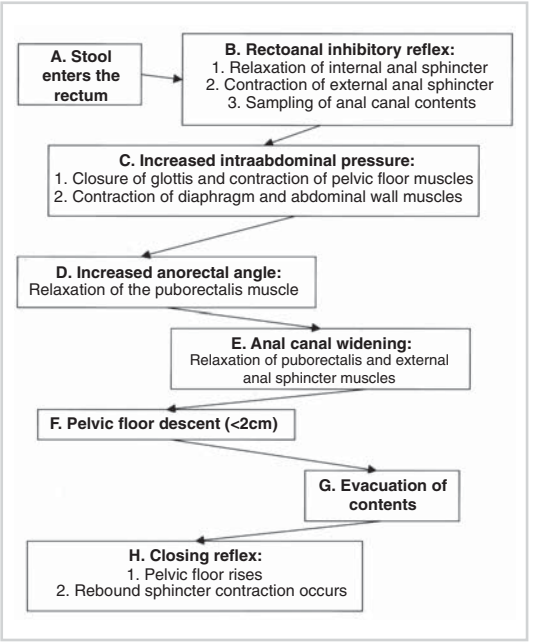

Figure 9.1. The steps of normal defecation.

contents are evacuated. Upon normal complete evacuation, the pelvic floor rises and sphincters contract once more in a "closing reflex."

Measurement Parameters

Appropriate parameters to be measured during defecography have evolved over time, based on the contributions of numerous authors. Accordingly, consistent objective measures and their implications are not yet universally accepted due to a lack of uniform technique.[3,5,17] However, the following definitions are generally considered standard based on their widespread use:

Anal canal length: The distance from the anal verge (defined by barium marking the skin or a marker placed on the perineum) to the rectum.

Anorectal angle: The angle between the axis of the anal canal and the posterior rectal wall (posterior anorectal angle) or the center of the rectum (central anorectal angle).

Perineal descent: The vertical movement of the anorectal junction from its position at rest. Reference points are the ischial tuberosities[5] or the pubococcygeal line drawn from the pubis to the tip of the coccyx.[6]

Peritoneocele: A caudal extension of the pouch of Douglas or rectouterine excavation to below the upper third of the vagina. A peritoneocele can contain fluid or omentum and is termed an enterocele when it contains bowel. Peritoneoceles can be further described as septal, vaginal, and rectal, based on anatomic features.[10]

Rectal intussusception: A descent of the entire thickness of the rectal wall, which can extend to the anal verge. When the rectal wall intussuscepts inferiorly through the anus, the condition is termed rectal prolapse.[18]

Rectocele: A rectocele is defined as an outpouching of the rectum that is more pronounced during straining and typically occurs anteriorly, although posterior rectoceles have also been described. More than 2 cm of outpouching may be considered abnormal.

Rectosacral gap: The horizontal distance between the posterior line of the rectum and the sacrum at S3.[17]

Rectovaginal space: The distance between contrast in the vaginal and contrast in the rectum.[18]

Sigmoidocele: Abnormal descent of a loop if sigmoid into the pelvis which may be first, second, or third degree (Fig. 9.2).[19]

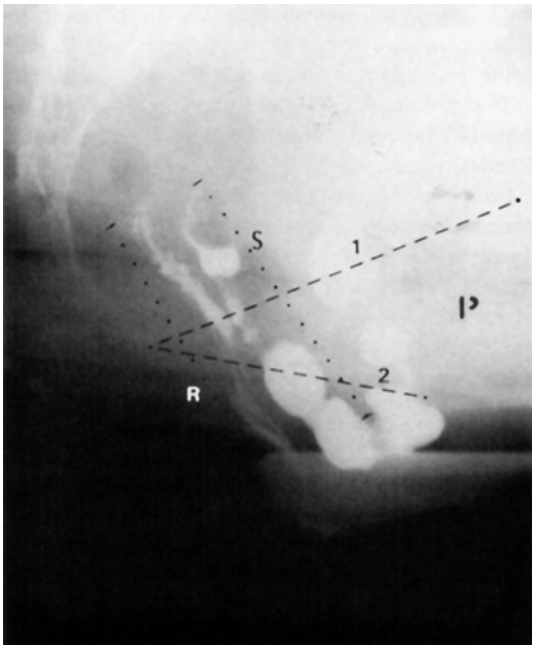

Figure 9.2. Measurement of the three degrees of sigmoidocele. (From Jorge et al.[19])

Interpretation: "Normal" Versus "Abnormal"

The most widely cited early study of "normal" volunteers was conducted by Mahieu and colleagues,[3] who retrospectively reviewed 56 defecograms deemed normal from 188 sequentially studied patients. These authors identified five radiologic signs consistently present in normal patients during defecation including (1) increase of the anorectal angle, (2) obliteration of the impression of the puborectalis muscle, (3) widening of the anal canal, (4) total or slightly incomplete evacuation of rectal contents, and (5) good resistance of the pelvic floor (Table 9.2). The authors also defined normal as the absence of pathologic findings. These five criteria have not been validated in any prospective study, nor were they formally validated in the cited study by a prospective application to retrospective data. Nonetheless, numerous subsequent investigators have used the five criteria as objective measures of normal defecography, and thus have contributed to their construct validity.

Shorvon and associates[17] studied 47 symptomatically normal volunteers who displayed a broad range of results with respect to anorectal angles and perineal descent. Some of the self-described normal subjects exhibited surprisingly pathologic anorectal function, such as fecal incontinence. The authors identified mucosal prolapse or intussusception in 50% of the subjects and rectoceles (defined as any bulge outside the anterior line of the rectum) in 81% of the nulliparous women. However, barium-soaked tampons were inserted into the vagina and thin barium was used to coat the rectal wall prior to placement of a thick paste—both are techniques that may alter results.[5,20]

Table 9.2. Cinedefecography findings indicating a normal test result

Finding during defecation	% normal patients ($n = 56$)
Anorectal angle increase	100
Obliteration of puborectalis muscle impression	96
Anal canal widening	100
Total vs. slightly incomplete evacuation	55 vs. 45
Pelvic floor descent <2 cm	84

Adapted from Mahieu et al.[3]

Table 9.3. Variability in "normal" measurements within and between studies

Measurement	Rest	Strain
Anorectal angle (degrees)	60–105 (Goei[22]) 83–131 (Goei[22]) 70–140 (Ekberg[23]) 65–134 (Mahieu[3])	— 106–134 (Goei[22]) 110–180 (Ekberg[23]) 105–164 (Mahieu[3])
Perineal descent		2 cm
Anal canal	22 mm men 16 mm women	17 mm (Shorvon[17]) 14 mm
Emptying		All or almost all
Rectocele		None (Mahieu[3]) <2 cm (Shorvon[17])
Rectosacral gap	10 mm (Shorvon[17])	

Table 9.3 shows some of the variation seen within and between studies attempting to establish normal measurement parameters. Given the difficulty of defining a normal result, how does one identify the abnormal? Generally, abnormal is characterized by subjective symptoms and measurement parameters outside of the broad "normal" categories. Results deemed abnormal might include (1) an obtuse or nonchanging anorectal angle, (2) nonrelaxation or paradoxical contraction of the puborectalis, (3) incomplete evacuation or a need for manual assistance to evacuate, (4) lack of or excessive perineal descent, (5) abnormal bowing of the rectal walls (rectal wall teacupping, internal prolapse, frank prolapse), or (6) an increasing distance between structures, suggesting a cystocele, sigmoidocele, enterocele, or peritoneocele.

Reproducibility

Variation in the reproducibility of specific defecography measurements remains an unresolved issue. To determine interobserver variation, four independent observers, two blinded to the patient's history, reviewed randomly sequenced videodefecographies performed in constipated patients. Two weeks after the initial assessment, intraobserver variation was determined by a repeat blinded review of unlabeled randomly sequenced studies. The results of interobserver accuracy for sigmoidocele, rectal sigmoidocele, intussusception, rectal prolapse, rectal empyting, opening of the anal canal, puborectalis contraction, and straightening of the anorectal angle and rectal empyting were 89.5%, 46%, 87.5%, 97.5%, 86.5%, 88.5%, 83%, and 80%, respectively. The intraobserver variations for these same variables

were 83.8%, 80%, 94.5%, 77%, 84.8%, 80.5%, and 85.5%, respectively. In summary, videodefecography had an overall accuracy of 82.3%.[24] Yang et al[25] reviewed the reproducibility of five measurements—posterior and central anorectal angles during rest, squeeze and strain, maximal width of the anal canal, maximal width of the rectal lumen, and size of the rectocele. The authors reported only fair interobserver agreement but high correlation among most intraobserver measurements, and these findings have been confirmed by other studies.[17,22] Ferrante and colleagues[7] noted significant interobserver variation in anorectal angle measurements between three interpreters but good intraobserver consistency, suggesting that variation in anorectal angle measurements may be due to subjective interpretation of the rectal axis along the curved rectal wall.

Ultimately, interpretation of defecography must rely on a constellation of measures, as well as the dynamic functional process. Improved standardization of measurement techniques clearly would contribute to more reproducible results, which would enhance interpretability. Additionally, understanding what is normal and acceptable to the individual patient is crucial to appropriate interpretation and treatment planning. In the next section, we discuss specific disorders diagnosed by defecography and their implications for treatment.

Anorectal Disorders: Diagnosis and Implications

Intussusception/Prolapse

Early defecographers recognized rectal intussusception (an abnormal telescoping descent of the rectum) as an antecedent to frank prolapse (a rectal eversion protruding through the anal orifice).[1,2,26] Defecography permits the diagnosis of prolapse or near prolapse in patients presenting with vague symptoms of bloody or mucus drainage, painful or ineffective straining at defecation, or a sensation of obstructed defecation. The ability to distinguish between mild to moderate intussusception and near frank prolapse has some value; while satisfactory treatment for intussusception is limited, a number of effective operations for prolapse have been developed. Defecography provides additional value by clarifying the presence of concomitant anatomic abnormalities, which may be addressed during a prolapse repair.

Rectocele

A rectocele is defined as greater than 2 cm of rectal wall outpouching or bowing while straining, and can precede or accompany rectal intussusception, as demonstrated in Figure 9.3. The rectocele can prevent passage of stool both by obstructing the anal orifice and by acting as a diverticulum to sequester stool. Patients with rectoceles commonly complain of the need for frequent sequential episodes of defecation, and even for manual compression or splinting of the anterior perineum or posterior vagina in order to completely evacuate. Additionally, with relaxation, patients may experience reduction of the rectocele and return of the sequestered stool to the lower rectum, potentially resulting in incontinence. Rectoceles are found in 25% to 50% of women, and are often asymptomatic.[23,27]

Van Dam and associates[28] investigated the utility of defecography in predicting the outcome of rectocele repair. Rectocele size, barium trapping, intussusception, evacuation, and perineal descent were measured during defecography exams of 74 consecutive patients with symptomatic rectoceles. The patients then underwent a transanal/transvaginal repair, followed by a 6-month-postoperative defecography and reassessment of the five most common presenting symptoms (excessive straining, incomplete evacuation, manual assistance required, sense of fullness, bowel movement less than three times per week). No postoperative defecograms demonstrated a persistent or recurrent rectocele; however, one third of patients had a poor result based on persistent symptoms. There was no association between defecography measurements and outcome of the repair. Still, the authors concluded that defecography serves three major purposes in the evaluation of a rectocele: preoperative evidence of its presence and size, documentation of additional pelvic floor abnormalities, and an objective assessment of postoperative changes.

Enterocele/Peritoneocele

A peritoneocele is a caudal invagination of the peritoneum, between the posterior vaginal wall

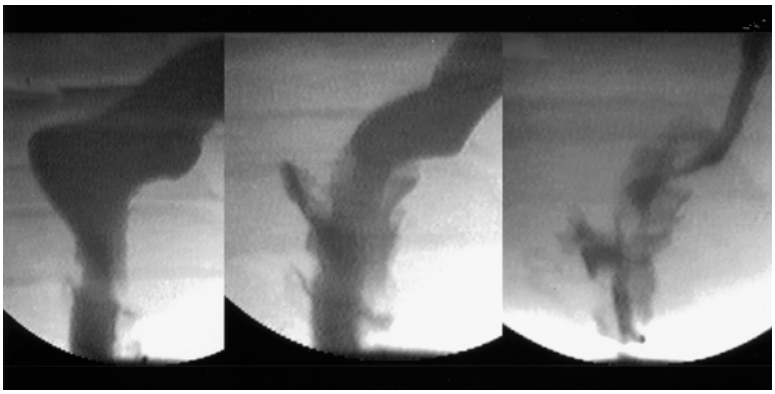

Figure 9.3. Rectal intussusception or internal prolapse, increasingly pronounced with straining. Note the initial appearance of an anterior rectocele, followed by the "teacup" appearance of the middle image.

and the anterior rectal wall, to a distance of >2 cm or inferior to the proximal one third of the vagina (Fig. 9.4). The peritoneocele may intermittently contain small bowel contents, resulting in an enterocele (Fig. 9.5). On defecography without peritoneography, a peritoneocele is suggested by an unexplained increase in the rectovaginal (or rectogenital) space during straining. Similarly, an enterocele is suggested by air-filled small-bowel loops within that space.

Increasing use of defecography has led to more frequent diagnosis of enteroceles; their prevalence is now estimated at 18% to 37%, and upward of 55% of patients with an enterocele have other concomitant pelvic floor disorders.[29] However, little is known of the actual impact enteroceles have on rectal emptying. Halligan and colleagues[30] prospectively studied 50 consecutive patients with constipation, and compared their results with 31 controls undergoing peritoneography for groin pain. Although a majority of constipated patients (77% versus 10% in the control group) had deep rectogenital pouches, only 58% filled with small-bowel contents during the study. Moreover, those patients with an enterocele evacuated more rapidly and completely than did the constipated patients with or without a deep pouch.

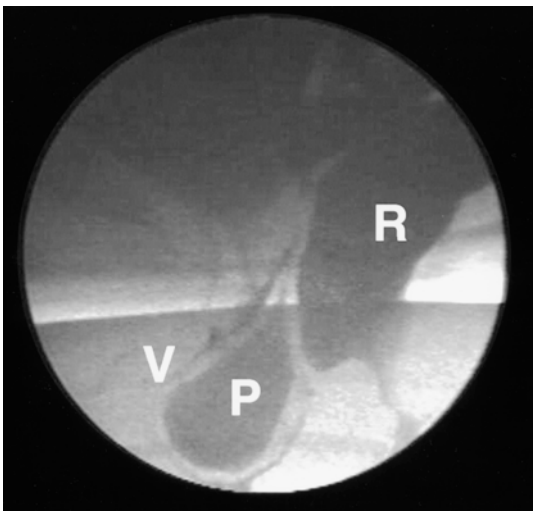

Figure 9.4. A peritoneocele extending through the vaginal introitus, seen with combined defecography and peritoneography. V, vagina; R, rectum; P, peritoneocele.

When is the diagnosis of an enterocele relevant? Among the 11% of U.S. women who will have a pelvic floor repair by age 80 years,[31] preoperative identification and concomitant repair of a peritoneocele or enterocele may help to prevent persistent symptoms or early recurrence of obstruction.[22] Nonetheless, among minimally symptomatic or asymptomatic patients, or among those in whom a repair is not otherwise warranted, the prudent surgeon must not overconstrue the importance of an incidentally identified enterocele.

Sigmoidocele

The existence and clinical implications of sigmoidocele are controversial. We have demonstrated that a deep rectovaginal pouch may contain small bowel at one time and sigmoid at another time, in the same patient. Jorge et al[19] maintain that, as opposed to the small bowel, the herniated sigmoid is more prone to stasis, owing to its larger diameter and more solid contents.

Jorge et al[19] undertook a study to assess the incidence and clinical significance of sigmoi-

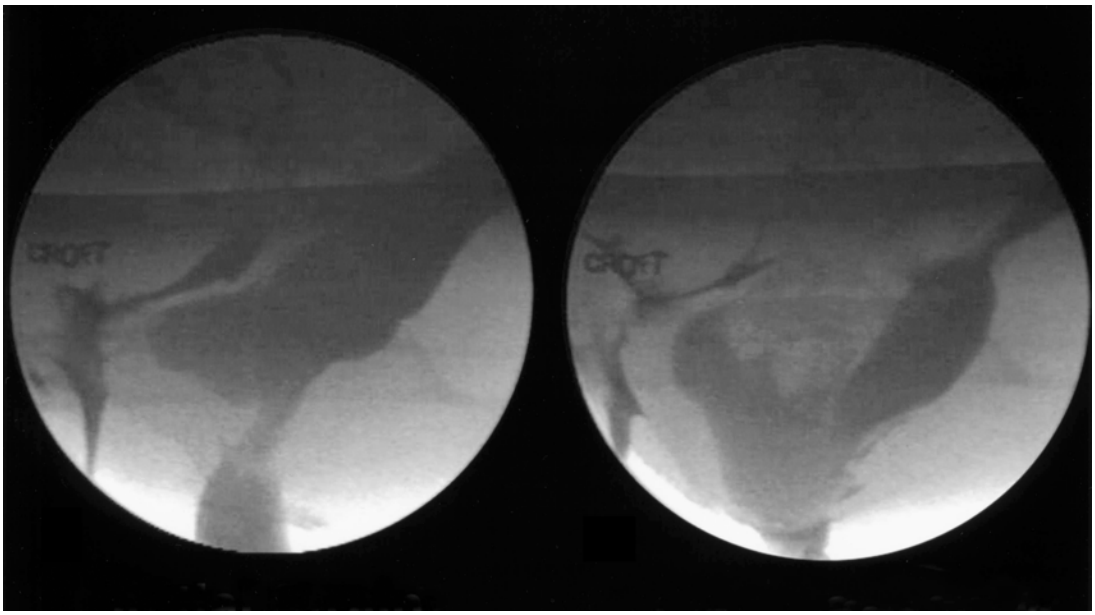

Figure 9.5. Deep rectovaginal pouch or septal peritoneocele. Upon straining, small bowel enters the pouch, forming an enterocele, and peritoneum extends caudally compressing the anal opening.

doceles as a finding during cindefecography. Twenty-four (5.2%) sigmoidoceles were noted during 463 cinedefecographic studies. Sigmoidoceles were classified based on the degree of descent of the lowest portion of the sigmoid loop during maximum straining in relation to the following anatomic landmarks: pubis, coccyx, and ischium. First-degree sigmoidocele was considered when the intrapelvic loop of sigmoid was observed on the cinedefecography but the sigmoid did not pass caudad to the pubococcygeal line; second-degree sigmoidoceles included sigmoid loops below the pubococcygeal line but above the ischeococcygeal line; third-degree sigmoidoceles consisting of loops of bowel transcending caudad to the ischiococcygeal line. Constipation symptoms were present in 20 of the 24 (83%) patients. The most common sensations were incomplete evacuation, straining, pelvic bloating, rectal pressure or fullness, infrequent bowel movements, and abdominal pain. Two thirds of these patients required assisted defecation including laxatives, enemas, and suppositories. Nine patients had first-degree, seven had second-degree, and eight had third-degree sigmoidoceles. The proposed classification system yielded excellent correlation among the mean level of the sigmoidocele, the degree of the sigmoid redundancy, and clinical symptoms. The clinical significance of third-degree sigmoidoceles were supported by the fact that all eight patients in that group were women with severe evacuatory difficulties, seven of whom had impaired rectal emptying on cinedefecography. All five patients with third-degree sigmoidoceles who underwent sigmoid resection reported significant symptomatic improvement at a mean follow-up ranging from 14 to 16 months.

Descending Perineum

Like other defecography measures, perineal descent is nonspecific and must be interpreted in context. An abnormal increase in perineal descent (typically greater than 2 cm) has been described among both incontinent patients and continent patients who strain during defecation.[32–34] These conflicting data underscore the poorly understood relationship between neuropathic pelvic floor damage and symptomatology.

Bartolo and associates[35] evaluated patients with perineal descent using manometric, radiographic, and neurophysiologic studies. When comparing 32 patients with incontinence and increased perineal descent with 21 patients with

obstructed defecation and increased perineal descent, the authors found no significant difference in the extent of perineal descent or neuropathic damage to the external anal sphincter. Patients who were incontinent had lower manometric pressures (both resting and squeeze pressures) while those individuals with obstructed defecation had normal manometric pressures. In a separate study, these authors also found that incontinent patients with increased perineal descent had severe denervation of both the puborectalis and the external sphincter compared to continent patients with increased perineal descent, who had partial denervation of the external sphincter only.[36] Miller and colleagues[34] evaluated sensation in two similar patient groups. Patients who were frankly incontinent actually had less perineal descent than continent patients with descent, but had severely impaired anal sensation.

Berkelmans et al[33] tried to determine if women with increased perineal descent and straining at stool were at risk for future development of incontinence. The authors identified 46 women with perineal descent who strained during defecation but were continent. Twenty-four of the 46 were followed after 5 years, and 13 of these (54%) had developed fecal incontinence, compared with three of 20 (15%) control patients. During their initial evaluation, the patients who previously strained and later developed incontinence had significantly greater perineal descent at rest and less elevation of the pelvic floor during maximal sphincter contraction than the women who strained but did not develop incontinence.

Thus, perineal descent may be a predictor of incontinence among patients with denervation of both the external sphincter and the puborectalis, and in patients with impaired anal sensation. Among patients with constipation, perineal descent and straining at stool may predict future fecal incontinence.

Dyskinetic Puborectalis

Dyskinetic puborectalis, paradoxical puborectalis, nonrelaxing puborectalis, and *anismus* are terms that describe the absence of normal relaxation of pelvic floor muscles during defecation, resulting in pelvic outlet obstruction. Defecographic evidence of a dyskinetic puborectalis includes a persistent posterior indentation of the puborectalis muscle, lack of perineal descent, a lack of straightening of the rectoanal angle, and poor opening of the anal canal.[37] Definition of specific measurement criteria (anorectal angle change, perineal descent) would be misleading due to the wide range of normal results.[38] During the exam, the patient may strain numerous times and evacuate only a small amount of contrast with each attempt or fail to empty any contrast at all. Straining against the pelvic floor or a non-opening anal canal can accentuate the anterior bowing of a rectocele or cause posterior rectal bowing. Once diagnosed, dyskinetic puborectalis is usually treated with biofeedback and bowel management. Patients who fail conservative treatment have been offered botulinum toxin injections into the puborectalis muscle with limited success.[39] Several studies have shown that neither electromyography nor cinedefecography is ideal relative to either specificity or sensitivity in the diagnosis of paradoxical puborectalis contraction.[15,23,27,40] Therefore, a combination of defecography and perhaps surface or intra-anal sponge electromyography may be the appropriate means of diagnosing of this problem.

Solitary Rectal Ulcer Syndrome

Defecography can clarify anatomic changes that contribute to the pathogenesis of solitary rectal ulcer syndrome and accordingly may be used to direct therapy. Kuijpers et al[41] determined that, among 19 patients with histologic features of solitary rectal ulcer syndrome, 12 had intussusception and five patients had inappropriate puborectalis muscle contraction on defecography exam. Intussusception can cause stretching of the submucosal vessels, ischemia, and ulceration. Straining against a nonrelaxing puborectalis muscle can cause internal prolapse, ischemia and ulceration.[26] Patients with solitary rectal ulcer syndrome and inappropriate puborectalis muscle contraction may be offered biofeedback, with surgery reserved for those with significant intussusception.[42] Goei and Baeten[22] studied pre- and postoperative defecograms in 11 patients with solitary rectal ulcers who were treated with a rectopexy. In nine patients the intussusception and rectal lesions were cured, and in two the intussusception and ulcer recurred. This syndrome remains a controversial area, and initial nonoperative treatment is often offered to all patients.

Incontinence

Defecography may indicate abnormalities of pelvic floor function that predispose a patient to incontinence, such as those that occur with outlet obstruction or prolapse. The anorectal angle, as a reflection of puborectalis muscle function, may be more obtuse in incontinent patients.[43,44] Kruyt and associates[44] reported on manometry and defecography performed on a diverse group of 160 consecutive patients. In this cohort, patients with anorectal angles greater than 130 degrees were more likely to leak contrast during the study and to have frank incontinence than patients with normal anorectal angles. However, others have found no difference in anorectal angle measurement between incontinent patients and normal controls.[35,45]

Rex and Lappas[46] compared manometry and defecography results from 50 consecutive symptomatic adults. In this study, leakage of contrast at rest and failure to reduce the anorectal angle during the defecography exam were specific but not sensitive predictors of decreased manometric pressures. However, incomplete evacuation or retention of contrast in rectoceles had excellent correlation with symptoms of outlet obstruction. The investigators concluded that defecography was most useful for incontinent patients with outlet obstruction symptoms.

Bielefeldt and associates[47] agree that defecography offers complementary information to manometry. In their study of 43 consecutive patients with fecal incontinence evaluated with manometry and defecography, a subgroup with severe fecal incontinence and an incompletely closed anal canal during defecography also had lower resting pressures. Severe anorectal angle changes, such as the loss of the puborectalis muscle indentation into the posterior rectum and an overly obtuse anorectal angle, were not reflected in manometric pressures suggesting that the functional integrity of the pelvic floor is not reflected in manometric data.

Specific Patient Populations

Male

Disorders of the pelvic floor are most commonly associated with females, presumably due to anatomic and physiologic burdens of childbearing. In an assessment of 2816 patients who had undergone defecography, Mellgren et al[29] noted that only 16% were male. Consequently, understanding of male pelvic floor issues has been limited by a lack of data and attention. Given the two major contributors to female pelvic floor disorders, obstetrical injury and age (which may simply be a proxy for decreased collagen), one might expect previous pelvic operation and age to play contributory roles in male pelvic floor issues as well.

Chen and colleagues[48] studied 40 men with rectoceles among 234 who underwent defecography for evacuation disorders. As expected, 40% of the men had previously undergone prostatic surgery and the mean age was 72 years. However, in contrast to females, whose rectoceles are nearly always anterior, males presented with 48% anterior and 52% posterior rectoceles. There was no discussion of controlling for age when evaluating the association between previous prostate surgery and rectocele. The authors acknowledged that the clinical significance of rectoceles and therapeutic strategies for men remain unknown.

Pouch Patients

Patients who have previously undergone total colectomy with ileal pouch–anal anastomosis are subject to a number of possible long-term complications, including symptoms of impaired pouch evacuation. Defecography can be an invaluable aid to accurate diagnosis and treatment planning in this setting. Stenosis of the pouch inlet or outlet and kinking of the efferent limb are the most common obstructive disorders.

Silvis et al[49] described planning of reoperation in five such patients, including developing a technique for transabdominal shortening of a long efferent limb with a linear stapler. They also described correction of an inlet stenosis identified by defecography and an extensive pouch revision in one patient with outlet stenosis. Defecography permitted complex, tailored surgery with good short-term relief of symptoms, although no long-term outcomes were available.

Pediatric

Between 3% and 8% of children have significant bowel dysfunction.[50] Since constipation is usually functional in this population, imaging

Table 9.4. Defecography results in children with constipation

Diagnosis	Puborectalis relaxation	Internal sphincter relaxation	Rectoanal inhibitory reflex (RAIR)	Rectum	Emptying
Hirschsprung's disease	Absent	Absent	Absent	Narrow	Very poor
Neuronal intestinal dysplasia	Present	Present	Absent	Massive bowel	Nonspecific
Intestinal pseudo-obstruction	Nonspecific	Nonspecific	Nonspecific	Nonspecific	Nonspecific
Ultrashort segment Hirschsprung's	Absent	Absent	Absent	Mega	Very poor
Megarectum*	Normal	Normal	Normal	Mega	Nonspecific

* Other causes of secondary megarectum and constipation in children include anal fissure, congenital anal anomalies with stricture, anterior anus, and myelomeningocele. All should have a normal internal sphincter relaxation.

studies are reserved for patients who do not respond to medical management. Defecography, barium enema, and manometry are complementary tests that help to focus a broad differential diagnosis including Hirschsprung's disease, neuronal intestinal dysplasia, intestinal pseudo-obstruction, and megarectum.

Defecography is feasible starting at age of 3 or 4 years. Abnormal findings in the pediatric patient include the presence or absence of megarectum, paradoxical relaxation, poor relaxation of the internal sphincter, or descent of the pelvic floor. Table 9.4 provides a framework for diagnosis based on defecography and manometry findings. The importance of a thorough workup is underscored when one considers that unnecessary biopsies can be avoided if imaging tests are normal.

Multiple Sclerosis

Among patients with multiple sclerosis, 50% to 70% report constipation or fecal incontinence and many complain of both.[51] Symptom overlap can make treatment particularly difficult. We start with rectal disimpaction and a whole-bowel cathartic, such as polyethylene glycol, followed by a bowel regimen of high-fiber diet, laxatives, and enemas. If the constipation proves intractable, defecography may reveal outlet obstruction due to a lack of pelvic floor relaxation.[52] Such patients may respond to biofeedback, especially those with limited disability and nonprogressive disease.[53]

Conclusion

Defecography is a radiographic examination of anorectal functional anatomy that remains useful despite its limitations. While defecography provides objective, reproducible evidence of the evacuatory process, it is vulnerable to the subjective interpretation of practitioners. Moreover, symptomatic and asymptomatic patients may have similar results, while two patients with similar symptoms may have very different results. These issues likely reflect the multifactorial etiology of obstructed defecation, which is strongly affected by underlying conditions, as described above. No single test provides all of the information necessary to fully assess constipation or rectal outlet obstruction; however, defecography can provide valuable information and permit exclusion of conditions not present (e.g., perineal descent syndrome, intussusception, nonrelaxing puborectalis).

Despite controversies regarding relevance and consistency, defecography has been regarded as a useful test since its introduction, and remains one of the best methods for evaluating the process of defecation. Ongoing efforts at standardization of definitions[37] and techniques will help to improve diagnostic reproducibility and allow pre- and postintervention comparison of patients in order to continue improving care.

References

1. Wallden L. Defecation block in cases of deep rectogenital pouch. Acta Chir Scand 1952;103(3):236–238.
2. Broden B, Snellman B. Procidentia of the rectum studied with cineradiography. A contribution to the discussion of causative mechanism. Dis Colon Rectum 1968;11(5):330–347.
3. Mahieu P, Pringot J, Bodart P. Defecography: I. Description of a new procedure and results in normal patients. Gastrointest Radiol 1984;9(3):247–251.
4. Kelvin FM, Maglinte DD, Benson JT. Evacuation proctography (defecography): an aid to the investigation of pelvic floor disorders. Obstet Gynecol 1994;83(2):307–314.
5. Ikenberry S, Lappas JC, Hana MP, Rex DK. Defecography in healthy subjects: comparison of three contrast media. Radiology 1996;201(1):233–238.

6. Mahieu P, Pringot J, Bodart P. Defecography: II. Contribution to the diagnosis of defecation disorders. Gastrointest Radiol 1984;9(3):253–261.
7. Ferrante SL, Perry RE, Schreiman JS, Cheng SC, Frick MP. The reproducibility of measuring the anorectal angle in defecography. Dis Colon Rectum 1991;34(1): 51–55.
8. Bernier P, Stevenson GW, Shorvon P. Defecography commode. Radiology 1988;166(3):891–892.
9. Altringer WE, Saclarides TJ, Dominguez JM, Brubaker LT, Smith CS. Four-contrast defecography: pelvic "flooroscopy." Dis Colon Rectum 1995;38(7):695–699.
10. Bremmer S, Ahlback SO, Uden R, Mellgren A. Simultaneous defecography and peritoneography in defecation disorders. Dis Colon Rectum 1995;38(9):969–973.
11. Gullmo A. Herniography. The diagnosis of hernia in the groin and incompetence of the pouch of Douglas and pelvic floor. Acta Radiol Suppl 1980;361:1–76.
12. Rafert JA, Lappas JC, Wilkins W. Defecography: techniques for improved image quality. Radiol Technol 1990;61(5):368–373.
13. Jorge JMN, Ger GC, Gonzalez L, Wexner SD. Patient positioning during cinedefecography: influence on perineal descent and other measurements. Dis Colon Rectum 1994;37:927–931.
14. Varma M, Warshaw A, Congilosi S. Evaluation of complex pelvic floor disorders with peritoneography (Abstract). Dis Colon Rectum 2000;43(5):A14.
15. Yeh CY, Pikarsky A, Wexner SD, et al. Electromyographic findings of paradoxical puborectalis contraction poorly correlate with cinedefecography. Tech Coloproctol 2003;7:77–81.
16. Goei R, Kemerink G. Radiation dose in defecography. Radiology 1990;176(1):137–139.
17. Shorvon PJ, McHugh S, Diamant NE, Somers S, Stevenson GW. Defecography in normal volunteers: results and implications. Gut 1989;30(12):1737–1749.
18. Bremmer S, Mellgren A, Holmstrom B, Lopez A, Uden R. Peritoneocele: visualization with defecography and peritoneography performed simultaneously. Radiology 1997;202(2):373–377.
19. Jorge JMN, Yang YK, Wexner SD. Incidence and clinical significance of sigmoidoceles as determined by a new classification system. Dis Colon Rectum 1994;37:1112–1117.
20. Wiersma TG, Mulder CJ, Reeders JW, Tytgat GN, Van Waes PF. Dynamic rectal examination (defecography). Baillieres Clin Gastroenterol 1994;8(4):729–741.
21. Hardcastle JD, Parks AG. A study of anal incontinence and some principles of surgical treatment. Proc R Soc Med 1970;63(Suppl):116–118.
22. Goei R, Baeten C. Rectal intussusception and rectal prolapse: detection and postoperative evaluation with defecography. Radiology 1990;174(1):124–126.
23. Ekberg O, Nylander G, Fork FT. Defecography. Radiology 1985;155(1):45–48.
24. Pfeifer J, Oliveira L, Park UC, Gonzalez A, Agachan F, Wexner SD. Are interpretations of defecography reliable and reproducible? Int J Colorectal Dis 1997;12:67–72.
25. Yang X, Partanen K, Farin P, Ji H, Soimakallio S. Reproducibility of five anorectal morphologic measurements in defecography. Acad Radiol 1994;1(3):224–228.
26. Rutter KR, Riddell RH, Christiansen J, et al. The solitary ulcer syndrome of the rectum. Clin Gastroenterol 1975;4(3):505–530.
27. Agachan F, Pfeifer J, Wexner SD. Defecography and proctography. Results of 744 patients. Dis Colon Rectum 1996;39:899–905.
28. van Dam JH, Ginai AZ, Gosselink MJ, et al. Role of defecography in predicting clinical outcome of rectocele repair. Dis Colon Rectum 1997;40(2):201–207.
29. Mellgren A, Bremmer S, Johansson C, et al. Defecography. Results of investigations in 2816 patients. Dis Colon Rectum 1994;37(11):1133–1141.
30. Halligan S, Bartram C, Hall C, Wingate J. Enterocele revealed by simultaneous evacuation proctography and peritoneography: does "defecation block" exist? AJR 1996;167(2):461–466.
31. Olsen AL, Smith VJ, Bergstrom JO, Colling JC, Clark AL. Epidemiology of surgically managed pelvic organ prolapse and urinary incontinence. Obstet Gynecol 1997;89(4):501–506.
32. Kelvin FM, Maglinte DD, Hornback JA, Benson JT. Pelvic prolapse: assessment with evacuation proctography (defecography). Radiology 1992;184(2):547–551.
33. Berkelmans I, Heresbach D, Leroi AM, et al. Perineal descent at defecography in women with straining at stool: a lack of specificity or predictive value for future anal incontinence? Eur J Gastroenterol Hepatol 1995; 7(1):75–79.
34. Miller R, Bartolo DC, Cervero F, Mortensen NJ. Differences in anal sensation in continent and incontinent patients with perineal descent. Int J Colorectal Dis 1989;4(1):45–49.
35. Bartolo DC, Read NW, Jarratt JA, Read MG, Donnelly TC, Johnson AG. Differences in anal sphincter function and clinical presentation in patients with pelvic floor descent. Gastroenterology 1983;85(1):68–75.
36. Bartolo DC, Jarratt JA, Read MG, Donnelly TC, Read NW. The role of partial denervation of the puborectalis in idiopathic faecal incontinence. Br J Surg 1983; 70(11):664–667.
37. Lowry AC, Simmang CL, Boulos P, et al. Consensus statement of definitions for anorectal physiology and rectal cancer: report of the Tripartite Consensus Conference on Definitions for Anorectal Physiology and Rectal Cancer, Washington, D.C., May 1, 1999. Dis Colon Rectum 2001;44(7):915–919.
38. Skomorowska E, Henrichsen S, Christiansen J, Hegedus V. Videodefaecography combined with measurement of the anorectal angle and of perineal descent. Acta Radiol 1987;28(5):559–562.
39. Ron Y, Avni Y, Lukovetski A, et al. Botulinum toxin type-A in therapy of patients with anismus. Dis Colon Rectum 2001;44(12):1821–1826.
40. Jorge JMN, Wexner SD, Ger GC, Salanga V, Nogueras JJ, Jagelman DG. Cinedefecography and electromyography in the diagnosis of non relaxting puborectalis syndrome. Dis Colon Rectum 1993;36:668–676.
41. Kuijpers HC, Schreve RH, ten Cate Hoedemakers H. Diagnosis of functional disorders of defecation causing the solitary rectal ulcer syndrome. Dis Colon Rectum 1986;29(2):126–129.
42. Christiansen J, Zhu BW, Rasmussen OO, Sorensen M, Goei R, Baeten C. Rectal intussusception and rectal prolapse: detection and postoperative evaluation with defecography. Dis Colon Rectum 1992;35(11):1026–1028; discussion 1028–1029.
43. Piloni V, Fioravanti P, Spazzafumo L, Rossi B. Measurement of the anorectal angle by defecography for the

diagnosis of fecal incontinence. Int J Colorectal Dis 1999;14(2):131–135.
44. Kruyt RH, Delemarre JB, Gooszen HG, Hermans J. Defecography and anorectal manometry. Eur J Radiol 1992;15(2):166–170.
45. Goei R. Anorectal function in patients with defecation disorders and asymptomatic subjects: evaluation with defecography. Radiology 1990;174(1):121–123.
46. Rex DK, Lappas JC. Combined anorectal manometry and defecography in 50 consecutive adults with fecal incontinence. Dis Colon Rectum 1992;35(11):1040–1045.
47. Bielefeldt K, Enck P, Zamboglou N, Moedder U, Erckenbrecht JF. Anorectal manometry and defecography in the diagnosis of fecal incontinence. J Clin Gastroenterol 1991;13(6):661–665.
48. Chen HH, Iroatulam A, Alabaz O, Weiss EG, Nogueras JJ, Wexner SD. Associations of defecography and physiologic findings in male patients with rectocele. Tech Coloproctol 2001;5(3):157–161.
49. Silvis R, Delemarre JB, Gooszen HG. Surgical treatment and role of dynamic defecography after ileal pouch–anal anastomosis: technical solutions to a difficult problem. Dis Colon Rectum 1997;40(1):84–88.
50. Fotter R. Imaging of constipation in infants and children. Eur Radiol 1998;8(2):248–258.
51. Wiesel PH, Norton C, Glickman S, Kamm MA. Pathophysiology and management of bowel dysfunction in multiple sclerosis. Eur J Gastroenterol Hepatol 2001;13(4):441–448.
52. Gill KP, Chia YW, Henry MM, Shorvon PJ. Defecography in multiple sclerosis patients with severe constipation. Radiology 1994;191(2):553–556.
53. Wiesel PH, Norton C, Roy AJ, Storrie JB, Bowers J, Kamm MA. Gut focused behavioural treatment (biofeedback) for constipation and faecal incontinence in multiple sclerosis. J Neurol Neurosurg Psychiatry 2000;69(2):240–243.

10

Compliance and Manovolumetry

Olof J. Hallböök and Rune I. Sjödahl

There in no single test that provides a complete picture of the complex mechanisms of defecation. A comprehensive battery of physiologic tests has gradually assumed an important position in the evaluation of patients with chronic severe constipation. The normal rectum demonstrates a receptive relaxation in response to distention, conferring its function as a reservoir. This chapter describes the manovolumetric method for rectal compliance measurement and discusses the clinical importance of rectal reservoir and sensory function in the investigation of patients with severe chronic constipation.

A major objective finding in constipated patients when compared with controls is the reduced sensation of filling of the rectum (Table 10.1).[1–10] Larger than normal volumes are required to distend the rectum sufficiently to evoke a sensation of filling and a desire to evacuate. This lack of sensitivity is suggestive of a primary neuropathy involving the afferent fibers arising from rather than being secondary to constipation.[11] Others have postulated that an excessive supraspinal inhibition of otherwise normal sacral cord function is a learned subconscious response.[9] This impaired sensitivity may explain the difficulty of eliciting the rectoanal inhibitory reflex in some patients with constipation who do not have Hirschsprung's disease. In addition, the sensitivity cannot be examined when the rectum is dilated, as there might be no contact between the balloon and the rectal wall.

Sensitivity is difficult to quantify. However, both thermal and electrical sensory thresholds can be measured. Despite the reproducibility of these elegant techniques, the teleologic ability of the anorectum to discriminate among various temperature or electrical impulses is indeed questionable. For this reason most physiologists prefer to measure sensation in terms of a functionally known variable volume. In the simplest terms, water at body temperature can be infused through the catheter into an intrarectal balloon. The levels of first sensation, fullness, and maximum tolerable volume (V) are measured. These same levels of sensation can be used when calculating rectal compliance. Compliance represents the rectal pressure (P) change that results from infusion of a given quantity of intrarectal content, in this case water. Thus the formula $(P1 - P2)/(V2 - V1)$ can be readily calculated. Despite the simplicity, reproducibility and functional correlation with this technique, reported findings in constipated patients vary greatly (Table 10.1). This may partly reflect differences among various institutions in laboratory technique and definition of the compliance value.

Assessment of Compliance

There are several ways to measure and calculate rectal compliance,[10,12,13] but there is still no generally accepted gold standard.[14] The most common method is to record the response of intrarectal pressure to progressive rectal distention. This generates a pressure–volume curve, and compliance is defined as the quotient of the change in volume and the change in pressure—the slope of the curve. The interpretations of the findings, however, are controversial.[15] The values obtained are of the threshold volume (volume at which sensation first occurred), fullness volume, and maximal tolerable volume, which vary. This

Table 10.1. Rectal reservoir and sensory function in chronic idiopathic constipation versus controls

Series	*n*	Compliance	Volume: first sensation	Volume: urge to defecate	Maximal tolerable volume
Read et al 1985[1]	55	Decreased*	Increased*	Increased*	Increased**
Bannister et al 1986[2]	34	NS	NS	Increased*	NS
Read et al 1986[3]	14	NS	NS	Increased**	NS
Shouler and Keighley 1986[4]	25	—	NS	Increased**	—
Roe et al 1988[5]	31	NS	Increased*	—	NS
Varma and Smith 1988[6]	15	Increased**	NS	—	NS
Waldron et al 1988[7]	44	Increased*	Increased*	Increased*	—
De Medici et al 1989[8]	64	NS	—	Increased**	—
Kerrigan et al 1989[9]	16	—	Increased*	Increased**	—
Wald et al 1989[10]	25	NS	Increased*	—	—

* $p < .05$; ** $p < .01$; NS, not significant versus controls; —, no data available.
The figures for compliance and volume are omitted in this table owing to difficulties in comparing laboratory techniques used in various institutions.

variation may reflect a learned cortical response, and may result in a misleading comparison of single values of compliance. Therefore, it may be better to compare the pressure–volume curve of the patient with the normal range (Fig. 10.1) or the mean curves among groups of subjects. Another possibility is to evaluate the pressure–volume quotient at defined distention pressure intervals, which can be accomplished with the manovolumetric method described below. Manovolumetry provides a more objective measurement of the rectal compliance, as it has no association with the subject's perception of a rectal balloon.[15]

Manovolumetry

In the manovolumetry system, the rectal volume is recorded as a dynamic response to a graded rectal distention at atmospheric pressure. This resembles the physiologic events in the intestine,

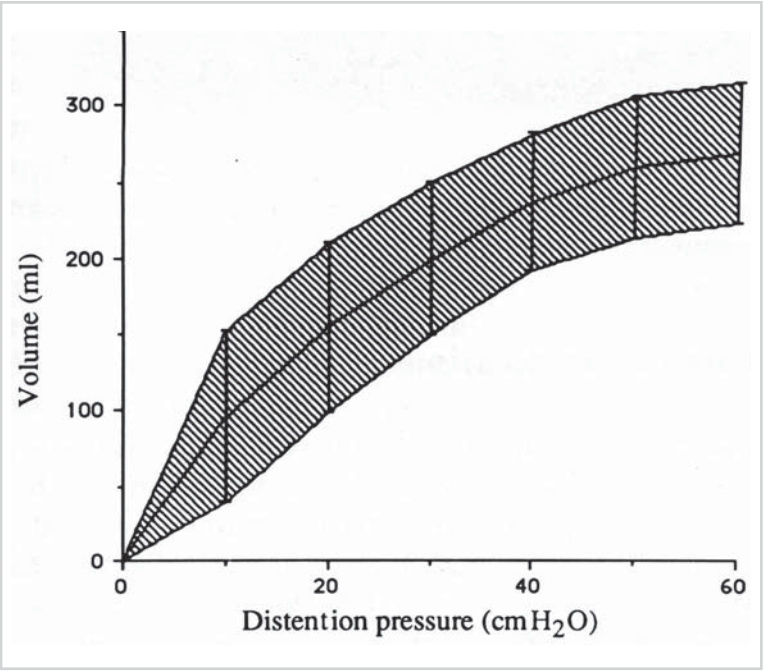

Figure 10.1. Pressure–volume response range in normal subjects ($n = 45$, mean ± SD) measured with the manovolumetry method. Reprinted from Hallbook O, Sjodahl R. Techniques of rectal compliance measurement. Semin Colon Rectal Surg 1992;3:88–91, ©1992, with permission from Elsevier.

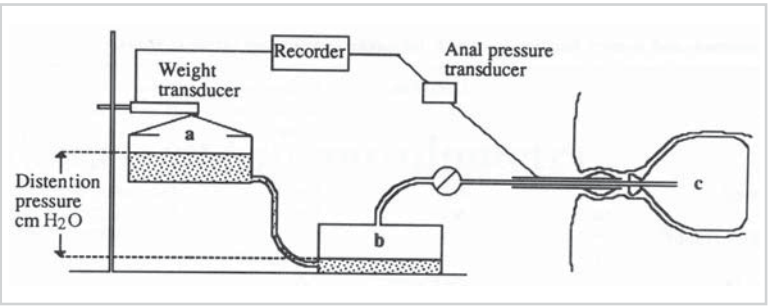

Figure 10.2. Design of the manovolumetry system. Reprinted from Hallbook O, Sjodahl R. Techniques of rectal compliance measurement. Semin Colon Rectal Surg 1992;3:88–91, ©1992, with permission from Elsevier.

which allow wide changes of volume with minimal corresponding changes in pressure. It differs from conventional systems where compliance is calculated by registration of pressure in response to distention with air or fluid.

The manovolumetry method was designed for investigation of reservoir organs.[16,17] It was described and evaluated for studies of anorectal function by Akervall et al[18] and Öresland et al.[19] The design is shown in Figure 10.2 and the disposable part of the system in Figure 10.3. As depicted in Figure 10.2, a water-filled reservoir (a) is open to air and suspended on a weight transducer. This vessel is in continuity via a tube to a closed-air reservoir (b), which is connected to a large, noncompliant plastic bag. This plastic bag is placed in the rectum (c). When the water reservoir is raised, pressure is generated in the air reservoir and consequently in the plastic bag. This pressure is equal to the difference between the levels of water in the two reservoirs. The amount of water flowing into the air reservoir is measured as weight reduction. This reduction is equal to the volume of the plastic bag, that is, the rectal volume. The water-filled reservoir is open to the air, meaning that the pressure in the rectum is kept constant despite variation in volume. An example of a manovolumetric recording is shown in Figure 10.4, which also shows a recording of the anal canal pressure made at the same time.

The manovolumetric method has the following properties:

1. Rectal distention with defined pressures allows dynamic registration of volume changes; thus compliance can be calculated in relation to defined pressure intervals.
2. The noncompliant plastic bag is sensitive to bowel wall contractions, making it suitable for motility studies.
3. Anal pressure is recorded simultaneously with rectal volume and motility, which allows assessment of the rectosphincteric reflexes.

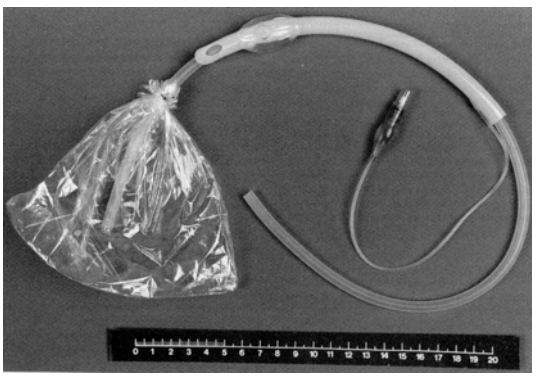

Figure 10.3. The disposable part of the manovolumetry system. A polyethylene bag (length 12 cm, volume 600 mL) hermetically tied to a tube, is placed in the rectum. An endotracheal tube (outer diameter 10 mm) is laced on the tube and used for anal canal pressure registration. Reprinted from Hallbook O, Sjodahl R. Techniques of rectal compliance measurement. Semin Colon Rectal Surg 1992;3:88–91, ©1992, with permission from Elsevier.

Electronic Barostat System

A polyethylene bag in the rectum is fixed to a multilumen tube, which is connected to a barostat device. The pressure in the bag is measured via a separate lumen of the tube. The barostat is connected to a computer, where the pressure, volume, and compliance (mL/mm Hg) are constantly monitored and recorded as the pressure–volume curve.

The bag can be distended in steps to either a fixed pressure (isobaric) or a fixed volume (isovolumetric). It is also able to keep the pressure in the rectal beg at a preselected level, which means that when the rectum relaxes, the system injects air, and when it contracts, the barostat

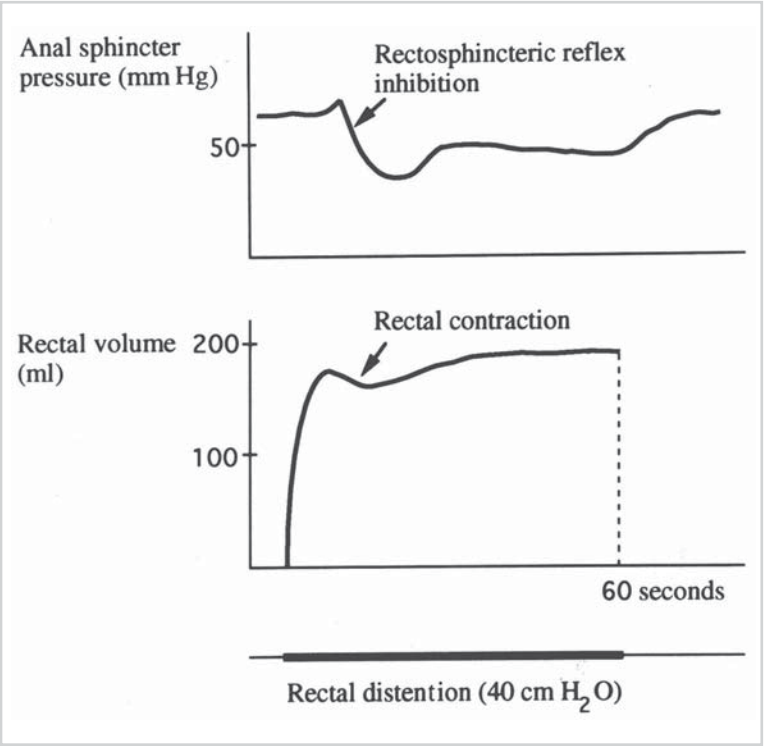

Figure 10.4. Manovolumetry. An example of rectal volume and anal pressure response to rectal distention with a preset distention pressure. A steady rate is accomplished within 60 seconds. (Modified from Akervall et al,[23] with permission of Springer.)

aspirates air. Thus, the barostat can measure rectal motor activity as changes in the intrarectal volume at a constant intrarectal pressure.[20,21]

Clinical Implications

Preoperative physiologic investigation is mandatory to select the very small subset of patients with chronic idiopathic constipation who will benefit from colectomy and ileorectal anastomosis.[22] With respect to rectal reservoir and sensory function in this category of patients, Akervall et al,[23] using the manovolumetric method, considered that rectal sensitivity is an important predictive variable for a favorable outcome after colectomy and ileorectal anastomosis. They also concluded that sensory abnormalities, which can be demonstrated by manovolumetry, might be overlooked if only the distending volume is recorded.

Preoperatively manovolumetry is more important with normal rectal compliance than with normal sphincter function. A stiff, poorly compliant rectum in combination with the loose bowel motions in the postoperative period puts considerable stress on the anal sphincters.

The presence of the rectoanal inhibitory reflex should exclude Hirschsprung's disease. In the absence of a megarectum, the finding of large distending volumes with little sensory awareness should raise the suspicion of spinal disease with the concomitant risk of incontinence if an ileorectal anastomosis is performed.[24]

Conclusion

Owing to the surrounding structures of the rectum and to neurohormonal influence, it is difficult to assess the mechanical properties of the rectal wall in vivo. Thus rectal compliance should be considered as a functional measurement.

The clinical relevance of rectal compliance in the management of constipation is not fully established. Measuring the rectal compliance has not been as important as was expected regarding the decision to operate but is still valuable. The trend is that surgery for constipation is per-

formed less often today. The role of the rectum in the pathophysiology of chronic idiopathic constipation is still poorly understood; further studies of rectal reservoir and sensory function are needed.

References

1. Read NW, Abouzekry L, Read MG, et al. Anorectal function in elderly patients with fecal impaction. Gastroenterology 1985;89:959–966.
2. Bannister JJ, Timms JM, Barfield LJ, et al. Physiological studies in young women with chronic constipation. Int J Colorectal Dis 1986;1:175–82.
3. Read NW, Timms JM, Barfield LJ, et al. Impairment of defecation in young women with severe constipation. Gastroenterology 1986;90:53–60.
4. Shouler P, Keighley MRB. Changes in colorectal function in severe idiopathic chronic constipation. Gastroenterology 1986;90:414–420.
5. Roe AM, Bartolo DCc, Mortensen NJM. Slow transit constipation. Comparison between patients with or without previous hysterectomy. Dig Dis Sci 1988;33: 1159–1163.
6. Varma JS, Smith AN. Neurophysiological dysfunction in young women with intractable constipation. Gut 1988;29:963–968.
7. Waldron D, Bowes KL, Kingma YJ, et al. Colonic and anorectal motility in young women with severe idiopathic constipation. Gastroenterology 1988;95: 1388–1394.
8. De Medici A, Badiali D, Corazziari E, et al. Rectal sensitivity in chronic constipation. Dig Dis Sci 1989;34:747–753.
9. Kerrigan DD, Lucas MG, Sun WM. Idiopathic constipation associated with impaired urethrovesical and sacral reflex function. Br J Surg 1989;76:748–751.
10. Wald A, Hinds JP, Caruana BJ. Psychological and physiological characteristics of patients with severe idiopathic constipation. Gastroenterology 1989;97:932–937.
11. Waldron DJ. Constipation. In: Kumar D, Waldron DJ, Williams NS, eds. Clinical Measurement in Coloproctology. London: Springer, 1991:97–108.
12. Roe AM, Bartolo DCC, Mortensen NJM. Diagnosis and surgical management of intractable constipation. Br J Surg 1986;73:854–861.
13. Varma JS, Smith AN, Busuttil A. Correlation of clinical and manometric abnormalities of rectal function following chronic radiation injury. Br J Surg 1985;72: 875–878.
14. Madoff RD, Orrom WJ, Rothenberger DA, et al. Rectal compliance: a critical reappraisal. Int J Colorectal Dis 1990;5:37–40.
15. Hallböök O, Sjödahl R. Technique of rectal compliance measurement. Semin Colon Rectal Surg 1992;3:88–91.
16. Martinson J. Studies on the efferent vagal control of the stomach. Acta Physiol Scand Suppl 1965;255:1–24.
17. Sundin T, Carlsson CA. Reconstruction of severed dorsal roots innervating the urinary bladder. An experimental study in cats. I. Studies on the normal afferent pathways in the pelvic and pudendal nerves. Scand J Urol Nephrol 1972;6:176–184.
18. Akervall S, Fasth S, Nordgren S, et al. Manovolumetry: a new method for investigation of anorectal function. Gut 1988;29:614–623.
19. Öresland T, Fasth S, Åkervall S, et al. Manovolumetric and sensory characteristics of the ileoanal J pouch compared with healthy rectum. Br J Surg 1990;77: 803–806.
20. Penning C, Steens J, van der Schaar PJ, et al. Motor and sensory function of the rectum in different subtypes of constipation. Scand J Gastroenterol 2001;36:32–38.
21. Steens J, Penning C, Brussee J. Prospective evaluation of ileoanal pouch characteristics measured by barostat. Dis Colon Rectum 2002;45:1295–1303.
22. Wexner SD, Daniel N, Jagelman DG. Colectomy for constipation: physiologic investigation is the key to success. Dis Colon Rectum 1991;34:851–856.
23. Akervall S, Fasth S, Nordgren S, et al. The functional results after colectomy and ileorectal anastomosis for severe constipation (Arbuthnot Lane's disease) as related to rectal sensory function. Int J Colorectal Dis 1988;3:96–101.
24. Bartolo DCC. Diagnostic procedures for incontinence, constipation. In: Philips SF, Pemberton JH, Shorter RG, eds. The Large Intestine: Physiology, Pathophysiology and Disease. New York: Raven Press, 1991:727–745.

11

Electromyography and Pudendal Nerve Terminal Motor Latency

Anders F. Mellgren, Jan Zetterström and Bengt Yngve Nilsson

Objective evaluation of the pelvic floor is important in the assessment of patients with evacuatory disorders. Electrophysiologic studies can provide both qualitative and quantitative data relative to nerve function in the pelvic floor. Electromyography (EMG) is used to assess the electrical activity in the striated sphincter muscle, and pudendal nerve terminal motor latency (PNTML) measures the nerve conduction in the pudendal nerve.

Electromyography of the Anal Sphincter

Electromyography records the electrical activity that is generated by functioning muscles. The first recordings were documented in the beginning of the 20th century,[1] and in 1930 Beck[2] recorded the EMG activity of the striated anal muscle. Anal EMG involves measurement of activity in striated muscle tissue, whereby information regarding the neuromuscular integrity such as denervation and reinnervation can be obtained. Normally, muscle fibers are depolarized by nerve impulses arriving at the motor nerve terminal. The muscle action potential that is subsequently generated and propagated along the length of the muscle fiber is the potential change of depolarization that is recorded by EMG.

The striated external anal sphincter is continuously active at rest; its activity normally increases during voluntary contraction and decreases during straining (Fig. 11.1).[3] The EMG activity in the external anal sphincter (EAS) is different from that in other muscles, as there is continuous and spontaneous EMG activity, even at rest.[4] This activity is constantly varied and increases with rectal distention and changes of body positioning. The EMG activity also usually increases during voluntary squeezing of the sphincter muscle, but ceases during relaxation of the EAS during pushing and evacuation.

Currently, there are four techniques used to record anal sphincter EMG: needle EMG, wire electrode EMG, single-fiber EMG, and surface EMG. The three first methods require insertion of a needle/wire into the external sphincter muscle in the sensitive anal area, but the fourth method causes little or no discomfort to the patient.

Needle Electromyography

Concentric needle EMG was introduced in 1929 by Adrian and Bronk[1] and is the traditional method of assessing EMG. The needle, which resembles a hypodermic needle, is inserted into the external anal sphincter while the patient is placed in the left lateral decubitus position. The needle can be advanced either into the EAS or deeper into the puborectalis muscle under the guidance of a finger inserted into the anal canal.

The uptake area of the electrode is quite small and includes only a few motor units; therefore, it is important to measure the activity in various locations in the muscle. The electrical activity is usually monitored during rest, squeezing, and simulated evacuation (pushing).

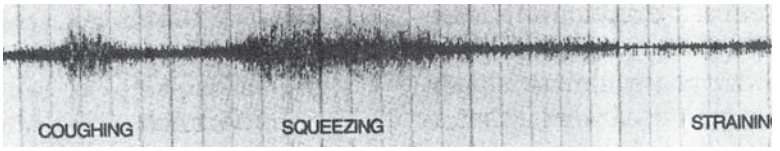

Figure 11.1. Normal surface electromyogram (EMG). The resting activity is normal and the activity is increased at coughing and squeezing, but not at straining.

Wire Electromyography

An alternative to concentric needle is the use of a thin silver or steel wire electrode with a skin electrode as reference. This technique is less painful for the patient; therefore, the measurements may be more reliable. The thin wire is usually inserted with the guidance of a lumbar puncture needle, while a hook at the tip of the wire is sometimes used to keep the wire keep in place.

Single-Fiber Electromyography

Single-fiber EMG is a special type of needle EMG that facilitates assessment of reinnervation in the external anal sphincter. The single-fiber EMG needle, having a very small electrode surface, measures the mean number of muscle fibers per motor unit within the electrode uptake area, also known as fiber density (FD). If an axon is injured, reinnervation (sprouting) from nearby axons will occur, which will increase the number of muscle fibers within the motor unit and thus increase FD.

Fiber density is the mean number of single fiber action potentials in 20 different positions within a muscle. It increases with age, and the upper normal limits are therefore adjusted to the patient's age: 1.52 (under the age of 30), 1.82 (age 30–65), 1.88 (age 66–70), and 2.20 (age 71–85).[5–7]

Surface Electromyography

Because of patient discomfort caused by the above-mentioned techniques, several centers prefer surface electrodes to study the electrical activity in the EAS (Fig. 11.2).[8,9] Surface EMG can be obtained either with surface electrodes placed on the perianal skin adjacent to the anal verge[8] or with an anal plug that is placed in the anal canal.[10] Surface electrodes record potentials summated from multiple motor units and therefore measure gross electric activity across relatively large areas. These methods have been demonstrated to be as accurate as needle EMG in patients with constipation.[9]

Role of Electromyography in the Evaluation of Constipation

Anal EMG is the most widely used method to identify patients who cannot appropriately relax their anal sphincters at attempted rectal emptying; this condition has been referred to by several terms, including paradoxical sphincter reaction (PSR), paradoxical puborectalis constraction (PPC), nonrelaxing puborectalis syndrome (NRPS), anismus, or spastic pelvic floor syndrome (Fig. 11.3). Anal EMG is also used in the treatment of PSR[11] by identifying patients with potential neuromuscular damage that can be related to chronic straining.[12]

Paradoxical Sphincter Reaction

Paradoxical sphincter reaction is a common finding in patients with rectal emptying difficulties and is considered by some authors to

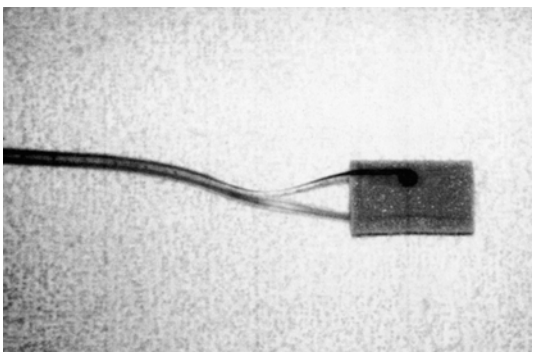

Figure 11.2. Anal plug surface electrode.

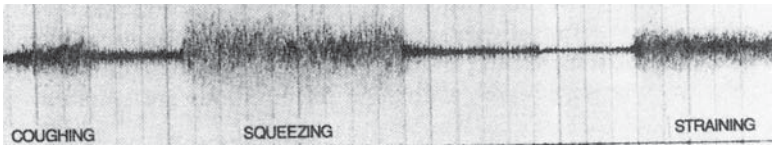

Figure 11.3. Surface EMG demonstrating paradoxical sphincter reaction. The EMG activity is increased also at straining (it would normally decrease).

be an important reason for obstructed defecation.[13] The dysfunction in the EAS and puborectalis muscle results in failure to relax at attempted defecation, resulting in a maintained or increased activity that can be registered on EMG. The PSR can also be diagnosed by defecography, anorectal manometry, palpation, and dynamic pelvic magnetic resonance imaging (MRI), although EMG is usually the preferred method.[14,15] The use of more than one modality to diagnose PSR is advisable because the results of these investigative methods do not always correlate with each other or with the patient's clinical symptoms.[15,16]

Some authors have suggested that PSR is caused by the embarrassing environment of the unphysiologic laboratory setting.[17,18] Pain caused by the needle electrodes has also been suggested to elicit a PSR.[17] However, in a study comparing needle electrodes with thin painless wire electrodes, PSR was recorded in all 10 patients independent of the type of electrode used.[14] Regardless of this finding, the laboratory setting does seem to influence the result. It has been shown that the incidence of PSR is reduced during ambulatory manometry, when the patient is able to evacuate in privacy at home.[19] Furthermore, it has been shown that the volume of the rectal balloon influences the presence of PSR.[20] When the volume in the rectal balloon was increased from 0 to 150 mL, PSR at straining was resolved in nine of 18 (50%) patients. Reports from several centers have shown improved evacuation after biofeedback training in patients with PSR.[11,21,22]

Pudendal Nerve Terminal Motor Latency

Pudendal nerve terminal motor latency (PNTML) is a measurement of time, or latency, from stimulation of the pudendal nerve at the level of the ischial spine to the muscle response in the external anal sphincter.[5,23] A disposable electrode is placed on the examiner's gloved index finger (Fig. 11.4) and inserted into the anal canal (Fig. 11.5). The stimulation is transrectally performed with the electrode located at the ischial spine while the response is recorded at the base of the examiner's finger. Recordings are made from both sides of the pelvis, as pudendal nerve damage may be asymmetric in some

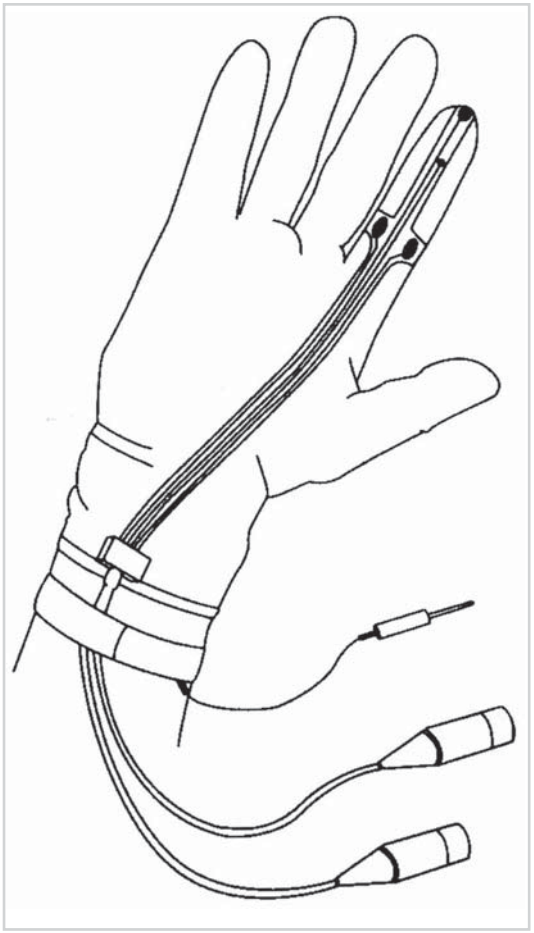

Figure 11.4. The St. Mark's pudendal electrode is placed on the examiner's gloved index finger. (From Tetzschner T, Sorensen M, Johnson L, Lose G, Christiansen J. Delivery and pudendal nerve function. Acta Obstet Gynecol Scand 1997;76:324–331, with permission from Blackwell Publishing.)

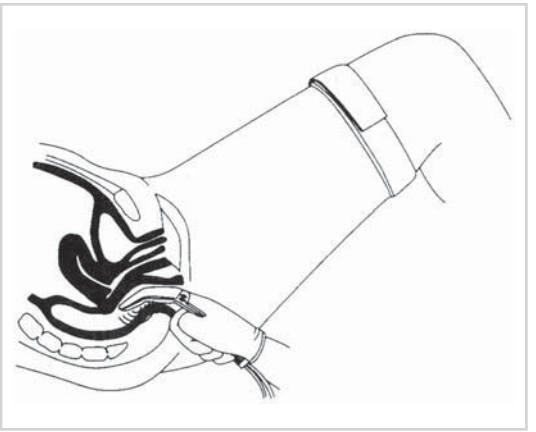

Figure 11.5. The St. Mark's pudendal electrode is inserted into the anal canal and rectum. The stimulation is performed transrectally with the electrode located at the ischial spine (From Tetzschner T, Sorensen M, Johnson L, Lose G, Christiansen J. Delivery and pudendal nerve function. Acta Obstet Gynecol Scand 1997;76:324–331, with permission from Blackwell Publishing.)

patients.[24] The latency of a normal pudendal nerve is 2.1 ± 0.2 msec, with a normal range of 2.5 msec; however, the latency increases with age.[23] Latency is dependent on the size and degree of myelination of the nerve fibers and neuropathies affecting the myelin such as diabetes, which affect the speed of conduction.

Pudendal nerve terminal motor latency is usually studied in patients with fecal incontinence as it may be of diagnostic value in these patients.[25,26] However, some patients with constipation have prolonged PNTML and, in one study, the overall incidence of pudendal neuropathy in constipated patients was 24%; patients with PSR had a higher incidence of bilateral neuropathy.[27] However, the role of PNTML measurements in constipated patients remains unclear, and this measurement is not always performed in the evaluation of patients with constipation.

Other Neurophysiological Techniques

Anorectal sensation may be evaluated by measuring the electrosensitivity. With this method, an electrode is placed into the rectum and the anal canal and a steadily increasing current is applied until the patient reports a threshold sensation. Transcutaneous electrical stimulation of the sacral plexus and transcranial magnetic stimulation of the motor cortex may add some information regarding the level of neurologic injury. These techniques are not widely used in the assessment of the pelvic floor.

Conclusion

Objective evaluation of the pelvic floor is an important part of the assessment of patients with defecation disorders. In this assessment, EMG is used to diagnose PSR and to assess the effect of biofeedback treatment. For practical reasons, surface EMG using an anal plug is usually preferred in this assessment. The role of PNTML and testing of anorectal sensation with electrosensitivity in constipated patients remains unclear.

References

1. Adrian ED, Bronk DW. The discharge of impulses in motor nerve fibers. In J Physiol 1929;67:119–151.
2. Beck A. Elektromyographische Untersuchungen am sphinkter ani. Arch Physiol 1930;224:278–292.
3. Porter NH. A physiological study of the pelvic floor in rectal prolapse. Ann R Coll Surg Engl 1962;31:379–404.
4. Floyd WF, Walls EW. Electromyography of the sphincter ani externus in man. J Physiol 1953;122:599–609.
5. Neill ME, Swash M. Increased motor unit fibre density in the external anal sphincter muscle in ano-rectal incontinence: a single fibre EMG study. J Neurol Neurosurg Psychiatry 1980;43:343–347.
6. Percy JP, Neill ME, Kandiah TK, Swash M. A neurogenic factor in faecal incontinence in the elderly. Age Ageing 1982;11:175–179.
7. Henry MM, Snooks SJ, Barnes PR, Swash M. Investigation of disorders of the anorectum and colon. Ann R Coll Surg Engl 1985;67:355–360.
8. O'Donnell P, Beck C, Doyle R, Eubanks C. Surface electrodes in perineal electromyography. Urology 1988;34:375–379.
9. Pfeifer J, Teoh T-A, Salanga VD, Agachan F, Wexner SD. Comparative study between intraoperative sponge and needle electrode for electromyographic evaluation of constipated patients. Dis Colon Rectum 1998;41:1153–1157.
10. Binnie NR, Kawimbe BM, Papachrysostomou M, Clare N, Smith AN. The importance of the orientation of the electrode plates in recording the external anal sphincter EMG by non-invasive anal plug electrodes. Int J Colorect Dis 1991;6:5–8.
11. Bleijenberg G, Kuijpers HC. Treatment of the spastic pelvic floor syndrome with biofeedback. Dis Colon Rectum 1987;30:108–111.
12. Snooks SJ, Barnes PRH, Swash M, Henry MM. Damage to the innervation of the pelvic floor musculature in

chronic constipation. Gastroenterology 1985;89:977–981.
13. Kuijpers HC, Bleijenberg G. The spastic pelvic floor syndrome. A cause of constipation. Dis Colon Rectum 1985;28:669–672.
14. Johansson C, Nilsson B-Y, Holmström B, Dolk A. Is paradoxical sphincter reaction provoked by needle electrode electromyography? Dis Colon Rectum 1991;34: 1109–1112.
15. Jorge JMN, Wexner SD, Ger GC, Salanga VD, Nogueras JJ, Jagelman DG. Cinedefecography and electromyography in the diagnosis of nonrelaxing puborectalis syndrome. Dis Colon Rectum 1993;36:668–676.
16. Johansson C, Ihre T, Holmstrom B, Nordstrom E, Dolk A, Broden G. A combined electromyographic and cineradiologic investigation in patients with defecation disorders. Dis Colon Rectum 1990;33:1009–1013.
17. Keighley MRB, Shouler P. Outlet syndrome: is there a surgical option? J R Soc Med 1984;77:559–563.
18. Jones PN, Lubowski DZ, Swash M, Henry MM. Is paradoxical contraction of puborectalis muscle of functional importance? Dis Colon Rectum 1987;30:667–670.
19. Duthie GS, Bartolo DCC. Anismus: the cause of constipation? Results of investigation and treatment. World J Surg 1992;16:831–835.
20. Lopez A, Holmstrom B, Nilsson BY, et al. Paradoxical sphincter reaction is influenced by rectal filling volume. Dis Colon Rectum 1998;41:1017–1022.
21. Dahl J, Lindquist BL, Tysk C, Leissner P, Philipson L, Järnerot G. Behavioral medicine treatment in chronic constipation with paradoxical anal sphincter contraction. Dis Colon Rectum 1991;34:769–776.
22. Gilliland R, Heymen S, Altomare D, Park UC, Vickers D, Wexner SD. Outcome and predictors of success of biofeedback for constipation. Br J Surg 1997;84: 1123–1126.
23. Swash M, Snooks SJ. Motor nerve conduction studies of the pelvic floor innervation. In: Henry MM, Swash M, eds. Coloproctology and the Pelvic Floor. Oxford: Butterworth-Heinemann, 1992:196–206.
24. Lubowski DZ, Jones PN, Henry MM. Asymmetrical pudendal nerve damage in pelvic floor disorders. Int J Colorect Dis 1988;3:158–160.
25. Kiff ES, Barnes PRH, Swash M. Evidence of pudendal neuropathy in patients with perineal descent and chronic straining at stool. Gut 1984;25:1279–1282.
26. Kiff ES, Swash M. Slowed conduction in the pudendal nerves in idiopathic (neurogenic) faecal incontinence. Br J Surg 1984;71:614–616.
27. Vaccaro CA, Cheong DM, Wexner SD, Salanga VD, Phillips RC, Hanson MR. Role of pudendal nerve terminal motor latency assessment in constipated patients. Dis Colon Rectum 1994;37:1250–1254.

12

Dynamic Magnetic Resonance Imaging and Nuclear Imaging

Adil E. Bharucha, Joel G. Fletcher, and John H. Pemberton

Defecation requires intraabdominal pressure coordinated with relaxation of the anal sphincters and pelvic floor muscles, particularly the puborectalis muscles. Pelvic floor motion can be imaged in real-time by barium fluoroscopy, radioisotope scintigraphy, or magnetic resonance imaging (MRI). Barium evacuation proctography was described in separate reports by Burhenne[1] in 1964 and Phillips and Edwards[2] in 1965. O'Connell et al[3] developed scintigraphy to quantify rectal evacuation after ileal pouch anal anastomosis with lesser radiation exposure compared to barium proctography. Dynamic MRI visualizes anorectal and pelvic floor motion during rectal evacuation without radiation exposure.[4]

Scintigraphic Defecography

Anorectal motion during evacuation is measured with a radioisotope-filled balloon within the rectum and anal canal.[5] Rectal evacuation is measured by filling the rectum with a radioisotope.

Procedure

A low-compliance, 16-cm long, latex balloon is inserted through the anal canal into the rectum (Fig. 12.1). The balloon is connected to a reservoir filled with 500 cc of water labeled with technetium-99m (^{99m}Tc). Radioactive markers are taped to the skin over the pubis anteriorly and over the tip of the coccyx posteriorly. With the patient in the left lateral decubitus position, static images are acquired over 15 seconds at rest, during squeeze, and during evacuation by a large-field-of-view gamma camera. The anal canal axis is defined by a line drawn through the middle of the balloon image of the anal canal. The rectal axis is defined by a line drawn parallel to the most inferior portion of the rectal image, just cephalad to the anal canal. The location of the anorectal junction is measured as the perpendicular distance from a line drawn between the pubococcygeal line to the most caudal aspect of the rectal image. In healthy persons, rectal evacuation is associated with widening of the anorectal angle and perineal descent (Fig. 12.2). In patients with symptoms of a functional defecation disorder, scintigraphy may reveal either reduced motion (i.e., anorectal angle change or descent), or increased perineal descent (i.e., descending perineum syndrome).[6,7]

To quantify rectal emptying, the rectum is filled with a 7.5% colloidal dispersion of aluminium magnesium silicate labeled with 1 mCi of ^{99m}Tc with patients in the left lateral decubitus position.[3,8] Images are obtained before evacuation (3-minute acquisition), during evacuation (2-second dynamic images over 4 minutes), and after evacuation (3-minute acquisition) on a commode. The percentage and rate of total ^{99m}Tc evacuation is calculated; less than 37% evacuation (i.e., 2 standard deviations below mean) is considered abnormal[3] (Fig. 12.3). The median evacuation time for seven asymptomatic subjects was 40 seconds.

Utility

By documenting abnormal (i.e., reduced or increased) anorectal motion during evacuation,

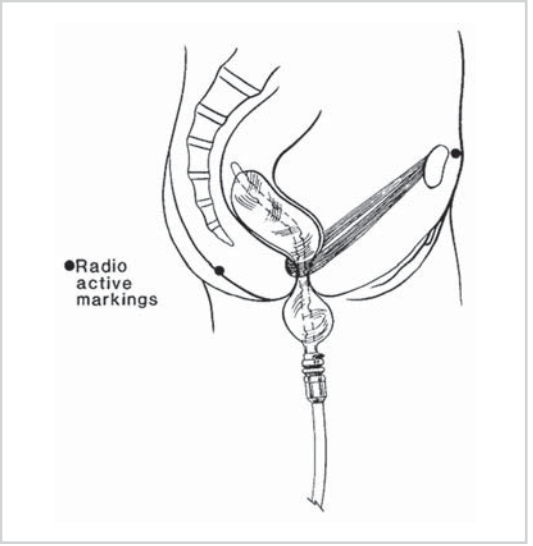

Figure 12.1. Diagram of the scintigraphic balloon device in place. The proximal portion of the balloon rests in the rectum, the central portion traverses the anal canal, and the distal portion projects beyond the anal verge. Radioactive markers are taped to the skin over the pubis anteriorly and over the tip of the coccyx posteriorly. (From Barkel et al,[5] copyright Lippincott Williams & Wilkins, 1988.)

scintigraphy is useful for confirming a clinically suspected functional disorder of defecation, with far less radiation than is delivered by standard fluoroscopic technique.[5,6] Anorectal scintigraphy has not been directly compared to barium evacuation proctography. However, in contrast to barium proctography, scintigraphic proctography cannot visualize anatomic disturbances during rectal evacuation such as a rectocele, enterocele, rectal intussusception, or uterine prolapse.

Magnetic Resonance Proctography

Magnetic resonance imaging (MRI) is a relatively new modality for imaging anal sphincter anatomy and pelvic floor motion during defecation and squeeze without radiation exposure.[9] The anal sphincters can also be visualized, preferably using an endoanal MRI coil.[10]

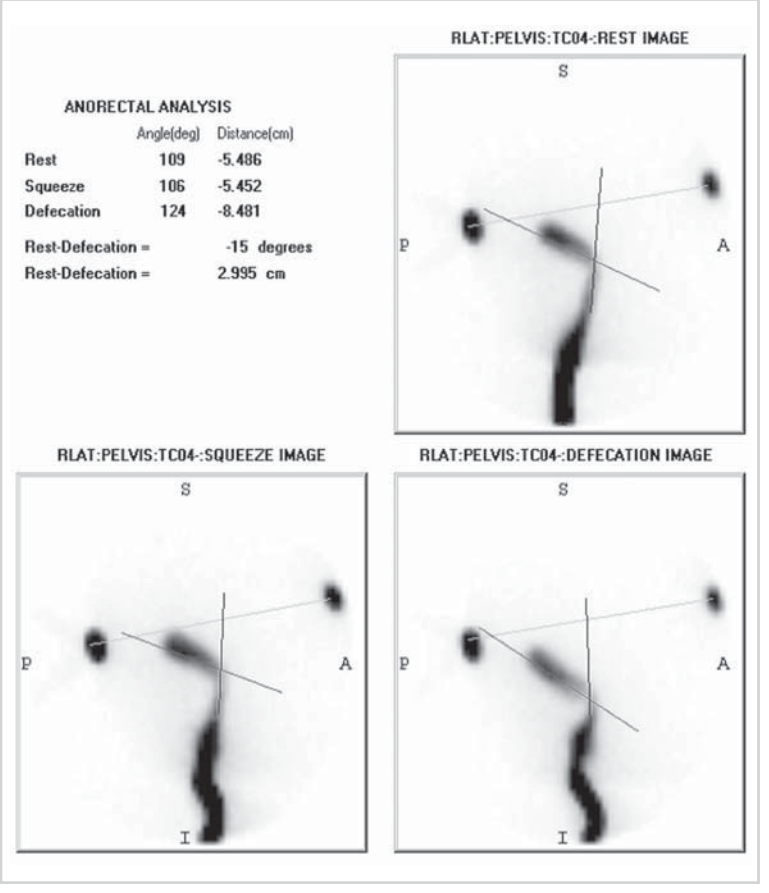

Figure 12.2. Scintigraphic evaluation of anorectal motion during evacuation and squeeze. Observe that the part of the balloon shaded black is outside the anal canal.

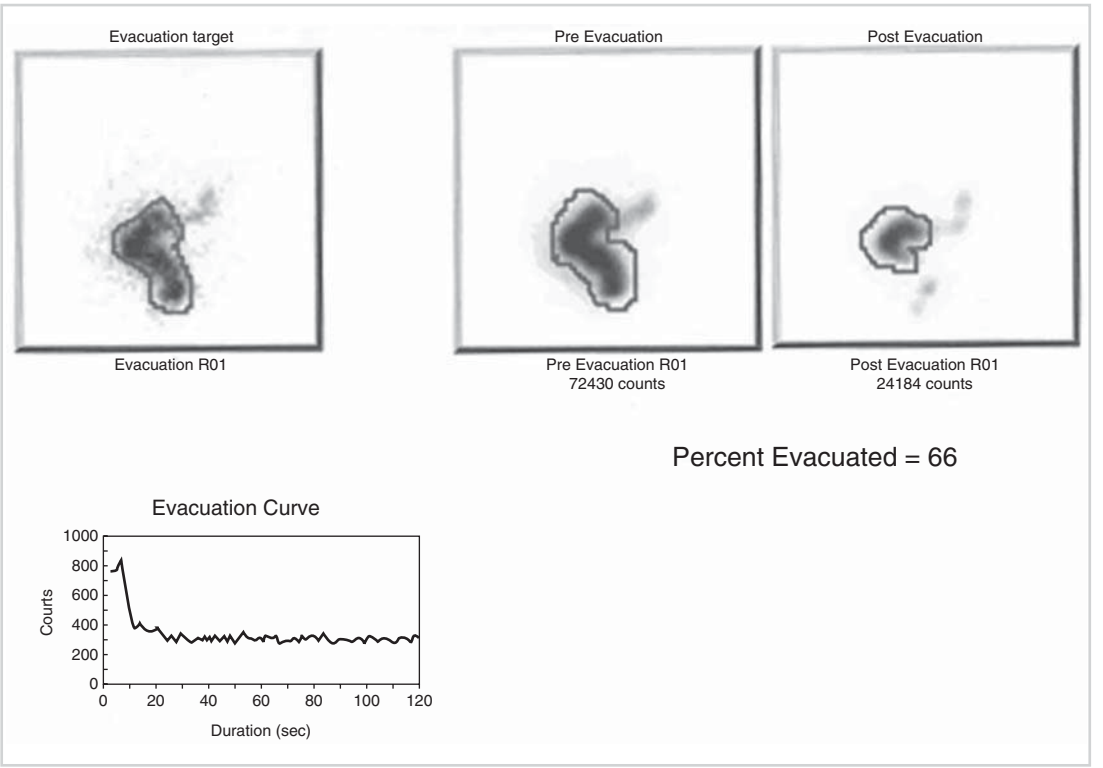

Figure 12.3. Scintigraphic evaluation of normal rectal evacuation.

Procedure

No preparation is necessary. After adding about 150 mL of ultrasound (US) gel to the rectum, anorectal and pelvic floor motion are visualized in real time while patients squeeze (i.e., contract) the pelvic floor muscles and expel rectal contents. Using a modified T2-weighted single-shot fast spin echo (SSFSE) imaging sequence or T2-weighted fast imaging with steady-state precession (FISP) MRI sequence, pelvic floor motion can be imaged at 1.2- to 2-second intervals.[11] Images can be reconstructed in real time, or shortly after acquisition, so that patients can be instructed or encouraged during maneuvers. After the evacuation sequence, patients are removed from the magnet and asked to empty the bladder and remaining rectal contents. Patients are then repositioned within the magnet to obtain additional dynamic sagittal images during the Valsalva maneuver, in order to maximize the detection of cystoceles and enteroceles.[12] Finally, contiguous coronal images are acquired at rest and during the Valsalva maneuver.[10]

Rapid image acquisition is necessary to visualize pelvic floor motion in real time because patients can maintain maximum rectal excursion during evacuation or puborectalis contraction when they squeeze for 15 to 30 seconds at most (Figs. 12.4 and 12.5). In contrast to scintigraphy or fluoroscopy, conventional, closed-configuration MR systems permit imaging in the supine position only. However, there is little difference in the detection of clinically relevant findings between supine MR and seated MR using open-configuration magnets. The exception is in detecting rectal intussusceptions for which seated MRI was superior.[13]

Similar to barium evacuation proctography, anorectal motion is quantified by measuring anorectal angles and anorectal junction during evacuation and squeeze maneuvers. Because the bony landmarks (e.g., pubis, sacrococcygeal junction) necessary to measure anorectal descent are more distinctly visualized during MRI, it is easier to make these measurements from MR compared to routine fluoroscopic images. A rectocoele is defined as an anterior bulge beyond the expected and extrapolated line

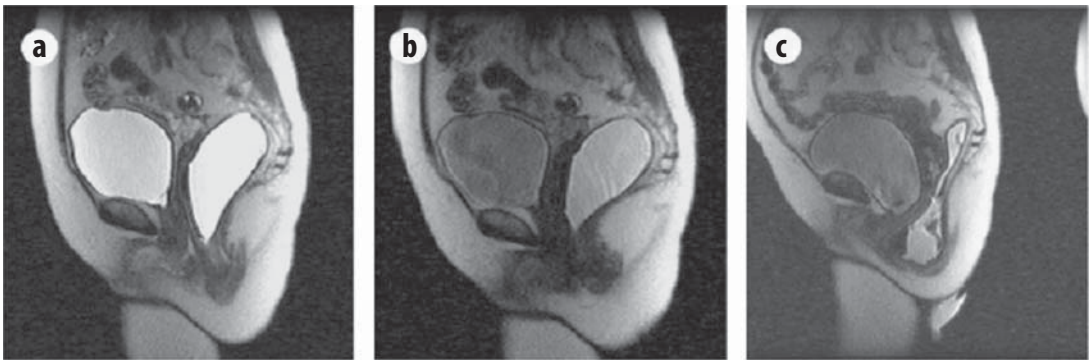

Figure 12.4. Magnetic resonance fluoroscopic images of the pelvis at rest (a), during squeeze (b), and simulated defecation (c) in a 52-year-old asymptomatic patient after filling the rectum with ultrasound gel. At rest, the pelvic floor was well supported; the anorectal angle was relatively obtuse (126 degrees). Pelvic floor contraction during the squeeze maneuver was accompanied by normal upward and anterior motion of the anorectal junction; the angle declined to 95 degrees. During rectal evacuation, the bladder base dropped by 2.5 cm below the pubococcygeal line; the 2.8-cm anterior rectocoele emptied completely and was probably not clinically significant; perineal descent (5 cm) was outside the normal range for evacuation proctography.

of the anterior rectal wall or a posterior bulge beyond the posterior wall.[14] A peritoneocele is characterized by protrusion of the peritoneal fat or fluid crossing the junction of the upper third and distal two thirds of the vagina, with separation of the rectovaginal septum. When this pouch contains small intestinal loops, it is described as an enterocoele (Fig. 12.6). Descent of the bladder base and either the cervix (when the uterus is present) or vaginal apex (for women who had a previous hysterectomy) are recorded relative to the pubococcygeal line.[14,15]

Utility

In asymptomatic women without a history of, or risk factors for, pelvic floor injury, anorectal motion parameters were comparable to previous studies using barium defecography (Table 12.1).[16] These normal values are derived from a group of women (mean age, 43; range 23–69 years) who did not have risk factors for anorectal trauma or bowel symptoms by detailed questionnaire. Observe that the normal range for anorectal angle change during evacuation was wide, perhaps because some asymptomatic subjects may have pelvic floor dysfunction. Normal values for anorectal motion may be technique dependent.[15] The utility of dynamic MRI for diagnosing functional disorders of defecation has not been thoroughly studied. An early study suggested that MR revealed disordered anorectal motion in 13 patients with symptoms of disordered defecation and normal routine anorectal physiologic tests.[17] More detailed studies suggest that dynamic MRI may have a

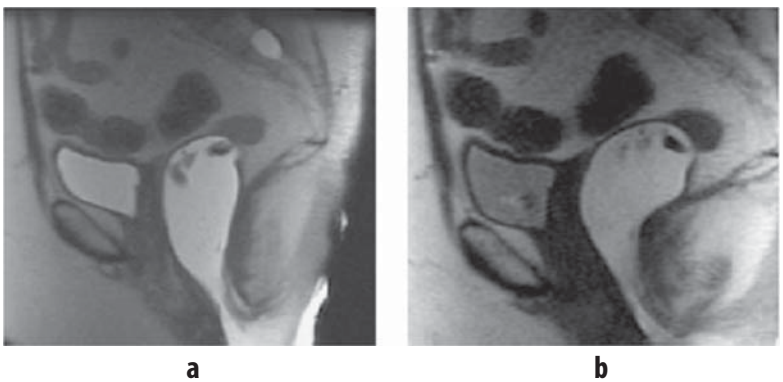

Figure 12.5. Pelvic magnetic resonance fluoroscopic images at rest (a) and squeeze (b) in a 57-year-old woman who has fecal incontinence. During squeeze, the puborectalis indentation on the posterior rectal wall was exaggerated compared to rest, and the anorectal angle declined from 143 degrees at rest to 90 degrees during squeeze; however, the anal canal remained patulous.

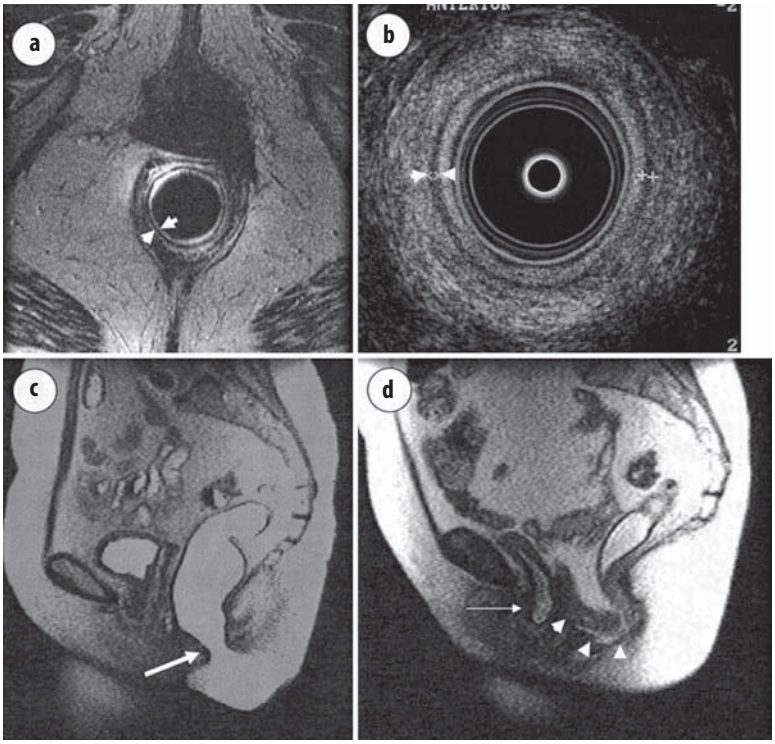

Figure 12.6. Endoanal T2-weighted fast spin echo imaging of the anal sphincters demonstrates marked diffuse thinning of the internal anal sphincter (arrowheads, a), along with correlative endoanal ultrasound (*arrowheads, b*). Dynamic MR proctography images at rest (*c*) demonstrates a patulous anal canal at rest (*arrow*). Dynamic MR proctography images during defecation *(d)* show a large enterocele *(arrowheads)*, with mesenteric fat and small bowel.

role when the diagnosis of an evacuation disorder cannot be confirmed by routine methods, for example, in patients with normal or increased perineal descent during a clinical examination, and a normal balloon expulsion test.[18] In addition to characterizing disordered squeeze or evacuation, dynamic MRI can also characterize pelvic organ prolapse, including rectocoele size, which is associated with increased perineal descent.[19] Lastly, patients find it useful to review images of evacuation for understanding the nature of their disorder, and the need for pelvic floor retraining.

Studies utilizing a relatively slow image acquisition sequence (i.e., every 4 to 31 seconds), found a poor correlation between MRI and barium proctography.[20,21] In contrast, when the acquisition time is 1.2 to 2.0 seconds, the correlation between dynamic MRI and colposystoproctography for all three pelvic floor compartments (anterior, middle, and posterior) was excellent.[22]

Table 12.1. Normal values for anorectal motion by dynamic mRI

Parameter	Mean	10^{th}, 90^{th} percentile values
Anorectal angle at rest	103 degrees	87, 124
Anorectal angle during evacuation	122 degrees	105, 138
Anorectal angle during squeeze	72 degrees	52, 85
Anorectal angle change during evacuation	19 degrees	−1, 40
Anorectal angle change during squeeze	−31 degrees	−13, −53
Location of anorectal junction at rest	2.2 cm	0.6, 3.9
Perineal descent during evacuation	3.3 cm	1.6, 5.1
Perineal ascent during squeeze	1.7 cm	1.0, 2.6

Negative values indicate a smaller angle during the maneuver compared to rest. Distances reflect perpendicular distance from the anorectal junction to the pubococcygeal line.

Acknowledgments

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References

1. Burhenne HJ. Intestinal evacuation study: a new roentgenologic technique. Radiol Clin 1964;33:79–84.
2. Phillips SF, Edwards DA. Some aspects of anal continence and defaecation. Gut 1965;6:396–406.
3. O'Connell PR, Kelly KA, Brown ML. Scintigraphic assessment of neorectal motor function. J Nucl Med 1986;27:460–464.
4. Lienemann A, Anthuber C, Baron A, Kohz P, Reiser M. Dynamic MR colposystorectography assessing pelvic-floor descent. Eur Radiol 1997;7:1309–1317.
5. Barkel DC, Pemberton JH, Pezim ME, Phillips SF, Kelly KA, Brown ML. Scintigraphic assessment of the anorectal angle in health and after ileal pouch-anal anastomosis. Ann Surg 1988;208:42–49.
6. Pezim ME, Pemberton JH, Levin KE, Litchy WJ, Phillips SF. Parameters of anorectal and colonic motility in health and in severe constipation. Dis Colon Rectum 1993;36:484–491.
7. Harewood GC, Coulie B, Camilleri M, Rath-Harvey D, Pemberton JH. Descending perineum syndrome: audit of clinical and laboratory features and outcome of pelvic floor retraining. Am J Gastroenterol 1999;94: 126–130.
8. Hutchinson R, Mostafa AB, Grant EA, et al. Scintigraphic defecography: quantitative and dynamic assessment of anorectal function. Dis Colon Rectum 1993;36:1132–1138.
9. Stoker J, Halligan S, Bartram CI. Pelvic floor imaging. Radiology 2001;218:621–641.
10. Fletcher JG, Busse RF, Riederer SJ, et al. Magnetic resonance imaging of anatomic and dynamic defects of the pelvic floor in defecatory disorders. Am J Gastroenterol 2003;98:399–411.
11. Busse R, Riederer S, Fletcher J, Bharucha A, Brandt K. Interactive fast spin-echo imaging. Magn Reson Med 2000;44:339–348.
12. Kelvin FM, Maglinte DD, Hale DS, Benson JT. Female pelvic organ prolapse: a comparison of triphasic dynamic MR imaging and triphasic fluoroscopic cystocolpoproctography. AJR 2000;174:81–88.
13. Bertschinger KM, Hetzer FH, Roos JE, Treiber K, Marincek B, Hilfiker PR. Dynamic MR imaging of the pelvic floor performed with patient sitting in an open-magnet unit versus with patient supine in a closed-magnet unit. Radiology 2002;223:501–508.
14. Shorvon PJ, McHugh S, Diamant NE, Somers S, Stevenson GW. Defecography in normal volunteers: results and implications. Gut 1989;30:1737–1749.
15. Goh V, Halligan S, Kaplan G, Healy JC, Bartram CI. Dynamic MR imaging of the pelvic floor in asymptomatic subjects. AJR 2000;174:661–666.
16. Bharucha AE, Fletcher JG, Harper CM, et al. Relationship between symptoms and disordered continence mechanisms in women with idiopathic fecal incontinence. Gut 2005; 54:546–555.
17. Healy JC, Halligan S, Reznek RH, et al. Magnetic resonance imaging of the pelvic floor in patients with obstructed defaecation. Br J Surg 1997;84:1555–1558.
18. Bharucha AE, Fletcher JG, Seide B, Riederer SJ, Zinsmeister AR. Phenotypic variation in functional disorders of defecation. Gastroenterology 2005;128: 1199–1210.
19. Pannu HK. Magnetic resonance imaging of pelvic organ prolapse. Abdom Imag 2002;27:660–673.
20. Healy JC, Halligan S, Reznek RH, et al. Dynamic MR imaging compared with evacuation proctography when evaluating anorectal configuration and pelvic floor movement. AJR 1997;169:775–779.
21. Vanbeckevoort D, Van Hoe L, Oyen R, Ponette E, De Ridder D, Deprest J. Pelvic floor descent in females: comparative study of colpocystodefecography and dynamic fast MR imaging. J Magn Reson Imag 1999;9:373–377.
22. Kelvin FM, Maglinte DD, Hale DS, Benson JT. Female pelvic organ prolapse: a comparison of triphasic dynamic MR imaging and triphasic fluoroscopic cystocolpoproctography. AJR 2000;174:81–88.

13
Biofeedback for Constipation

Dawn E. Vickers

Constipation, with its associated symptoms, is the most common chronic gastrointestinal complaint, accounting for 2.5 million physician visits per year[1] with a prevalence of 2% in the United States population.[2] Rome II diagnostic criteria for a diagnosis of constipation are specified in Table 13.1.[3] After identification and exclusion of extracolonic or anatomic causes, many patients respond favorably to medical and dietary management. However, patients unresponsive to simple treatment may require further physiologic investigation to evaluate the pathophysiologic process underlying the symptoms. Physiologic investigation generally includes colonic transit time study, cinedefecography, anorectal manometry, and electromyography (EMG),[4] which allows for definitive diagnosis of treatable conditions including anismus, colonic inertia, rectocele, and sigmoidocele.[5]

Anismus, also termed pelvic floor dyssynergia, spastic pelvic floor syndrome, paradoxical puborectalis contraction, and nonrelaxing puborectalis syndrome, accounts for an estimated 50% of patients with symptoms of chronic constipation.[6] Rome II diagnostic criteria for a diagnosis of pelvic floor dyssynergia are specified in Table 13.2.[3] This disorder of unknown etiology is characterized by failure of the puborectalis muscle to relax during defecation. Invasive surgical therapy or injection of botulinum neurotoxin[7] are associated with an unacceptable incidence of incontinence. In 1993, Enck's[8] critical review found that biofeedback has become widely accepted as the treatment of choice for anismus.

Biofeedback Defined

Schwartz et al[9] define the biofeedback process as "a group of therapeutic procedures which utilize electronic instruments to accurately measure, process, and feed back to persons and their therapists, meaningful physiological information with educational and reinforcing properties about their neuromuscular and autonomic activity, both normal and abnormal, in the form of analog, binary, auditory and/or visual feedback signals." This process helps patients develop a greater awareness of, confidence in, and an increase in voluntary control over physiologic processes. This result is best achieved with a competent biofeedback professional. Employing biofeedback instruments without proper cognitive preparation, instruction, and guidance is not appropriate biofeedback therapy. As with all forms of therapy, the therapist's skill, personality and attention to the patient affect the outcome.[9]

It has been suggested that when researchers understand the essential components of biofeedback training, research studies are often successful. These components are as follows: (1) The biofeedback instrument is no more and no less than a mirror. Like a mirror, it feeds back information, but has no inherent power to create change in the user. (2) To maximize results, biofeedback training, like any type of complex skill training, involves clear goals, rewards for approximating the goals, ample time and practice for achieving mastery, proper instruction, a variety of systematic training techniques, and feedback of information. (3) The individual

Table 13.1. Rome II criteria for diagnosis of constipation

In the preceding 12 months, the patient had two or more of the following for 12 weeks, which need not be consecutive:
- Straining >25% of defecations
- Lumpy or hard stools >25% of defecations
- Sensation of incomplete evacuation >25% of defecations
- Sensation of anorectal obstruction/blockage >25% of defecations
- Manual maneuvers to facilitate >25% of defecations (e.g., digital evacuation, support of the pelvic floor)
- <3 defecations per week
- Loose stools are not present, and there are insufficient criteria for irritable bowel syndrome

using the feedback must have a cognitive understanding of the process and goals, and positive expectations and positive interaction with the trainer, and must be motivated to learn.[10]

Practical Aspects of Biofeedback Therapy for Constipation

Practical aspects of using biofeedback therapy for pelvic floor muscle (PFM) dysfunction to treat symptoms of constipation and fecal incontinence include the technical, therapeutic, behavioral, and the pelvic muscle rehabilitation (PMR) components. The technical component involves the instrumentation used to provide meaningful information or feedback to the user. There are several technical systems available, and the advantages of any one device have not been scientifically tested. Devices include surface electromyography (sEMG), water-perfused manometry systems, and the solid-state manometry systems with a latex balloon. Although each system has inherent advantages and disadvantages, most systems provide reproducible and useful measurements. The choice of any one system depends on many factors, including cost and the goals of training. A solid-state system is preferable to a water-perfused system because there is no distraction or embarrassment from leakage of fluid, and the patient can be reoriented to a sitting position without adversely affecting calibration. Although this instrumentation is of proven effectiveness, this method is relatively cumbersome, complicated, and expensive. The sEMG instrumentation is widely used, proven effective, and suitable for office use.[11,12] Patients are able to remain fully clothed during the session and position changes are easily accomplished to assist with functional maneuvers. The therapeutic component involves the clinician's taking an active role by establishing a rapport with the patient, listening to concerns, reviewing the patient's medical history including current medications as well as over-the-counter and herbal preparations, reviewing bowel and bladder habits, educating the patient, and interpreting data.

Clinicians must have a complete understanding of bowel and bladder functioning considering the coexistence of multifactorial concomitant PFM dysfunction. In a patient with symptoms of urinary stress incontinence, nocturia, and difficulty voiding, Figure 13.1 shows the dysfunctional voiding pattern on the cystometrogram (CMG). The increased sEMG activity is indicative of outlet obstruction, inhibiting the detrusor contraction, thus requiring excessive straining by increasing intraabdominal pressure to empty the bladder. This consequently produces a dysfunctional defecation pattern and contributes to symptoms of constipation. Chronic straining with stool is another source of pelvic floor muscle denervation that contributes to pelvic floor muscle weakness and

Table 13.2. Rome II diagnostic criteria for a diagnosis of pelvic floor dyssynergia

The patient must satisfy diagnostic criteria for functional constipation (Table 13.1)
There must be manometric, EMG, or radiologic evidence for inappropriate contraction or failure to relax the pelvic floor muscles during repeated attempts to defecate
There must be evidence of adequate propulsive forces during attempts to defecate, and
There must be evidence of incomplete evacuation

EMG, electromyography.

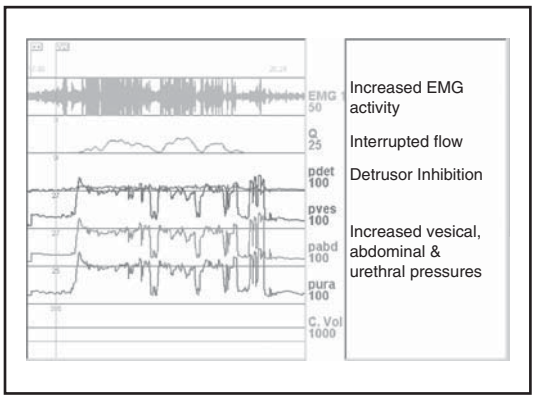

Figure 13.1. Voiding phase cystometrogram (CMG) recording.

incontinence.[13] Patients with fecal incontinence may complain of multiple daily bowel movements and a feeling of incomplete evacuation resulting in postdefecation seepage.[9] Many patients who present with constipation frequently have symptoms of urinary incontinence. Due to the coexistence of concomitant multifactorial PFM dysfunction associated with weak PFM and outlet obstruction, it is difficult to offer a specific standard biofeedback therapy protocol that is beneficial for all patients. Therefore, the clinician must address all bowel and bladder symptoms and develop an individualized program for each patient with progressive realistic goals. The behavioral component is aimed toward systematic changes in the patient's behavior to influence bowel and bladder function. Operant conditioning utilizing trial and error as an essential part of learning is merely one aspect of the learning process. Treatment is aimed at shaping the patient's responses toward a normal model by gradually modifying the patient's responses through positive reinforcement of successive approximations to the ideal response.[9] As a behavioral program, the patient's active participation is paramount in achieving subjective treatment goals, which include symptom improvement, quality of life improvement, and patient satisfaction. The PMR component involves designing an exercise program suitable for each patient to achieve the ultimate goal of efficient pelvic floor muscle function (Table 13.3).

Table 13.3. Exercise program suitable for each patient to achieve the ultimate goal of efficient pelvic floor muscle function: components of pelvic muscle rehabilitation (PMR) utilizing surface electromyography (sEMG) instrumentation

sEMG instrumentation
Signal detection
Signal processing
Data acquisition and display
sEMG evaluation
Abdominal muscles
Pelvic floor muscles
Pelvic muscle exercise principles
Overload
Specificity
Maintenance
Reversibility
Biofeedback treatment goals
Short-term
Long-term
Behavioral strategies
Patient education
Dietary modification
Habit training for difficult, infrequent, or incomplete evacuation
Urge suppression for urinary and fecal incontinence
Biofeedback-assisted pelvic muscle exercises
Kegel exercises: isolated pelvic muscle contractions
Beyond Kegel exercises: obturator and adductor assist
Quick contractions
Valsalva or push maneuver
Physiologic quieting techniques
Diaphragmatic breathing
Progressive relaxation techniques: hand warming

Surface Electromyography Instrumentation

There is no standardization for sEMG recordings among manufacturers of biofeedback instrumentation; therefore, it is important for clinicians to understand basic technical aspects such as signal detection, signal processing, data acquisition, and display.

Signal Detection

Surface electrodes summate the electrical action potentials from the contracting muscle and establish electrical pathways from skin contact of the monitored muscle site (Fig. 13.2).[9] The sEMG instrument receives and processes this electrical correlate of a muscle activity measured in microvolts (μV) (Fig. 13.3). Muscle contraction involves the pulling together of the two anchor points; therefore, active electrodes should be placed between anchor points along the long axis of the muscle.[9] The interelectrode distance determines the volume of muscle monitored. Various types of electrodes are used with sEMG devices for pelvic muscle rehabilitation. The most direct measure of the sEMG activity from the pelvic musculature occurs when using internal sensors. Binnie et al[14] compared fine-wire electrodes to sensors with longitudinal electrodes and circumferential electrodes during rest, squeeze and push. Internal sensors with longitudinal electrodes correlated better with fine-wire electrodes in all three categories (Fig. 13.4). Current internal sensors may detect one or two channels of sEMG activity. The two-channel multiple electrode probe (MEP) anal EMG sensor (Fig. 13.5) allows discrimination between proximal and distal external anal sphincter (EAS) activity, thereby allowing the clinician to target specific areas of EAS inactivity in the rehabilitation process.

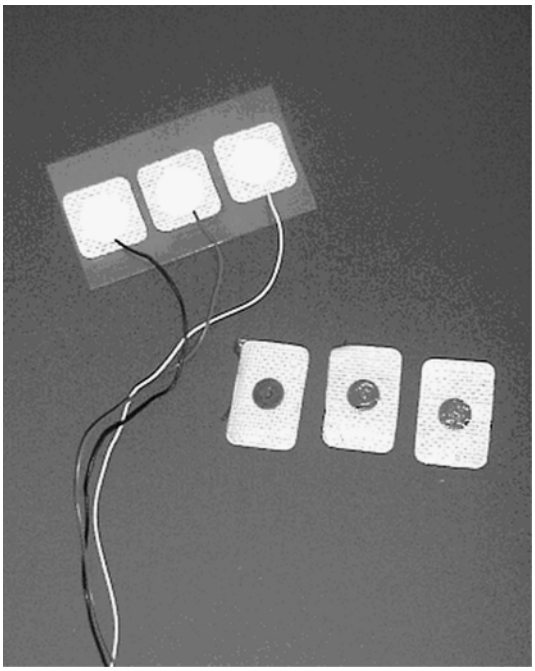

Figure 13.2. Disposable surface electromyograph (EMG) electrodes. (From Vickers D, Davila GW. Kegels and biofeedback. In: Davila GW, Ghoniem GM, Wexner SD, eds. Pelvic Floor Dysfunction: A Multidisciplinary Approach. London: Springer-Verlag, 2006:303–310.)

Signal Processing

The majority of the sEMG signal from the pelvic floor musculature is less than 100 hertz (Hz). The instrumentation should have the ability to filter noise interference allowing for a clear signal to be displayed. To detect the majority of the pelvic musculature signal, the instrumentation should have a wide bandwidth filter of 30 to 500 Hz. As the muscle fatigues, a shift to the lower frequencies (Hz) occurs; therefore, a wide bandwidth allows signal detection of low-amplitude contractions.[9] A 60 Hz "notch" filter rejects power-line interference. As all electronic instrumentation has internally generated noise, it is important for the clinician to know the internal noise level in order to distinguish noise from the sEMG signal.

Figure 13.3. The Orion platinum multimodality biofeedback system shows a typical display during a pelvic floor muscle (PFM) contraction. (Courtesy of SRS Medical, Redmond, WA.)

Figure 13.4. The SenseRx internal vaginal and anal sensors with longitudinal electrodes that maintain proper orientation to muscle fiber for accurate EMG monitoring. (Courtesy of SRS Medical, Redmond, WA.)

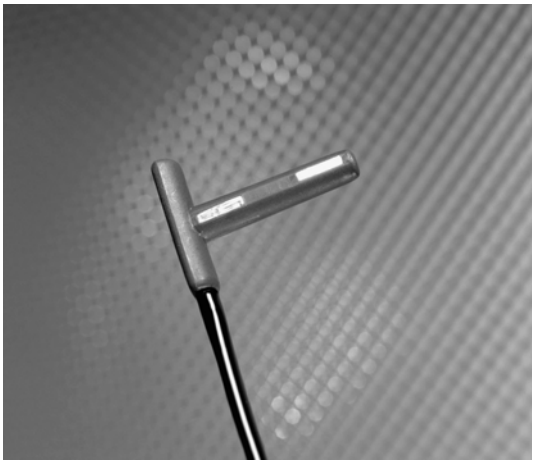

Figure 13.5. The multiple electrode probe (MEP) internal sensor. (Courtesy of SRS Medical, Redmond, WA. From Vickers D, Davila GW. Kegels and biofeedback. In: Davila GW, Ghoniem, GM, Wexner SD, eds. Pelvic Floor Dysfunction: A Multidisciplinary Approach. London: Springer-Verlag, 2006:303–310.)

Data Acquisition and Feedback Display

The sEMG instrument is designed to separate the electrical correlate of muscle activity from other extraneous noise and to convert this signal into forms of information or feedback meaningful to the user.[10] Adjusting the sensitivity settings of the feedback display permits the clinician to tailor the shaping process according to the patient's ability to perform an isolated pelvic muscle contraction. For example, if the sensitivity setting of the feedback display is 0 to 20 (μV), expanding the display to a scale of 0 to 10 (μV) provides reinforcement for submaximal contractions of weak muscles to help differentiate between abdominal contractions.

Surface Electromyography Evaluation

The abdominal and pelvic floor, the two channels of sEMG muscle activity, should be monitored simultaneously during the sEMG evaluation and the sEMG biofeedback-assisted pelvic muscle exercise training. Interpretative problems arise when monitoring only pelvic floor muscles without controlling changes in the intraabdominal pressure. The transmission of abdominal artifact to perennial measurements invalidates changes in the pelvic floor muscle measurements and can inadvertently reinforce maladaptive abdominal contractions.[9] The recommended surface electrode placement for monitoring abdominal muscle activity is along the long axis on the lower right quadrant of the abdominal oblique muscles. Perianal placement of surface electrodes may be used to monitor the pelvic floor muscles when internal sensors are inappropriate as in young pediatric patients.

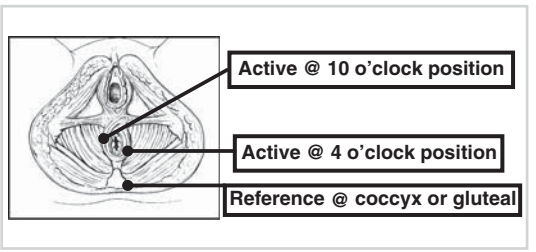

Figure 13.6. Surface perianal placement (From Vickers D, Davila GW. Kegels and biofeedback. In: Davila GW, Ghoniem, GM, Wexner SD, eds. Pelvic Floor Dysfunction: A Multidisciplinary Approach. Springer-Verlag London Ltd, 2006:303–310.)

Table 13.4. Abdominal and pelvic floor muscle surface electromyography (sEMG) evaluation

sEMG resting baseline
sEMG peak amplitude the contraction
sEMG mean amplitude of the contraction during a 10-second period
Duration of the contraction: 0 if <5 sec, 1 if 5 sec, 2 if >5 sec and ≤10 sec, 3 if >10 sec
sEMG muscle recruitment scale: 0, slow; 10, fast
Pelvic muscle isolation during contraction: 0, none; 10, good
Valsalva maneuver
Progress this week: 0, worse, to 10, excellent

Placing the active electrodes in the left and right anterolateral positions around the anal orifice and placing the reference electrode on the gluteus maximus or coccyx reduces artifact (Fig. 13.6). To obtain an evaluation, instruct the patient to simply relax, then to perform an isolated pelvic muscle contraction over a 10-second period, followed by performing a Valsalva maneuver; this sequence is repeated two to four times for accuracy (Table 13.4). During contraction, the abdominal muscle activity should remain relatively low and stable, indicating the patient's ability to isolate PFM contraction from abdominal contraction (Fig. 13.7). During the Valsalva maneuver, PFM muscle activity should decrease below the resting baseline to <2 μV, while the abdominal sEMG activity increases with elevated intraabdominal pressure (Fig. 13.8). These objective measurements are documented and reviewed with the patient. This also provides the clinician with initial objective measurements to gauge training and recommended home practice according to individual capabilities.

Pelvic Muscle Exercise Training Principles

Training principles that are important in any exercise program include the overload principle, the specificity principle, and the maintenance principle. The overload principle states that, for pelvic muscles to strengthen, they must be exercised beyond their limit. If muscles are underexercised, they are not challenged enough to increase in strength, endurance, or speed; therefore, length and resting tone remains the constant. The specificity principle states that the pelvic muscles are composed of fast- and slow-twitch fibers in roughly a 35% : 65% ratio; some fibers have a combination of fast- and

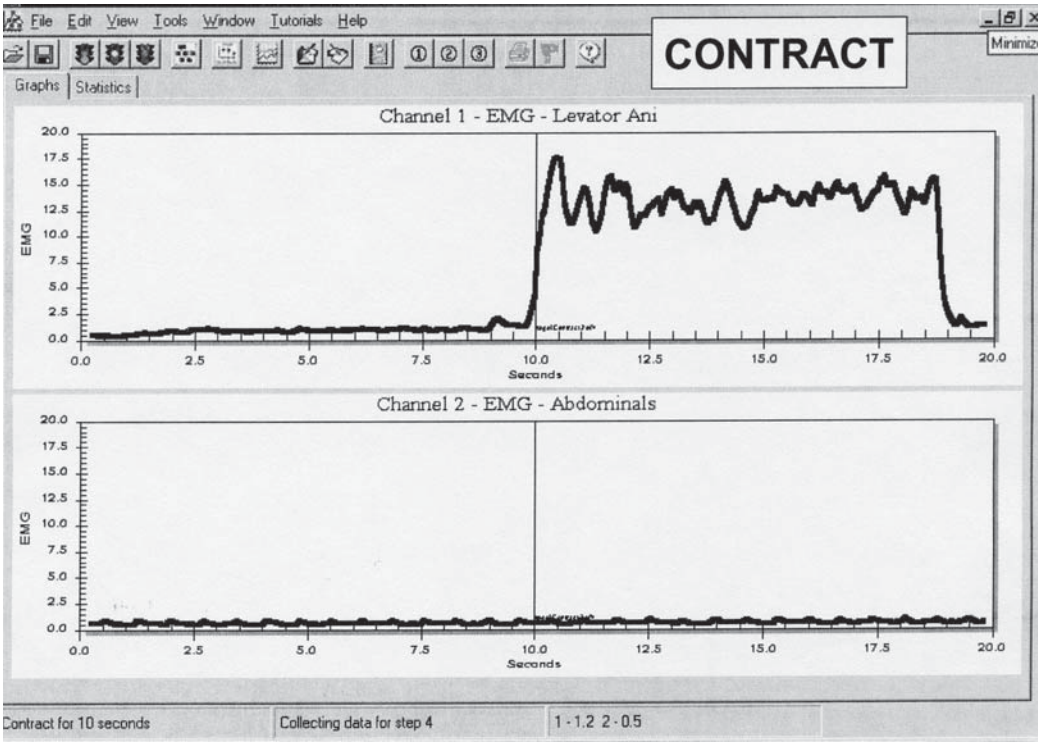

Figure 13.7. Channel 1: sEMG tracing of the PFM during contraction. Note the quick recruitment of appropriate PFM, ability to maintain the contraction, and ability to return to a normal resting tone. Channel 2: Abdominal sEMG tracing. Note the stability of the abdominal muscle activity.

slow-twitch components. Fast-twitch fibers improve in speed and strength with quick contractions, while slow-twitch fibers strengthen and gain optimal resting length and tone with longer "hold" contractions. Fast-twitch fibers fatigue quickly while slow-twitch fibers are designed for endurance and postural tone; therefore, repetitions are low for fast-twitch fibers and higher for slow-twitch fibers. The maintenance principle describes exercising for continence as a lifelong endeavor. The pelvic muscle strength is maintained by one daily 7- to 10-minute session. The reversibility principle states that, after exercising and symptomatic improvement, discontinuing exercises will result in symptom reoccurrence over time.[15]

Biofeedback Treatment Goals

After identifying functional problems and sEMG abnormalities, the clinician should prepare a treatment plan with specific short-term and long-term goals. Short-term goals describe the training components by which the patient may achieve the functional changes, whereas long-term goals refer to the expected functional outcomes (Table 13.5).[9]

Behavioral Strategies

Patient Education and Behavior Modification

Many misconceptions can be dispelled as patients gain a better understanding of their disorder. This education begins with reviewing the anatomy of the pelvic floor musculature and discussing normal bowel and bladder function with the use of visual aids. This exchange is followed by reassurance that irregular bowel habits and other defecatory symptoms are common in the healthy general population. Patients may exhibit

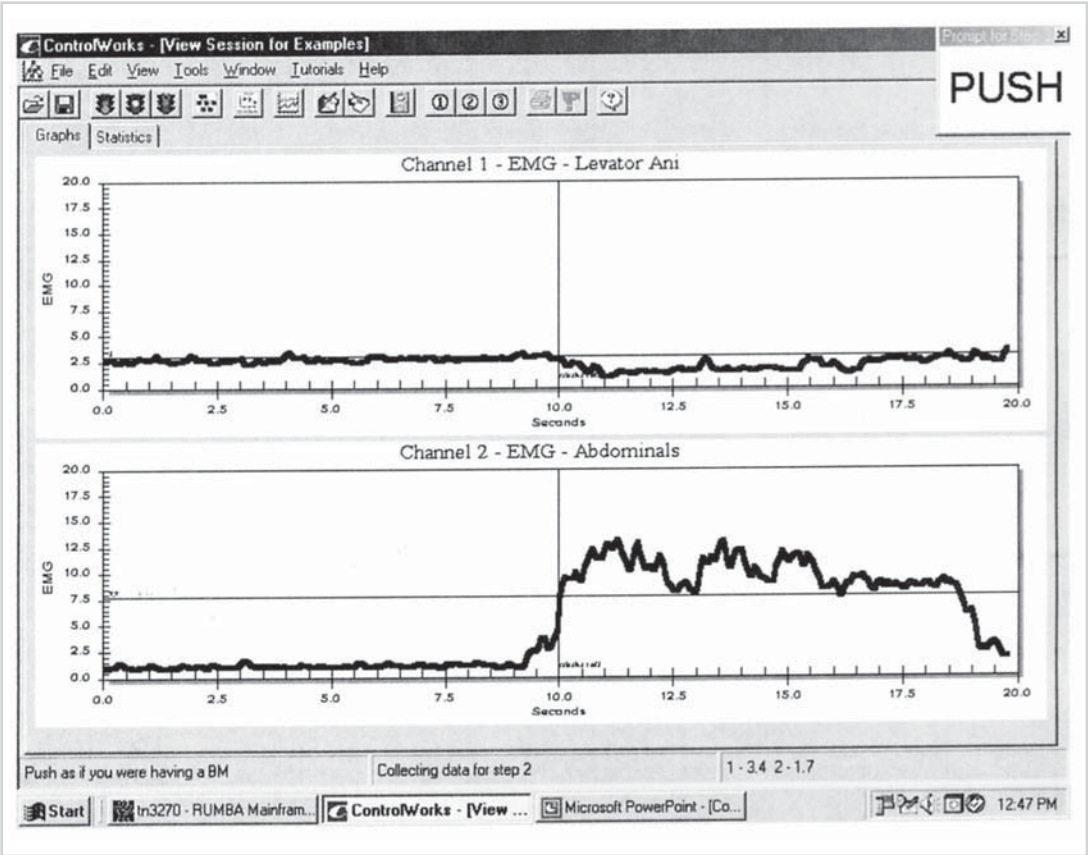

Figure 13.8. Channel 1: sEMG tracing of the PFM during a Valsalva maneuver. Note the decreased muscle activity. Channel 2: Abdominal sEMG tracing.

Table 13.5. Surface electromyography pelvic muscle rehabilitation treatment goals

Short–term goals
Reinforce pelvic floor muscle contractions isolated from abdominal and gluteal contraction
Reinforce pelvic floor muscle contractions toward greater amplitude and duration to improve strength and tone
Improve the coordination of pelvic floor muscle by shaping pelvic floor muscle contractions with short repose latency and immediate recovery to baseline after voluntary contraction ceases
Reduce chronically elevated pelvic floor muscle activity if implicated in perineal muscle pain, voiding dysfunction, or associated bowel disorders
Reduce straining pattern by reinforcing pelvic floor relaxation during defecation or micturation
To generalize skills learned in the office to the home situation
Long–term goals
Decrease laxative, enema, or suppository use
Increase number of spontaneous bowel movements
Decrease frequency of incontinent episodes
Improved symptoms of incomplete evacuation
Decreased straining

a variety of behavioral patterns. Some patients feel they need to have daily bowel movements and resort to laxative and enema misuse. Some patients may make several daily attempts straining to evacuate, while others may postpone the urge or make hurried attempts for convenience. Another frequently observed behavioral pattern, common among elderly women with symptoms of urinary incontinence, is the restriction of fluid intake to avoid leakage; in fact, this may worsen symptoms of constipation as well as symptoms of urinary incontinence. Reviewing a daily record of bowel habits guides the clinician to tailor education specifically to the underlying functional disorder.

Habit Training

Habit training is recommended for patients with symptoms of incomplete, difficult, or infrequent

evacuation. Patients are encouraged to set aside 10 to 15 minutes at approximately the same time each day for unhurried attempts to evacuate. The patient should not be overly concerned with any failure as another attempt later in the day is acceptable. This session is best initiated after a meal, which stimulates the gastrocolic reflex.[16]

The majority of commodes are approximately 35 to 40 cm in height; if a patient's feet or legs hang free or dangle above the floor while sitting, simulation of the squatting position will not be accomplished. Flexion of the hips and pelvis provides the optimal body posture. Full flexion of the hips stretches the anal canal in an anteroposterior direction and tends to open the anorectal angle, which facilitates rectal emptying. This position may be achieved by the use of a footstool to elevate the legs and flex the hips.[16]

Patients who have difficulty evacuating do not tolerate the symptoms of gas and bloating associated with fiber intake. Once emptying improves, these patients are encouraged to slowly begin weaning their laxative use and slowly adding fiber.

Dietary Modification

Dietary information is reviewed with all patients to assist in improving bowel function. Patients are provided with written informational handouts regarding foods that are high in fiber or foods that stimulate or slow transit. Offering creative fiber alternatives, which may be more appealing for patients to easily incorporate in their daily diet regimen, assists with compliance. Such alternatives include unrefined wheat bran that can be easily mixed with a variety of foods, cereals, muffins, as well as over-the-counter bulking agents. Adequate fluid intake and limiting caffeine intake is essential for normal bowel and bladder function; therefore, patients are encouraged to increase their fluid intake to 64 ounces per day unless otherwise prescribed by their physician.

Pelvic Muscle Exercise

Kegel Exercises

In the late 1940s, Arnold Kegel[17] developed a vaginal balloon perineometer to teach pelvic muscle exercises for poor tone and function of the genital muscles. He was instrumental in developing a standardized program for treating urinary stress incontinence. Kegel's program included evaluation and training utilizing visual feedback for patients to receive positive reinforcement as they monitored improvements in the pressure readings. Kegel also recommended structured home practice with the perineometer along with symptom diaries. His clinical use of these techniques showed that muscle reeducation and resistive exercises guided by sight sense are a simple and practical means of restoring tone and function of the pelvic musculature.[17]

Unfortunately, clinicians taught Kegel exercises without the use of instrumentation. Bump et al[18] showed that verbal or written instructions alone are not adequate, concluding that 50% of patients performed Kegel exercises incorrectly. There are disadvantages to teaching Kegel exercises without specific feedback from muscle contractions. There is a strong tendency to substitute abdominal and gluteal contractions for weak pelvic floor muscles. This incorrect manner of performing Kegel exercises is reinforced by sensory proprioceptive sensations, giving faulty feedback for the desired contraction, and, in effect, rendering the Kegel exercise useless.[9] For patients with fecal or urinary incontinence, abdominal contractions raise intra-abdominal pressure, thereby increasing the probability of an accident. For patients to begin performing isolated pelvic muscle contractions, they are instructed to contract their pelvic floor muscles without contracting abdominal, gluteal, or leg muscles, and to hold this contraction to the best of their ability. This is done while using the instrumentation display of the simultaneous sEMG activity of the abdominal and pelvic floor muscles for feedback. The patient must tighten the pelvic diaphragm (levator ani) in a manner similar to stopping the passage of gas or the flow of urine. Patients should be advised that the initial aim of treatment is not to produce a contraction of maximum amplitude, but to contract the pelvic floor muscle in isolation from other muscles without undue effort. To build muscle endurance, training proceeds with gradual increases in the duration of each contraction along with gradual increases in the number of repetitions. Rhythmic breathing patterns during contractions should be encouraged.

Recommended home practice is tailored according to the patient's ability and the degree of muscle fatigue observed during the session.

At each stage of treatment, patients are encouraged to practice these exercises daily without instrumentation feedback. While Kegel[17] asked patients to perform approximately 300 contractions daily during treatment and 100 during maintenance, there is no known optimal specific number of exercise sets. The goal of Kegel exercises is to facilitate rehabilitation of the pelvic floor muscles to achieve efficient muscle function. This includes normal resting tone, rapid recruitment of the pelvic floor muscles, sustained isolated pelvic muscle contraction, quick release to a normalized resting tone, and appropriate relaxation during defecation or micturation.

Beyond Kegels

The Beyond Kegel, a complete rehabilitation program for pelvic muscle dysfunction developed by Hulme, is based on the principle that the support system for the pelvic organs includes more than just the pelvic floor muscles. This support system, which is called the pelvic muscle force field (PMFF), includes the obturator internus, pelvic diaphragm (levator ani), urogenital diaphragm, and adductor muscles. In summary, these muscles function as an interdigitated and interrelated synergistic unit, rather than separated entities, to support abdominal organs, stabilize the lumbopelvic and sacroiliac region, and reflexively act for continence. Thus, as the obturator internus muscle contracts, it acts as a pulley, lifting the pelvic diaphragm and facilitating closure of the urogenital diaphragm. As the adductor contracts, it lifts the pelvic diaphragm through overflow (proprioceptive neuromuscular facilitation) principles via the close approximation of their attachments on the symphysis pubis. The balance and work/rest cycle of the obturator and adductor muscles function as an integral part of the urogenital continence system to maintain bladder and bowel continence and to facilitate effective and efficient elimination.

One portion of the Beyond Kegel protocol includes resistive exercises: (1) Obturator assist: Roll knees out against an elastic band and hold for a count of 10 seconds. Release for a count of 10 seconds. Practice 10 repetitions three times daily (Fig. 13.9). (2) Adductor assist: Roll knees inward on a soft ball and hold for a count of 10 seconds. Release for a count of 10 seconds. Practice 10 repetitions three times daily (Fig. 13.10).

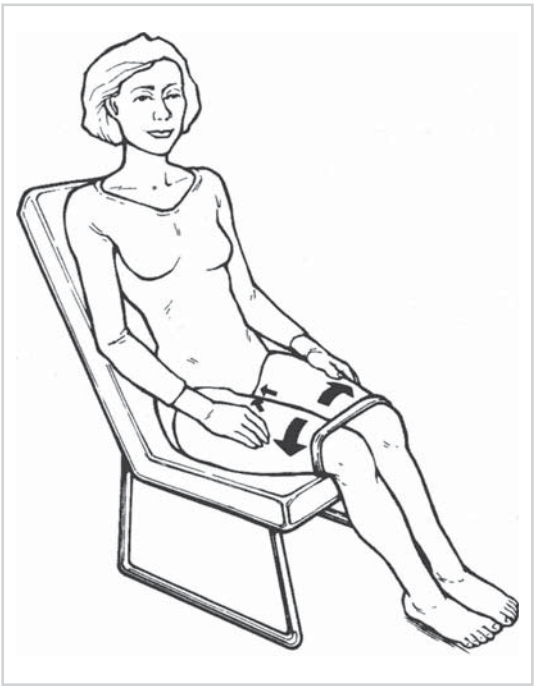

Figure 13.9. Beyond Kegel obturator assist resistive exercise.

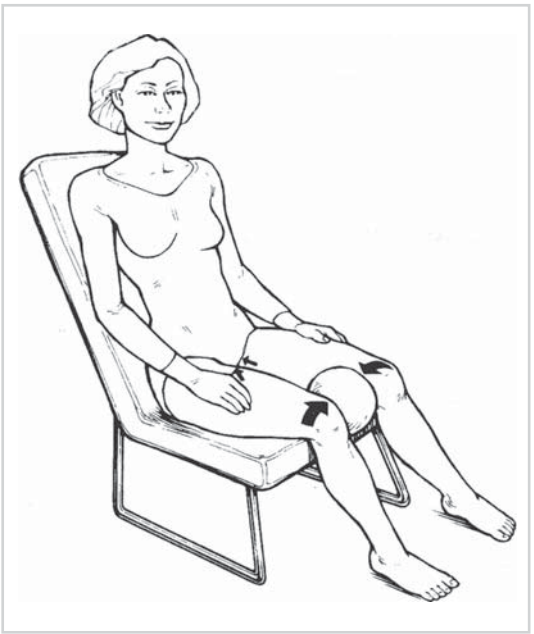

Figure 13.10. Beyond Kegel adductor assist resistive exercise.

This is a simple and effective beginning exercise for patients who are unable to perform isolated pelvic muscle contractions. As the pelvic muscles become more efficient, patients can progress to performing pelvic muscle contractions during the obturator assist and adductor assist 10-second hold. The Beyond Kegel protocols provide a detailed progressive pelvic muscle rehabilitation exercise program that has been shown to significantly improve and expedite the pelvic muscle rehabilitation process to achieve efficient muscle function.[15]

Quick Contract and Relax Exercises

This exercise improves the strength and function of the fast-twitch muscle fibers primarily of the urogenital diaphragm and external sphincter muscles. These fast-twitch muscle fibers are important for preventing accidents caused by increased intraabdominal pressure exerted during lifting, pulling, coughing, or sneezing. Once patients have learned to perform isolated pelvic muscle exercises, they are instructed to perform quick contract and release repetitions five to 10 times at the beginning and end of each exercise session they practice at home.[15]

Diaphragmatic Breathing Physiological Quieting

The breathing cycle is intimately connected to both sympathetic and parasympathetic action of the autonomic nervous system.[19] Bowel and bladder function is also mediated by the autonomic nervous system.[10] Conscious deep diaphragmatic breathing is one of the best ways to quiet the autonomic nervous system. This breathing effectively initiates a cascade of visceral relaxation responses. The aim of this exercise is to make the shift from thoracic breathing to abdominal breathing.[19] Patients are instructed to slowly inhale through the nose while protruding the abdomen outward as if the abdomen is a balloon being inflated or allowing the abdomen to rise. This maneuver is followed by slow exhalation through the mouth as the abdominal balloon deflates or as the abdomen falls. Patients are encouraged to practice this in a slow, rhythmical fashion. Visualization and progressive relaxation techniques in conjunction with diaphragmatic breathing may be used to accomplish lowering sympathetic nervous system tone, promoting quiet emotions and relaxed muscles, and ultimately promoting a quiet body.[20]

Anorectal Coordination Maneuver

Patients with symptoms of difficult, infrequent, or incomplete evacuation or those individuals with increased muscle activity while performing the Valsalva maneuver during the initial evaluation are taught the anorectal coordination maneuver. The goal is to produce a coordinated movement that consists of increasing intraabdominal (intrarectal) pressure while simultaneously relaxing the pelvic muscles. During the initial sEMG evaluation of the Valsalva maneuver, patients are asked to bear down or strain as if attempting to evacuate, which may elicit an immediate pelvic muscle contraction and closure of the anorectal outlet (Fig. 13.11). This correlates with symptoms of constipation including excessive straining and incomplete evacuation. The results of the sEMG activity observed on the screen display must first be explained and understood by the patient before awareness and change can occur. Change begins with educating the patient on diaphragmatic breathing, proper positioning, and habit training. Relaxation and quieting the muscle activity while observing the screen is reviewed. Initially patients are instructed to practice these behavioral strategies; however, some patients may continue to feel the need to "push" or strain to assist with expulsion. While observing the sEMG muscle activity on the screen, they are instructed to slowly inhale deeply while protruding the abdominal muscles to increase the intraabdominal pressure. They are then asked to exhale slowly through pursed lips. The degree of the abdominal and anal effort is titrated to achieve a coordinated relaxation of the pelvic floor muscles. Patients are encouraged to reproduce this maneuver during defecation attempts.

Biofeedback Sessions

The initial session at the Cleveland Clinic–Florida begins with a thorough history intake. The learning process begins with a description of the anatomy and physiology of the bowel and pelvic muscle function using anatomic diagrams

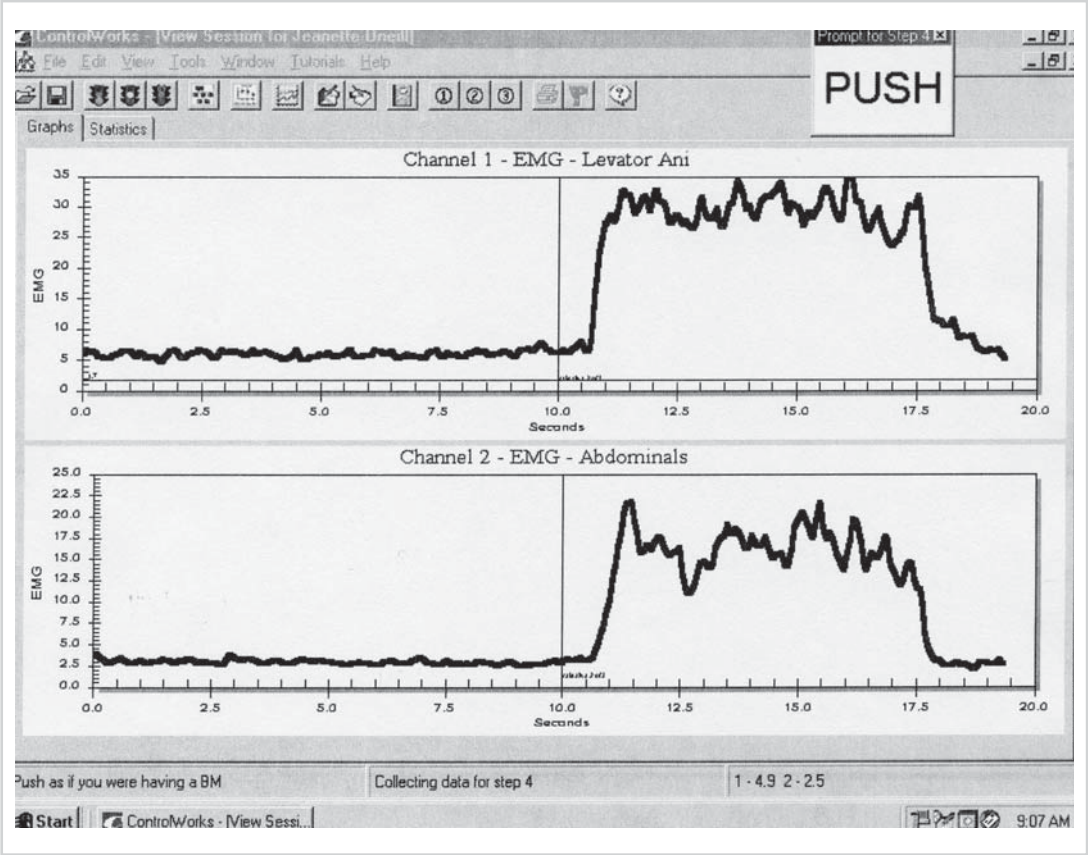

Figure 13.11. Channel 1: sEMG tracing of the PFM during a Valsalva maneuver. Note the increase muscle activity indicative of a paradoxical contraction. Channel 2: Abdominal sEMG tracing.

and visual aids. Verbal and written instructions are simplified for easy comprehension using layman's terminology. This is followed by a description of the biofeedback process, instrumentation, and PMR exercises. Patients should be aware that physicians cannot make muscles stronger or change muscle behavior. However, patients can learn to improve symptoms and quality of life by active participation and commitment to making changes. Results are not immediate; as with any exercise program, muscle improvement requires time and effort. Beginning goals of isolated pelvic muscle contractions are established and an example of sEMG tracing showing efficient muscle function is reviewed. Patients are given instructions on proper insertion of the internal sensor and remain fully clothed during the session. They are placed in a comfortable semi-recumbent position for training; however, internal sensors work in a variety of positions for functional maneuvers such as standing while reviewing urge suppression or sitting while performing the Valsalva maneuver. Surface electrodes are then placed on the right abdominal quadrant along the long axis of the oblique muscles, below the umbilicus used to monitor abdominal accessory muscle use. The cables are attached to the SRS Orion PC/12 (SRS Medical Systems, Inc., Redmond, WA) multimodality instrumentation that provides the ability to simultaneously monitor up to four muscle sites (Fig. 13.3). The EMG specifications include a bandwidth of 20 to 500 Hz and a 50/60-Hz notch filter. The sEMG evaluation is performed and reviewed with the patient.

Training for dyssynergia, incontinence, or pain begins with the systematic shaping of isolated pelvic muscle contractions. Observation of other accessory muscle use such as the gluteal or thighs during the session is discussed with the patient. Excessive pelvic muscle activity with an elevated resting tone >2 μV may be associated

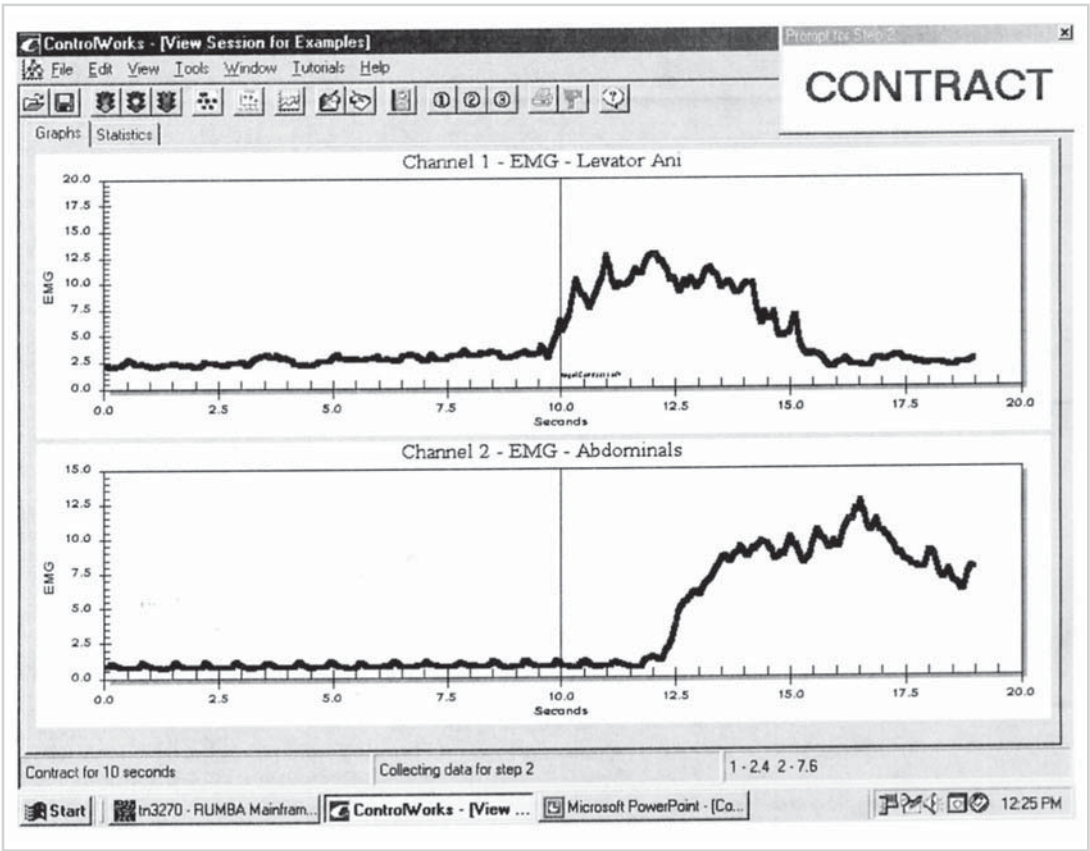

Figure 13.12. Channel 1: PFM sEMG tracing indicative of poor muscle function as seen with the slow recruitment, inability to maintain the contraction along with the recruitment of abdominal muscles seen in channel 2.

with dyssynergia, voiding dysfunction, and pelvic pain. Jacobson's progressive muscle relaxation strategy indicated that after a muscle tenses, it automatically relaxes more deeply when released.[21] This strategy is used to assist with hypertonia, placing emphasis on awareness of decreased muscle activity viewed on the screen as the PFM becomes more relaxed. This repetitive contract–relax sequence of isolated pelvic muscle contractions also facilitates discrimination between muscle tension and muscle relaxation. Some patients, usually women, have a greater PFM descent with straining during defecation associated with difficulty in rectal expulsion. Pelvic floor weakness may result in intrarectal mucosal intussusception or rectal prolapse, which contributes to symptoms of constipation. Furthermore, the PFM may not have the ability to provide the resistance necessary for extrusion of solid stool through the anal canal.[16]

Multifactorial concomitant PFM dysfunction accounts for the rationale to initiate all patients with isolated pelvic muscle rehabilitative exercises. Home practice recommendations depend on the observed decay in the duration of the contraction accompanied by the abdominal muscle recruitment (Fig. 13.12). The number of contractions the patient is able to perform before notable muscle fatigue occurs gauges the number of repetitions recommended at one time. Fatigue can be observed in as few as three to four contractions seen in patients with weak pelvic floor muscles. As an example of home practice, the patient performs an isolated pelvic floor muscle contraction, holds for a 5-second duration, relaxes for 10 seconds, and repeats three to 10 times (one set). One set is performed three to five times daily, at designated intervals, allowing for extended rest periods between sets. The lower the number of repetitions, the more

frequently interval sets should be performed daily. Excessive repetitions may overly fatigue the muscle and exacerbate symptoms. If patients are unable to perform an isolated contraction on the initial evaluation, they are given instructions for the Beyond Kegel exercises. The goal for patients is to be able to perform isolated pelvic muscle contractions alternating with the Beyond Kegel exercises, to ultimately achieve efficient PFM function. All patients are requested to keep a daily diary of bowel habits, laxative, enema or suppository use, fluid intake, number of home exercises completed, fiber intake, and any associated symptoms of constipation or incontinence.

Subsequent sessions begin with a diary review and establishing further goals aimed toward individualized symptom improvement. This is followed by an sEMG evaluation, which may include the addition of quick contract and release repetitions, Valsalva maneuver, or Beyond Kegel exercises depending on the patient's progress. These objective measurements gauge improvements in muscle activity that should be seen with each visit and occur prior to symptomatic improvement; this provides positive reinforcement for the patient to continue treatment. To assist with compliance, additional tasks should be limited to no more than three at any given time. These tasks, tailored to the individual needs, may include increasing the duration and number of PFM exercises, alternating Beyond Kegel exercises, habit training, physiologic quieting, anorectal coordination maneuvers, increasing fiber and fluid intake, increasing activity, or modifying laxative use or other methods of evacuatory assistance. Although the ideal goal may be to abolish all symptoms, this may not always be accomplished due to underlying conditions; however, individual goals are important, and some patients may be satisfied simply with the ability to leave home without fear of a significant fecal accident. Improved quality of life and patient satisfaction should be considered a treatment success.

Session Duration and Frequency

At the onset of biofeedback therapy, it may be difficult to ascertain how many sessions are required for successful training. The number of biofeedback training sessions should be customized for each patient depending on the complexity of the functional disorder as well as the patient's ability to learn and master a new skill. They are commonly scheduled from 1- to 1.5-hour visits once or twice weekly. Additionally, periodic reinforcement is recommended to improve long-term outcome.[21]

Adjunctive Treatment Method: Balloon Expulsion

Various adjunctive biofeedback treatment methods have been employed throughout the years. Balloon expulsion has been used as an objective diagnostic tool and reportedly enhances sensory awareness in patients with outlet obstruction. This training technique involves inserting a balloon into the rectum and inflating with 50 mL of air so that the patient has the sensation of the need to defecate. Adherent perianal placement of surface electrodes allows the patient to see the resultant sEMG pattern made by voluntary sphincter contraction. The patient is then asked to expel the balloon and if there is increased, rather than decreased, sphincter activity, the patient is instructed on straining without increasing sphincter activity.[22]

Efficacy of Biofeedback: Literature Review

When interpreting the clinical outcome of the studies listed in Table 13.6, one should keep in mind that there are no established guidelines regarding the number of sessions, teaching methods, clinician qualifications, type of equipment used, patient inclusion criteria, or subjective or objective data used to establish success—all of which vary considerably. Hyman et al's[23] critical review reports that, perhaps most importantly, there is no identified standard for training biofeedback clinicians to treat pelvic floor disorders. As with any therapy, the competence of the clinician is likely to have a significant impact on the outcome of treatment. Norton and Kamm[24] report that many patients lack the motivation or are unconvinced about the possible value of what they perceive to be simple exercises; therefore, the results of treatment are largely patient dependent, unlike drug or surgical therapy. Gilliland et al[25] reported that patient motivation and willingness

Table 13.6. Biofeedback studies in constipation

Author	*n*	Preevaluation	DX	Mean age	Feedback method	Sessions	Follow-up	Evaluation assessment	Percent improved	Defined Success
Emmanuel 2001[22]	49	BE, EMG, CTT, CRAFT, rectal laser Doppler flowmetry	IC	39	EMG + BD	4–7	28 mo	Diary, rectal Laser Doppler, BE, CTT cardiorespiratory autonomic function testing	59%	Pre- vs Postbiofeedback: <3 BM/week (27 vs 9) Need to strain (26 vs 9) Laxative or suppository (34 vs 9) Slow transit (22 vs 9) Rectal mucosal blood flow: improved vs not improved (29% vs 7%)
Dailianas 2000[34]	11	CTT, MN, DF, EMG	PPC	43	MN	2	6 mo	Diary	54.5%	Symptom improvement
Lau 2000[35]	173	DF	PPC	67	EMG	4–7	4–7	Diary	55%	Improved bowel function
Mollen 1999[36]	7	CTT, DF, BE, MN	PPC	30	NR	10	NR	MN	NR	Effects rectocolonic inhibitory reflex
McKee 1999[29]	30	DF, CTT, BEN, Colo, EMG, MN	PPC	35	MN	3–4	12 mo	Diary, BE	30%	Symptom improvement
Chiotakakou-Faliakou 1998[30]	100	CTT, MN, EMG	PPC + IC	40	EMG	4–5	23 mo	Phone interview	57%	Symptom improvement
Rieger 1997[31]	19	MN, DF, CTT, EMG, BE	IC	63	EMG + BD	6	6 mo	Interview	12.5%	>50% symptom reduction @ 6 mo
Glia 1997[37]	26	MN, DF, CTT, EMG, BE	PPC	55	EMG, MN	1–2/wk, < 10 wk	6 mo	Diary	58% 75% pts. completed therapy	Symptom improvement
Ko 1997[38]	32	EMG, DF, CTT, BE	PPC	50	EMG	4 (2–9)	7 mo	Diary	80%	Symptom improvement
Patankar 1997[39]	116	EMG, DF MN, CTT, DF, AUS	IC	73	EMG	8 (2–14)		Diary	73%	Satisfaction rate
Gilliland 1997[25]	194	EMG, DF, MN	PPC	71	EMG	11 (5–30)	72 mo	Return to normal (>3 unassisted BM per wk)	35% overall (63% pts completed therapy)	Normal bowel habits
Karlbohm 1997[40]	17	EMG,DF, MN, CTT	PPC	46	EMG, BE	8	14 mo	Questionnaire	43%	Improved rectal emptying
Rao 1997[41]	25	MN, DF, CTT, BE		50	MN, BE	2–10	<2 mo	Diary MN, BE	92%	>% Anal relaxation >Intrarectal pressure >Defecation index <BE time <Laxative use <Straining
Patankar 1997[42]	30			65.3	EMG	5–11	No	Diary EMG	84%	>Frequency of spontaneous BM >2/wk >EMG endurance and net strength of external anal sphincter

Park 1996[28]	68	MN, DF, CTT, EMG	PPC	65.9	EMG	11	No	Diary and questionnaire	25/85%	Improved or unimproved
Ho 1996[43]	62	MN, DF, CTT, EMG	PPC	48	MN, BE	4	14.9	Diary	90.3%	>Frequency of spontaneous BM <Laxative and enema use >Symptom improvement
Leroi 1996[44]	15	MN, EMG,	PPC	41.2	Psychotherapy, MN, EMG	16	6–10 mo	NR	66.7%	Complete recovery of symptoms
iproudhis 1995[45]	27	MN, DF, BE	PPC	46	MN, BE	1–10	1–36 mo	NR	51.8%	Complete disappearance of symptoms
Koutsomanis 1995[46]	60	CTT, EMG, BE	PPC	40.5		1–7	2–3 mo	Diary	50%	<EMG activity with Valsalva >Anismus index
Koutsomanis 1994[47]	20	MN, DF, CTT, BE	IC	34		2–6	6–12 mo	Diary	50%	>BM frequency <Straining >Symptom improvement
Bleijenberg 1987[48]	21	MN, EMG, DF, BE	PPC	37	EMG vs balloon	8–11	No	Diary Constipation score	EMG—73% BE—22%	Symptom improvement
Papachrysostomou 1994[49]	22	MN, DF, CTT, EMG, BE	PPC	42	EMG	>3	No	MN, DF, EMG Clinical improvement	89% vs 86%	<EMG activity >Improved DF >Rectal sensation
Keck 1995[50]	12	MN, DF, CTT, EMG, BE	IC	62	EMG	3	1–8 mo	Telephone interview	58%	Symptom improvement
Turnbull 1992[51]	7	MN, DF, CTT, EMG	PPC	35.7	MN, relax	4–5	2–4 yr	Diary	85.7%	Stool frequency <Symptoms bloating and pain
Fleshman 1992[52]	9	MN, DF, CTT, EMG, BE	PPC	49.4	EMG, BE, relax	2 × 6	>6 mo	BE, EMG	100%	<EMG activity during strain BE 60 cc Eliminate psyllium slurry
Wexner 1992[53]	18	MN, DF, CTT, EMG	PPC	67.7	EMG	9	1–17	Diary	88.9%	Spontaneous BM frequency <Laxative use
Dahl 1991[26]	9	MN, DF, CTT, EMG, BE	IC	41	EMG	5	6	Diary	77.8%	BM frequency <Laxative use
Kawimbe 1991[54]	15	MN, BE	PPC	45	EMG	2/d	6.2	DF, diary	86.7%	<Anismus index >Anorectal angle straining BM frequency
Lestar 1991[55]	16	MN, DF, BE, CTT, EMG	PPC	42.5	Defecometer	1	0	Defecometer	68.7%	Ability to expel balloon
Weber 1987[56]	22	MN	IC		MN	2–4	0	NR	18.2%	Daily spontaneous BM
Bleijenberg 1995[48]	10	DF, CTT, EMG	PPC	32	EMG, BE	Daily	7	NR	70%	Spontaneous BMs

MN, manometry; CTT, colon tranist time; Colo, colonoscopy; IC, idiopathic constipation; BE, balloon expulsion; DF, cinedefecography; BEN, barium enema; PPC, paradoxical puborectalis contraction; NR, not reported.

to comply with treatment protocols was the most important predictor of success.

Although feedback of information is essential for learning, the information itself, and the instrument providing the information, has no inherent power to create psychophysiologic changes in humans. Therefore, to establish a double-blind, placebo-controlled research protocol for biofeedback therapy, based on the principles used for medication trials, becomes inherently difficult. Studies based on understanding the essentials of biofeedback training are often successful.[10] In 1991, Dahl et al[26] defined their teaching methods of sensory awareness, shaping by teaching patients the correct sphincter responses, home practice, physiologic quieting methods, generalization, and weaning of equipment. There was a reported symptom improvement success rate of 78% for patients with anismus. Rao et al's[21] study is another example of defined teaching methods employing the essentials of biofeedback training and reporting 100% success; their defined success is >50% symptomatic improvement. They concluded that biofeedback therapy effectively improves objective and subjective parameters of anorectal function in patients with fecal incontinence. They noted that customizing the number of sessions and providing periodic reinforcement may improve success.

Treatment of Constipation

The many variants in these clinical trials may account for the wide range of success rates of 30% to 100% (Table 13.6). The number of treatment sessions varies significantly from one session of outpatient training to 2 weeks of daily inpatient training, followed by additional subsequent home training. Rao et al's[6] review noted that the end point for successful treatment has not been clearly defined and the duration of follow-up has also been quite variable. Enck and Musial[27] point out that comparing clinical symptoms prior to and after treatment usually assesses treatment efficacy; however, other studies have reported evaluation of sphincter performance during physiologic testing. Outcome was sometimes assessed by diary cards; however, reviews, telephone interviews, and questionnaires were more often used. These evaluation techniques are unreliable when the recorded event, such as defecation, is infrequent in nature.[27] Furthermore, diagnostic data from physiologic testing beyond confirmation of spastic pelvic floor syndrome is often not reported. Patient's concomitant conditions disclose a significant variance in inclusion criteria (e.g., presence of rectoceles, rectal sensory thresholds, previous surgery), which presumably contribute to the success of treatment.[27] Park et al[28] described two varieties of anismus, anal canal hypertonia, and nonrelaxation of the puborectalis muscle that appear to correlate with the success of biofeedback; specifically, anal canal hypertonia may be responsible for failure of biofeedback therapy. McKee et al[29] concluded that biofeedback for outlet obstruction constipation is more likely to be successful in patients without evidence of severe pelvic floor damage.

Biofeedback is a conservative treatment option for patients with idiopathic constipation, although some studies have had less favorable results. The most recent study, by Emmanuel and Kamm[22] in 2001, reported on 49 patients with idiopathic constipation pre- and postbiofeedback using objective measurements as well as patient symptom diaries, and found that symptomatic improvement occurred in 59% of patients. Twenty-two patients had slow transit before treatment, of whom 14 felt symptomatic improvement, and 13 developed normal colonic transit. There was a significant increase in rectal mucosal blood flow in patients who subjectively improved. The authors concluded that successful response to biofeedback for constipation is associated with specifically improved autonomic innervation to the large bowel and improved transit time. In 1998, Chiotakokowi-Faliakou et al[30] studied 100 patients treated with biofeedback and reported that 65% had slow transit and 59% had paradoxical puborectalis contraction on straining. Long-term follow-up at 23 months revealed that 57% of patients had felt their constipation improved. Reiger et al[31] evaluated the results of biofeedback to treat 19 patients with intractable constipation of no specific etiology and concluded that biofeedback had little therapeutic effect. In these cases, Wexner[32] reports patients remain symptomatic, requiring the inconvenience and expense of the use of cathartics. Engel and Kamm[13] showed that excessive straining has both acute and chronic effects on pudendal nerve latencies. Long symptom duration with intense straining would thus induce nerve damage. It has also been reported that the chronic use of laxatives induces changes in the

myenteric nerve plexa.[32] Wexner suggested an alternate course of action would be to explain to patients that, although success of only 40% to 60% can be anticipated, the success rate is determined by their willingness to complete the course of therapy. Patients should be counseled that biofeedback therapy is the only recourse other than the continued use of laxatives and cathartics.[36] Moreover, the lack of any known morbidity supports the logic of trying biofeedback despite the relatively low success rate.

Conclusion

Despite the many variants in the clinical trials for biofeedback, most experts agree that biofeedback is an attractive outpatient, conservative treatment option that is cost-effective, relatively noninvasive, easy to tolerate, morbidity free, and does not interfere with any future treatment options that may be recommended by the physician. It is gratifying to note that this simple technique can ameliorate symptoms and improve the quality of life in many patients with functional bowel and bladder symptoms attributed to pelvic muscle dysfunction. It should be available in every pelvic floor physiology unit.

References

1. Sonnenberg A, Koch TR. Physician visits in the United States for constipation. Dig Dis Sci 1989;34:606.
2. Sonnenberg A, Koch TR. Epidemiology of constipation in the United States. Dis Colon Rectum 1989;32:1–8.
3. Thompson WG, Longstreth GF, Drossman DA, Heaton KW, Irvien EJ, Muller-Lissner SA. Functional bowel disorders and functional abdominal pain. Gut 1999;45: 1143–1154.
4. Jorge JMN, Wexner SD. Physiologic evaluation. In: Wexner SD, Vernava AM III, eds. Clinical Decision Making in Colorectal Surgery. New York: Igaku-Shoin, 1995:11–22.
5. Wexner SD, Jorge JMN. Colorectal physiological tests: use or abuse of technology? Eur J Surg 1994;160:167–174.
6. Rao SSC, Welcher KD P, Leistikow JS. Obstructive defecation: a failure of rectoanal coordination. Am J Gastroenterol 1998;93:1042–1050.
7. Hallan RI, Williams NS, Melling J, Walron DJ, Womack NR, Morrison J. Treatment of anismus in intractable constipation with botulinum toxin. Lancet 1988;2: 714–717.
8. Enck P. Biofeedback training in disordered defecation: a critical review. Dig Dis Sci 1993;38:1953–1959.
9. Schwartz MS, et al. Biofeedback: A Practitioner's Guide, 2nd ed. New York: Guilford Press, 1995.
10. Shellenberger R, Green JA. From the Ghost in the Box to Successful Biofeedback Training. Greeley Co: Health Psychology Publication, 1986.
11. MacLeod JH. Management of anal incontinence by biofeedback. Gastroenterology 1987;93:291–294.
12. Rao SSC. The technical aspects of biofeedback therapy for defecation disorders. Gastroenterologist 1998;6:96–103.
13. Engel AF, Kamm MA. The acute effect of straining on pelvic floor neurological function. Int J Colorectal Dis 1994;9:8–12.
14. Binnie NR, Kawimbe BM, Papachrysotomou M, Clare N, Smith AN. The importance of the orientation of the electrode plates in recording the external anal sphincter EMG by non-invasive anal plug electrodes. Int J Colorectal Dis 1991;6:8–11.
15. Hulme JA. Beyond Kegels. Phoenix: Phoenix Publishing, 1997.
16. Lennard-Jones JE. Constipation. In: Feldman M, Friedman L, Sleisenger MH, eds. Sleisinger and Fordtran's Gastrointestinal and Liver Disease: Pathophysiology / Diagnosis / Management, 7th ed. Philadelphia: W.B. Saunders, 2002:81–209.
17. Kegel A. The physiologic treatment of poor tone and function of the genital muscles and of urinary stress incontinence. West J Surg Obstet Gynecol 1949;57: 527–535.
18. Bump RC, Hurt WG, Fantl JA, Wyman JF. Assessment of Kegel pelvic muscle exercise performance after brief verbal instruction. Am J Obstet Gynecol 1991;165: 322–329.
19. Basmajian JV. Biofeedback: Principles and Practice for Clinicians. Baltimore: Williams & Wilkins, 1989.
20. Charlesworth EA, Nathan RG. Stress Management: A Comprehensive Guide to Wellness. New York: Ballantine, 1985.
21. Rao SSC, Welcher KD, Happel J. Can biofeedback therapy improve anorectal function in fecal incontinence? Am J Gastroenterol 1996;91:2360–2365.
22. Emmanuel AV, Kamm MA. Response to a behavioral treatment, biofeedback in constipated patients is associated with improved gut transit and autonomic innervation. Gut 2001;49:214–219.
23. Hyman S, Jones KR, Ringel Y, Scarlett Y, Whitehead WE. Biofeedback treatment of fecal incontinence. Dis Colon Rectum 2001;44:728–736.
24. Norton C, Kamm MA. Outcome of biofeedback for faecal incontinence. Br J Surg 1999;86:1159–1163.
25. Gilliland R, Heymen S, Altomare DF, Park UC, Vickers D, Wexner SD. Outcome and predictors of success of biofeedback for constipation. Br J Surg 1997;84:1123–1126.
26. Dahl J, Lindquist BL, Leissner P, Philipson L, Jarnerot G. Behavioral medicine treatment in chronic constipation with paradoxical anal sphincter contraction. Dis Colon Rectum 1991;34:769–776.
27. Enck P, Musial F. Biofeedback in pelvic floor disorders. In: Pemberton JH, Swash M, Henry MM, eds. The Pelvic Floor: Its Function and Disorders. London: W.B. Saunders, 2002:393–404.
28. Park UC, Choi SK, Piccirillo MF, Verzaro R, Wexner SD. Patterns of anismus and the relation to biofeedback therapy. Dis Colon Rectum 1996;39:768–773.
29. McKee RF, McEnroe L, Anderson JH, Finaly IG. Identification of patients likely to benefit from

biofeedback for outlet obstruction constipation. Br J Surg 1999;86:355–359.
30. Chiotakakou-Faliakou E, Kamm MA, Roy AJ, Storrie JB, Turner IC. Biofeedback provides long term benefit for patients with intractable slow and normal transit constipation. Gut 1998;6:517–521.
31. Rieger NA, Wattchow DA, Sarre RG, et al. Prospective study of biofeedback for treatment of constipation. Dis Colon Rectum 1997;40:1143–1148.
32. Wexner SD. Biofeedback for constipation. Dis Colon Rectum 1998;41:670–671.
33. Smith B. Effect of irritant purgatives on the myenteric plexus in man and the mouse. Gut 1968;9:139–143.
34. Dailianas A, Skandalis N, Rimikis MN, Koutsomanis D, Kardasi M, Archimandritis A. Pelvic floor study in patients with obstructive defecation. J Clin Gastroenterol 2000;30:176–180.
35. Lau C, Heymen S, Alabaz O, Iroatulam AJN, Wexner SD. Prognostic significance of rectocele, intussusception, and abnormal perineal descent in biofeedback treatment for constipated patients with paradoxical puborectalis contraction. Dis Colon Rectum 2000;43:478–482.
36. Mollen RMHG, Salvioli B, Camilleri M, et al. The effects of biofeedback on rectal sensation and distal colonic motility in patients with disorders of rectal evacuation: evidence of an inhibitory rectocolonic reflex in humans. Am J Gastroenterol 1999;94:751–756.
37. Gila A, Gylin M, Gullberg K, Lindberg G. Biofeedback retraining in patients with functional constipation and paradoxical puborectalis contraction. Dis Colon Rectum 1997;40:889–895.
38. Ko CY, Tong J, Lehman RE, Shelton AA, Schrock TR, Welton ML. Biofeedback is effective therapy for fecal incontinence and constipation. Arch Surg 1997;132: 829–834.
39. Patankar SK, Ferera A, Larach SW, et al. Electromyographic assessment of biofeedback training for fecal incontinence and chronic constipation. Dis Colon Rectum 1997;40:907–911.
40. Karlbohm U, Hallden M, Eeg-Olofssson, Pahlman L, Graf W. Results of biofeedback in constipated patients. A prospective study. Dis Colon Rectum 1997;40:1149–1155.
41. Rao SSC, Welcher KD, Pelsan RE. Effects of biofeedback therapy on anorectal function in obstructive defecation. Dig Dis Sci 1997;42:2197–2305.
42. Patankar SK, Ferrera A, Levy JR, Larach SW, Williamson PR, Perozo SE. Biofeedback in colorectal practice. A multi center, statewide, three-year experience. Dis Colon Rectum 1997;40:827–831.
43. Ho YH, Tan M, Goh HS. Clinical and physiologic effects of biofeedback in outlet obstruction defecation. Dis Colon Rectum 1996;39:520–524.
44. Leroi AM, Duval V, Roussignol C, Berkelmans I, Reninque P, Denis P. Biofeedback for anismus in 15 sexually abused women. Int J Colorect Dis 1996;11:187–190.
45. Siproudhis L, Dautreme S, Ropert A, et al. Anismus and biofeedback: who benefits? Eur J Gastroenterol Hepatol 1995;7:547–552.
46. Koutsomanis D, Lennard-Jones JE, Roy AJ, Kamm MA. Controlled randomized trial of visual biofeedback versus muscle training without a visual display for intractable constipation. Gut 1995;37:95–99.
47. Koutsomanis D, Lennard-Jones JE, Kamm MA. Prospective study of biofeedback treatment for patients with slow and normal transit constipation. Eur J Gastroenterol Hepatol 1994;6:131–137.
48. Bleijenberg G, Kuijpers HC. Biofeedback treatment of constipation: comparison of two methods. Am J Gastroenterol 1995;89:1021–1026.
49. Papachrysostomou M, Smith AN. Effects of biofeedback on obstructed defecation—reconditioning of the defecation reflex. Gut 1994;35:252–256.
50. Keck JO, Staniunas RJ, Coller YES, et al. Biofeedback training is useful in fecal incontinence but disappointing in constipation. Dis Colon Rectum 1995;37:1271–1276.
51. Turnbull GK, Ritivo PG. Anal sphincter biofeedback relaxation treatment for women with intractable constipation symptoms. Dis Colon Rectum 1992;35:530–536.
52. Fleshman JW, Dreznik Z, Meyer K, Fry RD, Carney R, Kodner IJ. Outpatient protocol for biofeedback therapy of pelvic floor outlet obstruction. Dis Colon Rectum 1992;35:1–7.
53. Wexner SD, Cheape JD, Jorge JMN, Heyman SR, Jagelman DG. Prospective assessment of biofeedback for the treatment of paradoxical puborectalis contraction. Dis Colon Rectum 1992;35:145–150.
54. Kawimbe BM, Papachrysostomou M, Clare N, Smith AN. Outlet obstruction constipation (anismus) managed by biofeedback. Gut 1991;32:1175–1179.
55. Lestar B, Penninckx F, Kerremans R. Biofeedback defecation training for anismus. Int J Colorect Dis 1991; 6:202–207.
56. Weber J, Ducrotte P, Touchais JY, Roussignol C, Denis P. Biofeedback training for constipation in adults and children. Dis Colon Rectum 1987;30:844–846.

14

Medical Treatment of Constipation

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Constipation is commonly defined as the paucity of bowel movements. However, patients may have constipation regardless of the number of bowel movements in a unit of time. The inability to satisfactorily evacuate one's colon and rectum can be manifested by different degrees of abdominal discomfort associated with "normal" bowel habits, infrequent stools, or even overflow diarrhea. In addition, many other abdominal complaints are related to constipation, including pain syndromes, bloating, fullness, and even heartburn and dyspepsia.

It is not unusual for patients referred for constipation to present to the specialist having had at least one (and possibly multiple) full anatomic evaluation(s) of the bowel, including computed tomography (CT) scans, contrast studies, and colonoscopies. The reported results of these studies are usually normal, except for varying degrees of diverticulosis coli. Usually, a careful history suffices to reveal the underlying problem. Issues to be addressed in the history include bowel habits, frequency of bowel movements, ease or difficulty with evacuation, chronicity, childhood bowel habits, medications, and surgery. Careful attention to the use of pain medicines is required, because narcotic use is an often-overlooked cause of constipation-related problems.[1] Physical examination is typically unremarkable, but occasional patients can have palpable ascending or sigmoid colons secondary to stool accumulation. Rectal examination is often normal, but the presence of a large amount of firm stool at the distal rectum can occasionally help to direct therapy.

Interestingly, even patients who move their bowels every day or complain of diarrhea can be constipated, so a plain x-ray of the abdomen can be helpful in patients with vague complaints.[2] The standard radiology report does not include a comment on colonic stool content; therefore, the requesting physician should review the film.

Although routine labs such as complete blood count (CBC), comprehensive metabolic panel, and erythrocyte sedimentation rate (ESR) can be helpful, other tests such as thyroid-stimulating hormone are typically normal. New-onset constipation without an obvious predisposing factor, abnormal rectal exam with hemoccult positive stools, the presence of microcytic anemia on CBC, and an elevated ESR require further investigation, and if a colonoscopy has not been done relatively recently, it should be performed.

Anatomic and Physiologic Considerations

Three important functions of the colon are absorbing water once chyme is delivered from the small intestine and fecal storage and evacuation. The evacuation function has both voluntary and involuntary elements; when evacuation is hindered, constipation results.

Normal bowel function requires the coordination of motility, mucosal transport of water, as well as involuntary and voluntary defecation reflexes. Gastrointestinal motility is dependent on the electrophysiologic activity of smooth muscle cells, neural input from the intrinsic and autonomic nervous systems, hormonal

interactions, and coordinated smooth muscle contraction.

The gut exhibits two types of movement: propulsion and mixing. The basic propulsive movement is peristalsis, in which coordinated contractions of the circular as well as longitudinal muscles cause gastrointestinal contents to be pushed forward. The stimulus for peristalsis is distention of the intestine, which causes stretching of the bowel wall smooth muscle. As a result, the intestinal nervous system reacts by stimulating a contraction proximal to the food bolus, thus pushing it distally. In the colon the proximal segment functions in both a mixing and absorptive capacity: segmental mixing movements maximize the surface exposure and fluid absorption, whereas slow contractions distally propel the luminal contents. The distal colon functions primarily in a storage capacity.[3]

The intestinal smooth muscle is organized in two layers: a longitudinal outer layer and a circular inner layer. In the colon the longitudinal layer forms three bands, the taeniae that eventually form the external anal sphincter distally; the internal circular layer extends distally and eventually becomes the internal anal sphincter. The smooth muscle of the intestine generates intrinsic electrical signals that are translated into contractions. This mechanism is true in the stomach and small intestine, but due to the lack of gap junctions between muscle fibers in the colon, such intrinsic electrical signals usually fail to generate a synchronized contraction. Thus the motility of the colon is regulated by and dependent mainly on external stimuli. As in the rest of the gut, stretching the muscle fibers and cholinergic stimulation via extrinsic neural influences cause an excitatory effect, while noradrenaline and sympathetic stimulation are inhibitory.[3–5]

The intrinsic enteric nervous system lies entirely within the wall of the gut from the esophagus to the anus: the outer myenteric (Auerbach's) plexus and the inner submucosal (Meissner's) plexus. The myenteric plexus lies between the longitudinal and circular layers of the entire gut; its main function is control over motor activity. Stimulation increases the tone of the gastrointestinal (GI) wall, intensity and rhythm of contractions, and conduction velocity. The submucosal plexus controls local secretory and absorptive activity. More than a dozen neurotransmitters are released from nerve endings of enteric neurons. In addition to acetylcholine having an excitatory influence and norepinephrine a relaxing one, other neurotransmitters such as dopamine, serotonin, vasoactive intestinal peptide (VIP), substance P, and the endogenous opioid peptides leuenkephalin and met-enkephalin have excitatory or inhibitory activity. Other substances, including nitric oxide (NO), carbon monoxide (CO), amines, and purines also have inhibitory influence on GI motility. Gastrointestinal hormones such as gastrin, cholecystokinin (CCK) and motilin stimulate smooth muscle; somatostatin, glucagon, and gastric inhibitory peptide have inhibitory effects.

Extrinsic autonomic control of the gut is mediated through the vagus nerve for parasympathetic control from the esophagus to the proximal half of the colon, and the pelvic nerves via the sacral parasympathetics for control of the distal colon. Sympathetic fibers located in the thoracic and lumbar regions of the spinal cord reach the gut through the splanchnic nerves. Both the excitatory parasympathetics and inhibitory sympathetics synapse with neurons in the myenteric plexus and submucosal plexus.

Treatment of Constipation

The medical treatment of constipation is usually empiric and based on the experience of both the physician and patient. Patients who are chronically constipated usually bring to the doctor's office a history of various over-the-counter remedies that they have tried.[6] Currently, more frequently, a patient presenting to a specialist for constipation has often been evaluated with colonoscopy or other visualization studies of the colon. This chapter reviews the pharmacophysiology of a few medical therapies for constipation and previews some pharmaceuticals due out in the near future.

In a community practice it is appropriate to empirically treat patients with chronic constipation according to one's clinical judgment, assess the results, and if failure occurs, then decide on whether evaluation with physiologic studies or referral is indicated.

If the patient clearly is constipated (as determined by history or by x-ray), and cannot produce a spontaneous, moderate-sized movement, the treating physician should prescribe a cathartic-type laxative to clean out the colon before more conservative means are started. Once a patient has had a satisfactory evacuation

or if the patient is already having bowel movements at least every day or so, bulking agents should be instituted as foundational therapy.

Behavioral Considerations

Common causes of constipation include long-term voluntary restraint of evacuation, eventually leading to involuntary problems, highly efficient colonic dehydration of stools, and the inability to initiate defecation. There is strong evidence from the literature as well as everyday experience in the practice of medicine that many patients' problems with constipation and related symptoms originate from chronic voluntary restraint of evacuation. The exact profiles and underlying psychological stimuli for this behavior is beyond the scope of this chapter. However, treatment of constipation should include "reteaching" the patient proper bowel habits.

The concept of reteaching the colon should not be ignored. Patients who can achieve at least one evacuatory bowel movement every day or so will have significantly fewer symptoms, despite often years or even decades of problems with constipation-related complaints.

Reeducation of the colon often begins at the time of the first office visit, when the physician should discontinue some, if not all, of the pharmaceuticals, over-the-counter preparations, herbals, and other remedies that other practitioners have previously prescribed for the patient's abdominal symptoms. Over time, many patients accumulate a long list of various remedies that often counteract one another or are frankly counterproductive. Good examples include antispasmodics, which are frequently prescribed for the cramps of constipation. Unfortunately, all of the commonly prescribed antispasmodics have strong anticholinergic effects and are thus constipating.

Additionally, close examination of nongastrointestinal medications needs to be done so that if one or more drugs have a constipating effect, a substitute can be considered. The calcium channel blockers are a good example of a class of drugs used for hypertension that usually can be easily replaced by a less constipating agent.

The patient often benefits from a brief description of the normal physiology of evacuation. The colon is most active from a propulsive standpoint early in the morning (diurnal influences), and after meals. Having the patient choose one of those times to sit quietly on the commode and not straining but taking advantage of the increased activity is usually at least marginally helpful for the constipated patient.

Suppository and Enema Therapy

Patients who complain of pressure in the rectum or feel that they need help in initiating defecation often benefit from local therapy with water- or oil-based enemas or glycerin suppositories. These agents not only provide some lubrication to the area, but also cause reflexive contraction and evacuation of the distal colon and rectum from local mechanical effects. Patients often need reassurance about the safety and non–habit-forming aspects of this type of therapy.

Bulking Agents

Fiber supplementation should be foundational therapy for most if not all constipated patients.[7] A constipated patient should be started at a relatively low dose and slowly increased to a typical daily dose over several days to 1 week. Starting low will help to decrease bloating. After 2 to 4 weeks on therapy, if the patient is still having symptoms, the dose should be doubled in a split dose. Many patients have relief with fiber alone. Continued problems thereafter can be treated with occasional, mild laxatives. The nonresponders may need the addition of treatment for lactose intolerance, or evaluation to assess for colonic inertia, pelvic floor disorders, or postoperative causes.

Numerous bulk-forming laxatives are available as commercial, nonprescription preparations. Some agents may contain stimulant laxatives in conjunction with fiber. There are many sources for bulking agents such as Plantago seeds—psyllium, plant gums, guar, malt soup extract, and synthetic agents such as methylcellulose and polycarbophil. Table 14.1 lists some of these commercial agents. These agents are generally effective within 12 to 24 hours, but depending on individual transit time, they may require several days. Fiber intake should be accompanied by an adequate intake of fluids (at least 2 L daily), since constipation might worsen if water intake is insufficient. The amount of bulking agent and water intake

Table 14.1. Commercial bulk-forming agents

Active ingredient	Trade Name*	Comments
Psyllium	Konsyl	Highest fiber content
	Perdiem	
	Metamucil	Contains phenylalanine
	Fiberall	
	Syllact	
	Effer-syllium	
	Hydrocil	
Methylcellulose	Citrucel	
	Cologel	
	Hydrolose	
Plant gum	Kondremul	Contains mineral oil
	Genlax-S	Contains senna
Polycarbophil	Mitrolan	
	Equalactin	
	Fibercon	

* Konsyl®—Konsyl Pharmaceuticals Inc., Easton, MD (6 g fiber per dose).
Perdiem®—Novartis Consumer Health, Basel, Switzerland.
Metamucil®—Procter & Gamble, Cincinnati, OH (3.4 g fiber per dose).
Fiberall®—Heritage Consumer products, Brookfield, CT.
Syllact™
Effer-syllium™
Hydrocil®—Numark Laboratories, Inc., Edison, NJ.
Citrucel®—Merrell Pharmaceuticals Inc., Kansas City, MO (2 g fiber per dose).
Cologel™
Hydrolose™
Kondremul®—Barre-National, Inc., Baltimore, MD.
Genlax-S™
Mitrolan®—Wyeth Pharmaceuticals, Collegeville, PA.
Equalactin®—Numark Laboratories, Inc., Edison, NJ.
Fibercon®—Wyeth Pharmaceuticals, Collegeville, PA.

should be individually tailored for the patient, depending on the effect. If diarrhea results after a single dose, less fiber and less fluid should be ingested initially. The patient can easily monitor the response and adjust the doses after a brief educational encounter with the physician at the office.

Although there is an array of fiber products on the market, psyllium has been a mainstay of fiber therapy for decades. Usually, one can avoid the bloating associated with psyllium introduction by slowly increasing the dose over days or weeks, and starting therapy on a relatively empty colon. The end point of fiber therapy should be resolution of symptoms. This typically requires enough fiber for the patient to have softer, bulkier stools at least once every day or so. If patients reach the maximum recommended dose without success, then either a different type of fiber preparation can be substituted or a mild laxative can be taken on the days that they do not move their bowels.

Magnesium

An example of a safe, mild laxative is the class of agents with magnesium as the active ingredient. Magnesium-based therapy can often provide a nonprescription aid for constipated patients. Magnesium promotes bowel evacuation by causing osmotic retention of fluid and distension of the colon, thus stimulating increased peristaltic activity. Patients with renal failure should generally avoid magnesium products.

Therapy—Past, Present, and Future

When bulking agents with or without a mild laxative do not provide relief for the constipated patient, the treating physician has a myriad of treatments, prescription and over-the-counter, to turn to. If the patient's complaints do not suggest anatomic problems or such problems are excluded by other investigations, then continued medical therapy is warranted. Even for patients with pelvic floor disorders or structural bowel problems likely related to chronic constipation and straining, often conservative measures with medications is warranted, since surgical repair is typically seen as a last resort and is frequently not 100% successful at relieving symptoms.

Below are a few examples of second-line medications for the treatment of constipation. Practitioners should always be ready to use treatments empirically for lactose intolerance when patients continue to complain of cramps or pain even when first-line therapies help the patient to have more frequent bowel movements. In a referral practice, up to 50% of referred patients have lasting relief from sometimes decades of discomfort with the use of daily psyllium supplementation and a commercial lactase preparation with meals.

Therapies of the Past

Senna

The most popular herbal medicines in the health food industry are those agents that are used to correct bowel irregularities and relieve

constipation.[8–10] Senna is a herb that has been used for medicinal purposes for millennia. It is a shrub of the plant family Leguminosae.

The active ingredients of senna were first isolated and characterized in the early 1940s. These were two glycosides that were attributed to the anthraquinone family and named sennosides A and B. They are essentially prodrugs. When ingested, they travel through the alimentary tract chemically unchanged until they reach the colon. In the colon they undergo hydrolysis through the action of bacterial β-glycosidases and a further reduction to the final active substances rhein-anthrone and rhein.[11–14] Their precise mode of action is unknown, although a dual effect has been observed: an increase in the colonic motility with a net reduction in water absorption.[15] Oral administration of senna pod extract dose-dependently reversed net absorption of water, sodium, and chloride to net secretion, and also increased potassium secretion in a rat model. It also stimulated the output of prostaglandin E_2 into the colonic lumen as well. Both effects were significantly inhibited by pretreatment with indomethacin.[16] Later it was shown that the addition of calcium channel blockers to indomethacin completely blocked the diarrhea caused by rhein anthrone.[17] These observations imply that the laxative effect of senna may be attributed, at least in part, to secretion of water and electrolytes into the colonic lumen, and that this secretion is mediated by calcium ions and prostaglandin E_2. More recently it was suggested that the above-mentioned effects might be mediated by the inhibitory action of senna on nitric oxide synthase.[18] In physiologic conditions, endogenous nitric oxide is a proabsorptive molecule that exerts its effect on the enteric nervous system, the suppression of prostaglandin formation, and the opening of K^+ channels. Thus, the inhibition of nitric oxide formation produces the opposite effect that results in diarrhea.

Since the administered product must reach the colon to be activated, the effect is limited to the large intestine and usually occurs 6 to 12 hours following oral administration.

Contrary to the common belief that natural or herbal medicines are universally harmless and safe, some herbal products may cause serious, even fatal complications.

Anthraquinone laxatives may produce excessive diarrhea accompanied by severe abdominal pain. The urinary excretion of the compounds may cause abnormal discoloration of the urine (light brown turning red with increasing pH), usually without impairment of the renal function. Prolonged use of anthraquinone laxatives causes a melanotic pigmentation of the colonic mucosa called melanosis coli. The mechanism of this phenomenon is deposition of lipofuscin and ceroid products of apoptosis in macrophages of the colonic mucosa. This pigmentation is reversible 4 to 12 months after cessation of laxative use.[19–21] There is a general consensus that melanosis coli is a harmless condition. It does not correlate with higher rates of colorectal cancer, although a higher detection rate of adenomatous polyps was demonstrated in one study.[22] This may be due to the fact that even tiny adenomas (that do not usually contain the pigment) are easier to visualize when the dark colonic mucosa serves as a background.

Cathartic colon is a historic, radiologic term for the anatomic changes in the colon secondary to prolonged use of stimulant laxatives. These alterations are characterized by loss of haustral folds, a finding that might suggest neuronal injury or damage to colonic longitudinal musculature caused by these agents. Furthermore, the gradual adaptation and tolerance to senna, as demonstrated by the need for larger doses to produce the same effect after prolonged use, may be attributed to these changes. Those findings are reversible as well.[23,24]

Current Therapies

More recent additions to the formulary for the treatment of constipation include osmotic agents and drugs active in neuroendocrine modification at the level of the intrinsic neural pathways of the colon.

Polyethylene Glycol

Polyethylene glycol electrolyte lavage solutions (PEG-ELS) have been used for cleansing the GI tract before diagnostic and surgical procedures.[25–27] The effect produced by those solutions prompted clinicians to use them for treating constipation; however, it was shown that while ingesting a large volume of solution for bowel cleansing, there was no net absorption of water or electrolytes. The ingestion of smaller volume

might result in absorption of the salt component of the solution—a situation that may be hazardous for patients with congestive heart disease and chronic renal failure.[28–31]

In the late 1990s a new laxative was introduced into clinical practice. MiraLax™ PEG 3350, National Formulary powder for solution (Braintree Laboratories, Braintree, MA) is a tasteless, osmotic laxative, and unlike the above-mentioned lavage solutions, it does not contain salt. It has been gaining increasing popularity, and was subjected to many clinical trials with promising results.[32–35] It is remarkably nontoxic, and large quantities can be ingested without deleterious side effects.[36,37] It has no effect on active absorption or secretion of glucose or electrolytes and there is no evidence of tachyphylaxis.[38] The usual dose is 17 g of powder in 8 ounces of liquid per day for adults, with an expected bowel movement occurring after 2 to 4 days of use.

Serotonin and the Gastrointestinal Tract

Serotonin (5-hydroxytryptamine, 5-HT) has long been known to play an integral role in gastrointestinal neurotransmission.[39] Serotonin is formed by the hydroxylation and decarboxylation of tryptophan and is converted to its active form in the nerve terminals (Fig. 14.1).

The GI tract contains approximately 95% of the total body serotonin.[40] Although 5-HT is found in a subpopulation of myenteric interneurons, the vast majority is located in subcellular granules located in the enterochromaffin (EC) cells. The EC cells are located in the epithelial layer of the mucosa in close contact to the enteric nerve endings. The serotonin in the EC cells is released when the cells are stimulated by chemical or mechanical stimuli such as increased intraluminal pressure or vagal stimulation. This in turn activates nerve endings in the enteric nervous system and initiates the peristaltic reflex.[41]

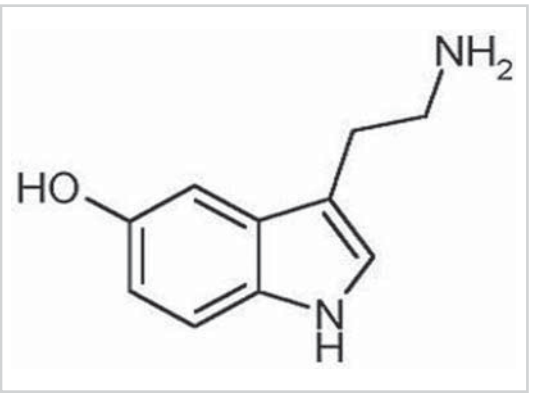


Figure 14.1. Serotonin.

Serotonin has a wide array of effects on the GI tract largely due to the presence of multiple subtypes, which appear to be present on several classes of myenteric neurons, smooth muscle cells, and enterocytes. In general, the release of 5-HT has been found to be directly modulated by ligand-gated and G-protein–coupled receptors, which have at least 15 serotonin receptor subtypes that mediate its effect.

The selective, partial 5-HT4 agonist Tegaserod is one of a new class of compounds called the aminoguanidine indoles. Structurally, Tegaserod is very similar to serotonin and stimulates the release of calcitonin gene-related peptide from enteric neurons. This augments the peristaltic reflex, enhances intestinal secretion, and reduces visceral hypersensitivity. Tegaserod interacts with enteric 5-HT4 receptors, resulting in amplification of this process.

In an industry-sponsored, multinational randomized trial, researchers assessed the efficacy of Tegaserod in 1348 adults of whom 90% were females.[42] These subjects had complaints of chronic constipation, which was defined as a weekly average of fewer than three spontaneous bowel movements. These patients received 2 mg, 6 mg, or placebo twice a day for 12 weeks. The study showed that Zelnorm® (Tegaserod) caused a statistically significant improvement and increased the frequency of spontaneous bowel movements and relieved symptoms including straining, hard stool, incomplete evacuation, and abdominal discomfort.

Recently Tegaserod has been approved for chronic constipation in men.

Therapies of the Future

In the not-too-distant future, patients and their physicians may be spared the sometimes tremendously difficult problem of narcotic-induced constipation. To date, the narcotic antagonists have been effective peripherally, but

have been unhelpful because they reverse the intended, central effect of the analgesic.

Narcotic administration is perhaps the most common cause of iatrogenic constipation. Three types of receptors for opioid peptides have been identified as having effects on human gastrointestinal function: μ, κ, and λ receptors. They all belong to the family of G-protein–coupled receptors, and reduce intracellular cyclic adenosine monophosphate (cAMP) by inhibiting adenylate cyclase.[43]

At the membrane level, they reduce neuronal excitability by hyperpolarization resulting from increased potassium permeability of the membrane, and neurotransmitter release by inhibition of voltage-gated calcium channels. The overall effect is inhibitory. These actions result in a reduction in acetylcholine release, with an overall inhibitory effect on the neuron.[44]

Opioid receptors are widely distributed in the central and peripheral nervous system, the intestinal musculature, and other tissues. They are found in high concentrations in the dorsal horn of the spinal cord where they process and relay afferent nociceptive signals to the central nervous system. In the brain, they are mainly in areas involved in pain transmission. μ-Receptors are the principal mediators of the analgesic action of endogenous and exogenous opioids, as well as the major side effects of sedation, bowel dysfunction, respiratory depression, and dependence. Localization studies of the human gut have shown that μ-receptor activity is localized to myenteric and submucosal neurons and to immune cells of the lamina propria.[45]

Generally, opioids interfere with normal GI motility by delaying transit, by stimulating nonpropulsive motility, segmentation and tone, and by stimulation of sphincters such as the pylorus. These effects are mainly mediated by κ and μ receptors.[46] Delay in colonic transit contributes significantly to the constipating effect of opioids, prolonging content-mucosa contact time and enhancing absorption.

Alvimopan is a new selective, competitive, peripherally acting μ-receptor antagonist, with limited oral bioavailability. It can reduce opioid-induced bowel symptoms without antagonizing centrally mediated opioid effects. Its action is against peripheral receptors, and it has a negligible central effect. Gonenne et al[47] have recently shown that Alvimopan blocks the effects of the opioid analgesic codeine on small-bowel and colonic transit in humans. Furthermore, Alvimopan alone significantly accelerates colonic transit in healthy volunteers when compared to placebo.

Conclusion

In a community practice, uncomplicated constipation should be approached in a stepwise manner. Although most patients may have their own methods to deal with acute problems, they occasionally need a one-time oral cathartic or large-volume enema in the beginning of treatment, to start with a "clean slate." In these situations, prior to treatment, confirmation of constipation is usually easily accomplished by reviewing an abdominal x-ray.

Most patients' symptoms of constipation can be treated with daily fiber supplements and behavior modification. Of the remaining patients, many respond to rectally administered glycerin suppositories, enemas, or the judicious use of an oral stimulant, such as magnesium or senna.

For those continuing with symptoms despite conservative management, the practitioner will have to decide whether to proceed with prescription therapy such as polyethylene glycol or Tegaserod, or refer the patient for physiologic-anatomic testing with marker studies and defecography.

In the near future, effective therapy for narcotic-induced constipation will likely be available. Until then, aggressive, nonspecific therapy accompanied by minimization or elimination of the offending substance is warranted.

References

1. McMillan SC, Tittle M. A descriptive study of the management of pain and pain-related side effects in a cancer center and a hospice. Hosp J 1995;10:89–108.
2. Sandler RS, Drossman DA. Bowel habits in young adults not seeking health care. Dig Dis Sci 1987;32:841.
3. Huizinga JD, Daniel EE. Motor functions of the colon. In: Philips SF, Pemberton JH, Shorter RG, eds. The Large Intestine: Physiology, Pathophysiology, and Disease. New York: Raven Press, 1991:93–114.
4. Kellow JE, Borody TJ, Phillips SF, Tucker RL, Haddad AC. Human interdigestive motility: variations in patterns from esophagus to colon. Gastroenterology 1986;91(2):386–395.
5. Huizinga JD. Electrophysiology of human colon motility in health and disease. Clin Gastroenterol 1986; 15(4):879–901.

6. Sonnenberg A, Koch TR. Physician visits in the United States for constipation: 1958–1986. Dig Dis Sci 1989; 34:606.
7. Locke GR III, Pemberton JH, Phillips SF. AGA technical review on constipation. Gastroenterology 2000;19: 1766–1768.
8. Eisenberg DM, Davis RB, Ettner SL, et al. Trends in alternative medicine use in the United States, 1990–1997: results of a follow-up national survey. JAMA 1998;280(18):1569–1575.
9. Vickers A, Zollman C. ABC of complementary medicine: herbal medicine. BMJ 1999;319(7216):1050–1053.
10. Smart HL, Mayberry JF, Atkinson M. Alternative medicine consultations and remedies in patients with the irritable bowel syndrome. Gut 1986;27(7):826–828.
11. Okada T. Über den metabolismus der Senna—Abführung. Tohoku J Exp Med 1940;38:33–41.
12. Fairbairn JW. Chemical structure, mode of action and therapeutical activity of anthraquinone glycosides. Pharm Weekbl 1965;100(51):1493–1499.
13. Lemli J. Senna—an old drug in modern research. Pharmacology 1988;36(suppl 1):3–6.
14. Franz G. The senna drug and its chemistry. Pharmacology 1993;47(suppl 1):2–6.
15. Leng-Peschlow E. Dual effect of orally administered sennosides on large intestine transit and fluid absorption in the rat. J Pharm Pharmacol 1986;38(8):606–610.
16. Beubler E, Kollar G. Stimulation of PGE2 synthesis and water and electrolyte secretion by senna anthra_ quinones is inhibited by indomethacin. J Pharm Pharmacol 1985;37(4):248–251.
17. Yamauchi K, Yagi T, Kuwano S. Suppression of the purgative action of rhein anthrone, the active metabolite of sennosides A and B, by calcium channel blockers, calmodulin antagonists and indomethacin. Pharmacology 1993;47(suppl 1):22–31.
18. Izzo AA, Mascolo N, Capasso F. Nitric oxide as a modulator of intestinal water and electrolyte transport. Dig Dis Sci 1998;43(8):1605–1620.
19. Benavides SH, Morgante PE, Monserrat AJ, Zarate J, Porta EA. The pigment of melanosis coli: a lectin histochemical study. Gastrointest Endosc 1997;46(2): 131–138.
20. Nadal SR, Calore EE, Manzione CR, Puga FR, Perez NM. Effects of long-term administration of senna occidentalis seeds in the large bowel of rats. Pathol Res Pract 2003;199(11):733–737.
21. van Gorkom BA, Karrenbeld A, van Der Sluis T, Koudstaal J, de Vries EG, Kleibeuker JH. Influence of a highly purified senna extract on colonic epithelium. Digestion 2000;61(2):113–120.
22. Nusko G, Schneider B, Ernst H, Wittekind C, Hahn EG. Melanosis coli—a harmless pigmentation or a precancerous condition? Z Gastroenterol 1997;35(5):313–318.
23. Joo JS, Ehrenpreis ED, Gonzalez L, et al. Alterations in colonic anatomy induced by chronic stimulant laxatives: the cathartic colon revisited. J Clin Gastroenterol 1998;26(4):283–286.
24. Campbell WL. Cathartic colon. Reversibility of roentgen changes. Dis Colon Rectum 1983;26(7):445–448.
25. Davis GR, Santa Ana CA, Morawski SG, Fordtran JS. Development of a lavage solution associated with minimal water and electrolyte absorption or secretion. Gastroenterology 1980;78(5 pt 1):991–995.
26. Goldman J, Reichelderfer M. Evaluation of rapid colonoscopy preparation using a new gut lavage solution. Gastrointest Endosc 1982;28(1):9–11.
27. DiPalma JA, Brady CE 3rd. Colon cleansing for diagnostic and surgical procedures: polyethylene glycol-electrolyte lavage solution. Am J Gastroenterol 1989;84(9):1008–1016.
28. Andorsky RI, Goldner F. Colonic lavage solution (polyethylene glycol electrolyte lavage solution) as a treatment for chronic constipation: a double-blind, placebo-controlled study. Am J Gastroenterol 1990; 85(3):261–265.
29. Velio P, Bassotti G. Chronic idiopathic constipation: pathophysiology and treatment. J Clin Gastroenterol 1996;22(3):190–196.
30. Corazziari E, Badiali D, Habib FI, et al. Small volume isosmotic polyethylene glycol electrolyte balanced solution (PMF-100) in treatment of chronic nonorganic constipation. Dig Dis Sci 1996;41(8):1636–1642.
31. Hammer HF, Santa Ana CA, Schiller LR, Fordtran JS. Studies of osmotic diarrhea induced in normal subjects by ingestion of polyethylene glycol and lactulose. J Clin Invest 1989;84(4):1056–1062.
32. DiPalma JA, DeRidder PH, Orlando RC, Kolts BE, Cleveland MB. A randomized, placebo-controlled, multicenter study of the safety and efficacy of a new polyethylene glycol laxative. Am J Gastroenterol 2000; 95(2):446–450.
33. Cleveland MV, Flavin DP, Ruben RA, Epstein RM, Clark GE. New polyethylene glycol laxative for treatment of constipation in adults: a randomized, double-blind, placebo-controlled study. South Med J 2001;94(5): 478–481.
34. Loening-Baucke V. Polyethylene glycol without electrolytes for children with constipation and encopresis. J Pediatr Gastroenterol Nutr 2002;34(4):372–377.
35. Di Palma JA, Smith JR, Cleveland M. Overnight efficacy of polyethylene glycol laxative. Am J Gastroenterol 2002;97(7):1776–1779.
36. Kinservik MA, Friedhoff MM. The efficacy and safety of polyethylene glycol 3350 in the treatment of constipation in children. Pediatr Nurs 2004;30(3): 232–237.
37. Rowe VK, Wolf MA. Glycols. In: Clayton GD, Clayton FE eds. Patty's Industrial Hygiene and Toxicology. New York: John Wiley, 1982:3844–3852.
38. Shaffer CB, Critchfield FH. The absorption and excretion of the solid polyethylene glycols (carbowax compounds). J Am Pharm Assoc Sci Ed 1947;36:152–157.
39. Vialli MM, Ersapmer V. Ricerche sul secreto delle cellule enterocromaffini. IX Intorno alla natura chimica della sostanza specifica. Boll Soc Med Chir Pavia 1937;51: 1111–1116.
40. Erspamer V. Occurrence of indolealkyamines in nature. In: Erspamer V, ed. Handbook of Experimental Pharmacology: 5-Hydroxytryptamine and Related Indolealkyamines. New York: Springer-Verlag, 1966: 132–181.
41. Grider JR, Kuemmerle JF, Jin JG. 5-HT released by mucosal stimuli initiate peristalsis by activating 5-HT4/5-HT1p receptors on sensory CGRP neurons. Am J Physiol 1996;270:778–782.
42. Johanson JF, Wald A, Tougas G, et al. Effect of tegaserod in chronic constipation: a randomized, double-blind,

controlled trial. Clin Gastroenterol Hepatol 2004;2: 796–805.
43. De Schepper HU, Cremonini F, Park MI, et al. Opioids and the gut: pharmacology and current clinical experience. Neurogastroenterol Motil 2004;16:383–394.
44. Kurz A, Sessler DI. Opioid-induced bowel dysfunction: pathophysiology and potential new therapies. Drugs 2003;63:649–671.
45. Kaufman PN, Krevsky B, Malmud LS, et al. Role of opiate receptors in the regulation of colonic transit. Gastroenterology 1988;94:1351–1356.
46. Pasternak GW. Pharmacological mechanisms of opioid analgesics. Clin Neuropharmacol 1993;16:1–18.
47. Gonenne J, Camilleri M, Ferber I, et al. Effect of alvimopan and codeine on gastrointestinal transit: a randomized controlled study. Clin Gastroenterol Hepatol 2005;3:784–791.

15

Surgical Treatment of Colonic Inertia

Shing W. Wong and David Z. Lubowski

History

Colectomy for constipation was initially proposed by William Arbuthnot Lane (Fig. 15.1).[1] In a subsequent "Address on Chronic Intestinal Stasis," Lane[2] described ileosigmoid or ileorectal bypass procedures (leaving the colon intact) when constipation was accompanied by headaches and lethargy resulting from "autointoxication." The objective evidence of autointoxication was said to include pigmentation of the skin and malodorous perspiration. Lane proposed colectomy with anastomosis to the descending colon or the rectum when abdominal pain was also a prominent feature. In his first series of 39 cases, operative mortality was 18%, and 29 patients (74%) were noted to be satisfied with the operation. Lane was a proficient technical surgeon for the time, but he caused colectomy for constipation to fall into disrepute by performing the procedure for such diverse conditions as tuberculosis, thyrotoxicosis, and migraines, and it was rarely performed in the ensuing decades. Almost a century later there has been a resurgence of interest in the operation.

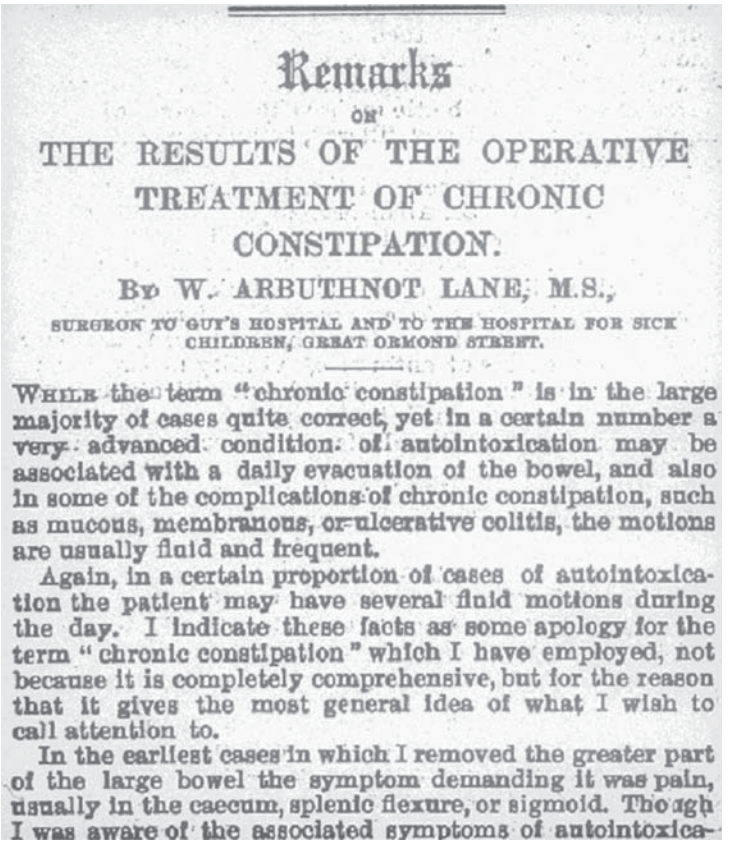
Although Lane's definitions of success were arbitrary, he did discover that if the whole colon was not removed, constipation would frequently recur. Initially, he resected the colon up to the splenic flexure, believing that gravity would aid the movement of feces down the vertical descending colon and sigmoid colon. However, he discovered that with the passage of time, symptoms would recur and he would need to remove the residual colon except for the rectum. This procedure remains the favored surgical treatment of colonic inertia.

Definition of Colonic Inertia

Colonic inertia is the failure of the colon to propel stool toward the rectum, including the failure to produce mass movement of stool around the time of defecation. The condition manifests as a syndrome of infrequent bowel actions, bloating, abdominal pain, and systemic symptoms including lethargy and nausea. Colonic motor activity is abnormal, with reduced high-amplitude propagating contractions, and transit time through the colon is prolonged.[3–5] There is failure to enhance colonic phasic pressure activity by a meal or stimulant, and impaired propagated colonic contractile response to bisacodyl and cholinergic agents.[6–8] Preston and Lennard-Jones[7] postulated that the relative inactivity of the colon may be due to a congenital or acquired disorder of the myenteric plexus. Bassotti and colleagues[8] found that patients with slow-transit constipation displayed an impaired colonic motor response to strong cholinergic stimulation (edrophonium chloride) in the descending colon when compared with healthy subjects.

Surgical Treatment

Surgical treatment for constipation is only indicated when symptoms are very severe and all conservative measures have failed after a reasonable length of time. It should always be remembered that major abdominal surgery may potentially be associated with significant morbidity. It is our policy to use a combination laxative regimen in large doses and ensure



Remarks

ON

THE RESULTS OF THE OPERATIVE TREATMENT OF CHRONIC CONSTIPATION.

By W. ARBUTHNOT LANE, M.S.,

SURGEON TO GUY'S HOSPITAL AND TO THE HOSPITAL FOR SICK CHILDREN, GREAT ORMOND STREET.

WHILE the term "chronic constipation" is in the large majority of cases quite correct, yet in a certain number a very advanced condition of autointoxication may be associated with a daily evacuation of the bowel, and also in some of the complications of chronic constipation, such as mucous, membranous, or ulcerative colitis, the motions are usually fluid and frequent.

Again, in a certain proportion of cases of autointoxication the patient may have several fluid motions during the day. I indicate these facts as some apology for the term "chronic constipation" which I have employed, not because it is completely comprehensive, but for the reason that it gives the most general idea of what I wish to call attention to.

In the earliest cases in which I removed the greater part of the large bowel the symptom demanding it was pain, usually in the caecum, splenic flexure, or sigmoid. Though I was aware of the associated symptoms of autointoxica-

Figure 15.1. Arbuthnot Lane first reported the results of colectomy for constipation. Front page, *British Medical Journal*, 1908.

compliance, before recommending surgery. A bulking agent together with an osmotic laxative and a stimulant agent taken together daily are generally prescribed. Laxative resistance, or significant nausea or pain associated with the drugs, signals failure of conservative therapy.

This chapter discusses the surgical treatment of colonic inertia (idiopathic slow-transit constipation) where the colon is of normal diameter. Idiopathic megacolon and Hirschsprung's disease are excluded from the discussion. Before recommending surgery it is critical to exclude other treatable causes of constipation, which are shown in Table 15.1. Constipation-predominant irritable bowel syndrome is excluded on symptomatology using the Rome II criteria and by confirming that the patient has slow colonic transit using markers or isotope scintigraphy.[9–11] The standard treatment for slow-transit constipation is colectomy with ileorectal anastomosis (ileoproctostomy), but there are alternative surgical options besides colectomy that are outlined in detail in other chapters.

Antegrade Colonic Enema

Antegrade irrigation of the colon may be used as an alternative to colectomy or a stoma in patients with severe laxative-resistant constipation.[12] Malone et al[13] first described the technique of antegrade colonic enema (ACE) in 1990, using the reversed appendix as the conduit with the amputated tip tunneled into the cecum as a continence mechanism. This was a modification of the Mitrofanoff procedure of using the appendix as a nonrefluxing conduit to catheterize the bladder. The ACE technique is particularly useful in patients who have constipation as well as anal sphincter weakness, where the use of laxatives is complicated by incontinence. We have previously used the reversed appendix technique

Table 15.1. Etiology of constipation

- Dietary
  - Inadequate fiber
- Social
  - Immobility
  - Environmental changes (hospitalization, vacation)
  - Elderly
- Endocrine and metabolic
  - Hypothyroidism, pregnancy, hypercalcemia, diabetes, hypokalemia, uremia, hypopituitarism, lead poisoning, porphyria
- Central and peripheral nervous system pathology
  - Autonomic neuropathy (diabetes), porphyria, Parkinson's disease
- Drugs
  - Iron supplements, calcium channel blockers, anticholinergics, antidepressants, narcotic agents, nonsteroidal antiinflammatory drugs, laxative abuse
- Psychiatric
  - Depression, psychoses, anorexia nervosa
- Gastrointestinal
  - *Structural*
    - Colonic obstruction: neoplasm, diverticular disease, inflammatory bowel disease, volvulus, intussusception
    - Anal outlet obstruction: stenosis, fissure
  - *Functional*
    - Normal transit: constipation-predominant irritable bowel syndrome
    - Slow-transit constipation
      - Idiopathic
      - Intestinal pseudo-obstruction
      - Hirschsprung's disease
      - Megacolon
    - Obstructed defecation
      - Hypertonic internal sphincter
      - Rectocele
      - Pelvic floor weakness
      - Anismus
      - Idiopathic

of Malone, but more recently have found the technique of simply invaginating the nonreversed appendix base using a series of purse-string sutures to be successful. Regardless of which technique is employed, it is important to have well-coordinated patient training with irrigation techniques.

Sacral Nerve Stimulation

Although the study numbers are still small and follow-up currently short-term, sacral nerve stimulation has shown a potentially promising role in the treatment of intractable idiopathic constipation. The technique probably acts via parasympathetic nerve stimulation, but other factors including modulation of rectal sensation may be important. In one small study, stimulation produced an increased bowel frequency and improved evacuation.[14] This method is addressed in detail in another chapter.

Subtotal Colectomy

Subtotal colectomy and ileorectal anastomosis (IRA) result in improvement in the frequency of evacuation in over 90% of patients, with a high degree of satisfaction in the majority of cases.[15–23] Severe diarrhea occurs in up to 10% of cases, which may be associated with incontinence if anal sphincter tone is reduced. Subtotal colectomy with cecorectal or ileosigmoid anastomosis is associated with recurrent constipation in up to 30% of cases. A number of outcome measures need to be examined in detail.

Bowel Frequency

Most large studies show a satisfactory mean or median stool frequency after colectomy and ileorectal anastomosis (Table 15.2). In a review of the literature, Knowles and colleagues[24] found the overall median stool frequency to be 2.9 per day (range 1.3 to 5). Mean daily stool frequency was noted in one study to decrease over time from five to four to three per day at 1 month, 6 months, and 12 months, respectively.[25] Another study found an improvement from 3.7 per day at 27 months to 2.5 per day at 5 years.[26] In our study of 52 patients at a mean of 3.5 years, each patient had at least one bowel motion daily, with a median of four stools per day, and 69% of patients passed four or less bowel motions daily.[19]

Table 15.2. Mean or median stool frequency after colectomy and ileorectal anastomosis

First author	No. of patients	Stools/24 hours
Wexner[45]	16	3.5
Vasilevsky[23]	52	2.8
Yoshioka[30]	40	Med 3
Kamm[31]	38	2
Pemberton[15]	59	Med 4
Lubowski[19]	59	3.7
Piccirillo[16]	54	3.7
Platell[17]	87	5
Nyam[18]	74	4
Bernini[61]	106	2.8

The possibility of developing severe diarrhea is perhaps the main concern with this procedure. Diarrhea has fairly wide definition parameters, but the incidence reported by Knowles et al[24] in 16 series ranged from 0% to 46% with a median of 14%. Regular use of antidiarrheal medication has been used as a marker of severity. Pemberton et al[15] found a mean stool frequency of two per day and none of the patients required antidiarrheal medication after 12 months follow-up. Piccirillo et al[16] found that only 17% of 54 patients required antidiarrheal medication, while in our study 27% of patients used medication but only 10% did so regularly.[17–19]

Recurrent Constipation

The incidence of recurrent constipation varies quite considerably in the literature. This measure is an important end point for success after colectomy. The definition of constipation used after colectomy is variable and may contribute to the wide range reported; the definition of Drossman et al,[27] most commonly used elsewhere in the literature (two or fewer stools per week and/or straining at stool more than 25% of the time) is often not followed after colectomy. Knowles and colleagues[24] reported a median constipation rate of 9% (range 0–46%) from 15 series. It is difficult to identify the precise reasons for these wide variations but several factors may be relevant. Follow-up time is important since function after subtotal colectomy may deteriorate with time. Selection criteria for surgery may explain some differences. It is possible that in some series in which objective evidence of slow-transit constipation was not obtained in all cases, patients with irritable bowel syndrome and normal colonic transit were included. We used radioisotope scintigraphy to select patients, with recurrent constipation occurring in 2%.[19] Although radioisotope studies may not offer any advantage over radiopaque marker studies in assessing colonic transit, they may assist in identifying patients with significant small bowel involvement. Recurrent constipation has been found to be more common in patients with generalized intestinal dysfunction. One study found that 11 of 16 such patients developed recurrent constipation in contrast to only one of 21 patients with colonic inertia alone.[28]

An important reason for differences in recurrent constipation rates may be the type of operation used. There are several studies that confirm low recurrence rates of 0% to 2% after anastomosis to the rectum.[15,16,18,19] Other studies that included a mix of ileorectal, cecorectal, and ileosigmoid anastomoses have reported rates of 11% to 32%.[29–31] Indeed, Lane first reported failure of colectomy with anastomosis to the splenic flexure, and recurrent constipation after ileosigmoid anastomosis has since been documented. Pemberton et al[15] found that one of two patients who underwent a colectomy and ileosigmoid anastomosis developed recurrent constipation within 4 months and required further resection with ileorectal anastomosis. Hasegawa et al[32] reported the same experience in four of eight patients who had an ileosigmoid anastomosis. Vasilevsky et al[23] performed an anastomosis between the ileum and the distal sigmoid colon in 46 of 52 patients with chronic constipation and found an average bowel frequency of 2.8 per day. Although only two patients underwent resection of the residual sigmoid colon with ileorectal anastomosis, 11% and 20% of the patients required laxatives or enemas, respectively.

Other authors have found that patients with an ileorectal anastomosis tended to have more diarrhea and incontinence than did those patients who had an ileosigmoid anastomosis.[33] However in our view, this outcome seems less than the risk of recurrent constipation with a lesser resection.

Cecorectal anastomosis (CRA) seems to have a high failure rate, often accompanied by distention of the cecum and failure to evacuate.[22,34] In a series of five patients who underwent cecorectal anastomosis, two patients presented within 2 years with persistent constipation after cecal dilatation, one of whom developed a cecal volvulus and both were later converted to IRA.[30] Fan and Wang[35] noted recurrent constipation at 4 and 6 months in both patients who underwent cecorectal anastomosis but not in 22 other patients who had an IRA. Hasegawa et al[32] reported that two of nine patients who initially had a cecorectal anastomosis were later converted to an ileorectal anastomosis because of persistent constipation. Platell et al[17] had the same experience with three of 10 patients, although the precise indications for the conversions were not given in their study.

There are a number of theoretical advantages of CRA over IRA. The CRA preserves the terminal ileum and ileocecal valve in addition to the cecum. However, Fasth and colleagues[34] found that preserving the ileocecal valve did not alter

the mean daily fecal volume. The terminal ileum is important for the absorption of electrolytes, water, bile salts, and vitamin B_{12}. A patent ileocecal valve may slow the transit of fecal contents into the rectum and prevent bacterial overgrowth in the small bowel. However, Yoshioka and Keighley[30] found no differences between seven patients with CRA and seven patients with IRA in small bowel transit times or abdominal distention.

Despite the general published results, there are still some advocates of CRA over IRA. A French study compared IRA in six patients with CRA in 12 patients.[36] It found that patients with a CRA had better functional results with no cases of diarrhea, fecal incontinence, or postoperative small-bowel obstruction. Three patients in the IRA group required antidiarrheal treatment, one patient had episodic incontinence, and three patients required a laparotomy for bowel obstruction. It has been suggested that the cecum may fill the pelvis and prevent small bowel adhesions to that area and hence obstruction. Sarli et al[37] have described a novel antiperistaltic CRA without rotation, in which the apex of the cecum is joined to the top of the rectal stump. The authors found satisfactory results in 10 women with a mean preoperative bowel frequency of once per 10 days compared with postoperative frequency of 1.3 (range 0.5–3) per day at 1-year follow-up. All patients reported normal continence and none used antidiarrheal medications. Longer follow-up and more widespread trials of this method are required to see if these excellent results are maintained.

Incontinence

The median incontinence rate was 14% (range 0–52%) in Knowles et al's[24] review. In our study six patients (12%) had significant incontinence after surgery.[19] Five had normal anal sphincter function but incontinence was precipitated by very high stool frequency in three cases. Pikarsky et al[26] found that the incidence of incontinence decreased from 24% at short follow-up to 17% at longer follow-up and attributed this improvement to a more solid stool consistency with the passage of time.

Abdominal Pain

Most studies report that at least 50% of patients have persistent or worsened abdominal pain after subtotal colectomy and some authors have argued against the operation on the basis of failure to cure this symptom. Postoperative abdominal pain ranged from 0% to 90% in the review by Knowles et al.[24] The two studies reporting an incidence of 90% may be incorrect since in one study six of 18 patients after partial colectomy and 15 of 24 patients after subtotal colectomy had persistent pain.[38] The other study defined persisting pain as pain occurring at least twice during the month before the interview.[39] Kamm et al[31] compared two groups of patients after subtotal colectomy with short follow-up (mean 1 year) and long follow-up (mean 5 years) to determine whether the unwanted effects of surgery resolve with time. They found that the incidence of pain was equivalent in both groups, suggesting that postoperative pain persists. Redmond et al[28] noted a similar finding but only in patients who also had abnormal motility of the upper gastrointestinal tract. They found that no patients with isolated colonic inertia experienced pain by the fifth postoperative year, while 70% of patients with generalized gastrointestinal dysfunction continued to experience pain at 2, 5, and 10 years' follow-up.

There is no doubt that pain is a significant part of the syndrome of slow-transit constipation and must be carefully considered when selecting patients for surgery. We believe that patients who have very severe pain and equivocal slow transit on isotope study are probably on the irritable bowel syndrome end of a spectrum of conditions and should be excluded from surgery since their dominant symptom (pain) will not be cured. On the other hand, most patients with severe slow transit will have some pain, and we found that although pain persisted in 52% after surgery, there was a statistically significant improvement in the severity of pain (Fig. 15.2). The mean postoperative pain score was low, at 1.98. We believe that this is a useful observation since patients can be reassured that they are unlikely to have persisting severe pain. [It is the book editors' practice to advise all patients that pain will remain present or even worsen after surgery.]

Bloating

The incidence of abdominal bloating varies in different studies. It was noted to be unchanged after surgery in two studies.[17,30] Pluta et al[40]

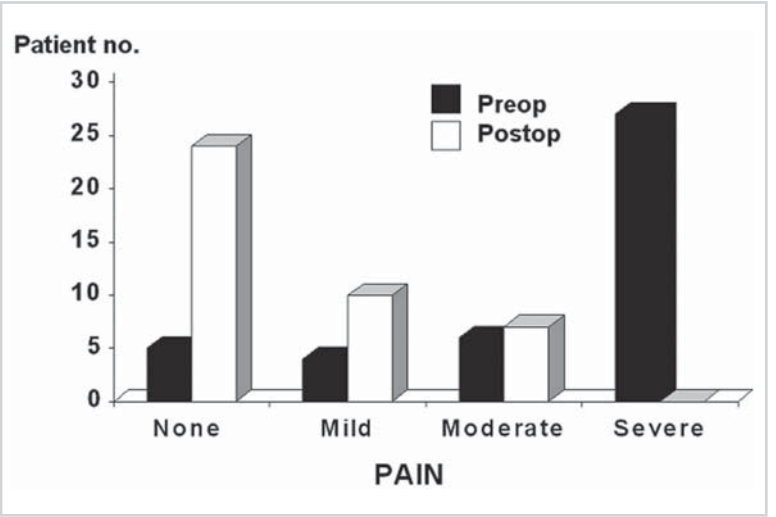


Figure 15.2. Pain categories before and after colectomy for colonic inertia. There was a significant shift to the less severe categories of pain after surgery, with no patient remaining in the severe category.

reported that in 24 patients with severe bloating preoperatively, postoperative bloating continued to be severe in two patients, significant but less in five, minor in nine, and absent in eight. Kamm et al[31] found 45% had persistent bloating after surgery, and Preston et al[22] found it in 10 of 16 patients after subtotal colectomy. Conversely, Piccirillo et al[16] reported no patients with postoperative bloating despite 65% of their patients complaining of bloating preoperatively, and the authors attributed these good results to strict patient selection. In another study the preoperative incidence of bloating was 60%, which remained unchanged at 27 months but decreased to 23% at long-term follow-up of at least 5 years.[26] This improvement was attributed to small-bowel adaptation. [However, it is the book editors' practice to advise all patients that bloating will continue or worsen following colectomy.]

Patient Satisfaction and Success Rates

Ultimately, patient satisfaction is the critical factor determining the success of surgery. Knowles et al[24] reported patient satisfaction or success rates in 31 studies ranging from 31% to 100% (median 86%). The method used for outcome assessment across studies was quite variable, based on patient reports in 14 studies, on function in six, and a combination of the two in five studies; no criteria were stated in six studies. We would question some of the figures quoted; for example, Hasegawa et al[32] reported 29 of 61 patients (48%) to be asymptomatic and an additional 16 of 61 patients (26%) to be improved, yet Knowles et al[24] quoted a 39% success rate for Hasegawa's paper. There are a number of large studies from separate centers that show patient satisfaction rates of 80% to 90% (Table 15.3). We found that 47 of 52 patients (90%) were satisfied with the operation in response to direct questioning, and would elect to have the operation done again.[19] The five patients dissatisfied with the operation were the one patient in the study who had an anastomotic leak, the one patient who developed recurrent constipation, which required an ileostomy, and three patients with incontinence.

Table 15.3. Percentage of patients satisfied with the outcome of colectomy for constipation

First author	Satisfied (%)
Belliveau[65]	83
Preston[22]	81
Wexner[45]	94
Leon[66]	77
Vasilevsky[23]	79
Yoshioka[30]	58
Pemberton[15]	100
Lubowski[19]	90
Beck[67]	100
Piccirillo[16]	94
Platell[17]	77
Nyam[18]	90

A number of factors may predict a more favorable patient satisfaction rate. The results appear to be better when patients undergo colonic transit studies and thorough pelvic floor function testing, presumably by excluding patients with irritable bowel syndrome. Nyam et al[18] noted the success rate ranged from 58% to 79% in six studies where surgery was performed without physiologic testing. In five studies where selection was based on objective physiologic assessment, successful outcome ranged from 88% to 100%.

Redmond et al[28] noted that 90% of patients with motility abnormalities restricted to the colon had a successful outcome, but only 13% of patients with generalized intestinal dysmotility had prolonged relief. Patient satisfaction with surgery may deteriorate with time, especially if further surgery is required for recurrent constipation or other complications such as diarrhea and incontinence. Mollen et al[41] noted that the early postoperative satisfaction rate of 76% dropped to 52% at 1-year follow-up, with this group of patients having a high reoperation rate in which seven of 21 patients required an ileostomy or ileoanal pouch.

Small-Bowel Obstruction

Small-bowel obstruction after subtotal colectomy for colonic inertia is common and frequently requires surgical intervention. The median small-bowel obstruction rate is 18% (range 2–71%), with a median re–operation rate of 14% (0–50%).[24]

The incidence of small-bowel obstruction after colectomy and ileorectal anastomosis seems to be higher when the procedure has been carried out for constipation rather than for other conditions: after resection for large-bowel tumors it was 2% and for inflammatory bowel disease 9%.[42] The reason for these differences is unclear but small bowel inertia as a part of generalized intestinal involvement in patients with colonic inertia may explain the higher incidence in this group. Another possible reason may be that resection for carcinoma involves ligating the vessels closer to their origins, with fewer ligatures and less denuded peritoneal surface to form adhesions. One study had contrary conclusions, with no difference noted in the incidence of small-bowel obstruction among the three groups of patients who underwent subtotal colectomy for colonic inertia, Crohn's disease, and familial adenomatous polyposis or other neoplasia.[43]

The reason for the frequent requirement of surgical intervention after obstruction is also unclear but a significant proportion of these cases may be due to small intestinal pseudo-obstruction. Mollen et al[41] noted that patients who have an ileostomy because of colonic inertia frequently experience periods of absent ileostomy output followed by attacks of severe diarrhea, thus mimicking mechanical obstruction. They also found that in all four patients who required a laparotomy for small-bowel obstruction, no clear mechanical cause was found. The reported small-bowel resection rates were also very low; with no resections in 52 patients undergoing laparotomy in five studies and one in 12 patients in another study.[17,18,22,23,31,41]

Surprisingly, the rate of small-bowel obstruction has not been shown to significantly increase over time, perhaps suggesting that it will occur early or not at all. This idea would perhaps support the notion of small-bowel dysmotility being a factor. Obstruction occurred in four of 38 patients after a mean follow-up of 20 months and seven of 74 patients after a mean follow-up of 56 months.[15,18] Long-term follow-up studies (longer than 5 years) have reported small-bowel obstruction in six of 30 patients from the Cleveland Clinic (Florida)[26] and in eight of 40 patients in our unit (unpublished data).

Operative Morbidity

Serious sepsis seems to be uncommon after colectomy for constipation, but the potential must always be carefully factored into the decision to undertake abdominal surgery for benign disease. We had one anastomotic leak in a series of 52 patients, requiring temporary ileostomy.[19] Webster and Dayton[25] reported two anastomotic leaks in 48 patients, and Lahr et al[44] had one anastomotic leak in 109 patients who underwent colectomy with or without pelvic floor repair. Pluta et al[40] reported two pelvic abscesses in 24 patients, and Yoshioka and Keighley[30] had pelvic abscesses in three of 40 patients, two of which were due to confirmed anastomotic leaks. One study had a higher sepsis rate, with three anastomotic leaks and 11 pelvic abscesses in 96 patients.[17] Mortality has also been reported in the literature, with two among 52 patients[23] and two in 96 patients.[17]

Prolonged ileus is a commonly described postoperative event and occurs more frequently in patients with a detectable motility abnormality of the upper gastrointestinal tract.[28] Deep vein thrombosis does not seem to be more common than in other abdominal surgery, although it is not recorded in some publications. In our series one patient had deep vein thrombosis and two had pulmonary emboli.[19]

Quality of Life

Quality of life after colectomy for colonic inertia has not been well documented in the majority of studies and should be an important component of future studies. Wexner et al[45] found an improvement of quality of life in their 16 patients who underwent subtotal colectomy; initial activity limitations attributed to the patients' bowel habits improved after the operation and the numbers of patients with social, vocational, physical, or sexual activity limitations were all reduced after surgery. Nyam et al[18] assessed quality of life, although they did not use a validated instrument; parameters assessed were sex life, social activity, sports, housework, recreation, family relationships, and travel, which were scored 1 to 5. Overall quality of life was good or improved (scores of 3 or more) in 89% of patients at 6 months, and this improvement was seen in all aspects of lifestyle surveyed and it persisted at 3 and 5 years.

One study examined the relationship between functional outcome and quality of life using a validated modified 36-item gastrointestinal quality of life index.[32] The authors noted no correlation between frequency of bowel movement and quality of life score, but found a statistically significant negative impact on quality of life scores with each of the symptoms of abdominal pain, diarrhea, and incontinence. In addition, they found that a permanent ileostomy correlated with significantly lower scores. They found no correlation between quality of life and a previous history of psychiatric illness. Ninety-three percent of their patients indicated that they would undergo the surgery again.

Long-Term Follow-Up

Functional results after subtotal colectomy for colonic inertia may improve or deteriorate over time. Long-term follow-up is usually reported as a mean 5-year follow-up, but this statistic may leave a substantial number of patients with short follow-up. We have recently assessed the outcome in patients who underwent colectomy for slow-transit constipation with at least 5 years' follow-up; 40 of 82 patients had been followed for 5 years (median 7.9 years, range 5–14.7 years) (unpublished). The median stool frequency was three per day (range 1–14), with 58% passing three or fewer stools per day and 75% four or fewer stools. Seventeen percent of the patients were using medications: 8% for constipation and 9% for diarrhea. Abdominal pain persisted in 40% of patients but there was a statistically significant improvement in the severity of the pain (Fig. 15.2). Six patients had incontinence, with three of these having high stool frequencies. Ninety percent of the patients were satisfied and would elect to have the operation performed again.

Another study reported 30 patients with a minimum 5-year follow-up (range 61–122 months) found a mean stool frequency of 2.5 per day (range 1–6).[26] Four patients required regular medications, two for constipation and two for diarrhea. Twenty-five patients (83%) reported perfect continence and the remainder had less than one incontinent episode per month. Four patients complained of pelvic pain, three of whom had pain before surgery but noted a decrease in intensity since the operation. Seven patients (23%) experienced persistent bloating after surgery. All of the above functional results were improved when compared with the results at 27 months' follow-up. All patients regarded their outcome as excellent.

A study with a median follow-up of 7 years (range 2–20) showed overall disappointing results,[32] which were related to impaired evacuation or overt psychiatric disease/psychological disturbance. The overall permanent stoma rate was 23%. However, a satisfactory outcome was achieved in 95% of psychologically stable patients with slow transit alone and no impaired evacuation. All patients in whom a colectomy for constipation is planned should be counseled as to the eventual potential for a permanent ileostomy.

Trial of Ileostomy

It has been suggested that a trial period with a loop ileostomy may give some indication about

the likelihood of reducing pain and about the possibility of severe diarrhea developing after colectomy. The procedure is best performed laparoscopically. If the ileostomy output is not excessive, then perhaps an acceptable stool frequency may be anticipated. Because no study has accurately addressed this method, we cannot comment with any veracity, but anecdotally it has been helpful as a staging procedure in isolated cases.

Conclusions for Colonic Resection

Subtotal colectomy and ileorectal anastomosis are effective in relieving constipation in patients with colonic inertia. Careful selection of patients with physiologic investigations to exclude those with irritable bowel syndrome or significant small-bowel dysmotility is important. Patients should be fully informed about the risk of sepsis, albeit small, and about a possible poor functional outcome. Severe pain may be significantly reduced in properly selected patients. Segmental colectomy offers the possibility of avoiding the risk of severe diarrhea but is still associated with recurrent constipation in up to 18% of cases, requiring a further major procedure. More precise isolation of the abnormally functioning part may improve the prospect for segmental resection.

Segmental Colonic Resection

If a particular segment of the colon could be reliably identified as the cause of constipation, then segmental colectomy could offer some advantage by preventing severe diarrhea or incontinence that occurs in a small number of cases after subtotal colectomy and ileorectal anastomosis. Another potential advantage of a limited colonic resection is a reduction in the deperitonealized area that may reduce the risk of postoperative adhesions. In general, the published functional results of segmental colectomy have been unsatisfactory.

The segment of colonic inertia may be confined to the right or left colon.[46] Results of segmental resections are poor if cases are not selected on the basis of detailed transit studies.[24] Lane and Todd[47] reported successful outcome in four of six patients who underwent subtotal colectomy, one of two who underwent left hemicolectomy, and one of six who underwent a sigmoid colectomy. Preston et al[22] found in their study that the five patients who underwent partial colectomy (sigmoid colectomy, three; left hemicolectomy, two) were not improved. In contrast, Kamm et al[48] showed promising results from left hemicolectomy in two cases selected on the basis of isotope studies.

There are other proponents of segmental colon resections for colonic inertia. DeGraaf et al[38] had a prospective series of patients who underwent partial left hemicolectomy and compared them with those individuals who underwent a subtotal colectomy. They selected patients for left hemicolectomy if total transit time was prolonged but transit in the right colon was normal. Recurrent constipation was seen in three of 18 patients who underwent left hemicolectomy and in seven of 24 patients who underwent subtotal colectomy. An end stoma was created in four patients in each group because of poor function. Diarrhea and fecal incontinence developed in two of 14 and five of 20 patients, respectively (although postoperative stool frequency was not given), and satisfaction with the operation was expressed by 12 of 18 and 15 of 24 patients, respectively. The authors advocated selection of the operation from the segmental colonic transit studies because the clinical outcome in the two groups was similar.

In a study from Taiwan, patients underwent left ($n = 24$), right ($n = 4$), or subtotal ($n = 12$) resection according to the distribution of markers in the colon, determined by assessing the location of the majority (>95%) of retained markers on an abdominal x-ray at day 7 after ingestion.[49] Surprisingly, only three of the 28 patients who underwent segmental resection developed recurrent constipation and underwent subtotal colectomy, although this still represents a 10% failure rate. The functional results of all 40 patients were very impressive, with 90% of patients having one bowel movement per day and the rest had only two motions, although the follow-up was only 3 months.

A recent Swedish study that prospectively followed 28 patients who underwent segmental colonic resection (26 left and two right hemicolectomies) showed good symptomatic relief with a reduced risk of side effects.[50] Six patients who also had a sutured rectopexy together with the left hemicolectomy were included. Patients were selected on the basis of a marked delay in either the right or left colon and a less impaired

delay in the rest of the colon on oral indium 111 (^{111}In)-labeled scintigraphic transit study. The authors felt that this study was superior to the radiopaque marker method because different colonic segments in a long colon may be difficult to identify on a single abdominal x-ray. The median stool frequency increased from one to seven per week with a reduction in laxative and enema usage, but five operations (18%) failed and required further surgery for constipation. Fecal continence improved in eight patients and deteriorated in five. Diarrhea (nine bowel motions daily) occurred in one patient after a left hemicolectomy. Impaired rectal sensation was found to correlate with a poor outcome, affecting all five patients whose operation failed, and only four of 23 patients had a successful outcome.

Hasegawa et al[32] reported results of colectomy with a median follow-up of 7 years. Eight of 13 patients who underwent segmental colectomy required further surgery for constipation, and only three of 13 patients (23%) in the segmental colectomy group were asymptomatic compared with 23 of 48 patients (48%) in the subtotal colectomy group.

Ileoanal Pouch

Ileoanal pouch is sometimes required for recurrent constipation after subtotal colectomy and has occasionally been performed as the initial treatment. In Yoshioka and Keighley's[30] series, six of 40 patients underwent restorative proctocolectomy after developing recurrent constipation with megarectum and impaired rectal sensation after subtotal colectomy. With an ileal pouch, bowel frequency ranged from two to eight per day and all patients had normal continence.

A subsequent series from the same hospital reported 13 patients who underwent restorative proctocolectomy for constipation, five as a primary procedure associated with megacolon and constipation.[51] The other eight patients had recurrent constipation after previous subtotal colectomy for slow transit. Eleven of the 13 patients had good function. The complication rate was high, with two anastomotic leaks and four patients developing small-bowel obstruction. At follow-up (2 months to 6 years) the mean frequency of defecation was 4.8 (day) and 1.2 (night). Although there was no severe incontinence, some patients experienced daytime and nighttime soiling.

Other studies with small patient numbers have also had some success. Nicholls and Kamm[52] noted improvement in bowel function after this operation in two patients, although one required catheterization to assist evacuation. Christiansen and Rasmussen[53] performed a restorative proctocolectomy in one of 12 patients who developed obstructed defecation after subtotal colectomy, with a satisfactory outcome. In another study, five patients who had a restorative proctocolectomy were improved with average bowel frequency of 4.8 per day.[54]

Mollen et al[41] reported persistent abdominal symptoms in three patients after an ileoanal pouch procedure for failed symptom control after subtotal colectomy, and Hasegawa et al[32] found that all five patients who underwent restorative proctocolectomy because of persistent constipation after subtotal colectomy eventually had their pouch excised.

Ileostomy and Colostomy

End ileostomy may be required in patients with recurrent constipation after subtotal colectomy for colonic inertia. In some instances, it may be the primary treatment for these patients either as a definitive procedure, or as mentioned previously as a prelude to another operation. Failure after colectomy may result in the need for a stoma: Hasegawa et al[32] found that 14 of 61 patients (23%) eventually had a permanent stoma. They noted that the permanent stoma rate was significantly higher in patients with psychological disease. One study found that six of 44 patients who underwent subtotal colectomy had a subsequent ileostomy, three for persistent constipation, two for diarrhea, and one for diarrhea with incontinence.[31] Yoshioka and Keighley[30] noted that six of 40 patients eventually required an ileostomy, and Ghosh et al[39] reported three of 21 patients had an ileostomy but continued to be symptomatic after the ileostomy possibly as a result of global intestinal dysfunction.

Initial diversion and subsequent colonic manometry was used as a guide in children to either resect the colon or close the stoma.[55] Initial ileostomy[8] or colostomy[4] was performed in 12 children with intractable constipation and abnormal colonic manometry. Manometry was again performed at a mean of 15 months later. In four patients with a gastrocolonic response and high-amplitude propagating contractions

(HAPCs), closure of the ileostomy without colectomy was successful in preventing further constipation. In four patients with a gastrocolonic response but HAPCs only in the right colon, left hemicolectomy cured three patients. In two patients with no gastrocolonic responses or HAPCs, subtotal colectomy and ileorectal anastomosis were performed, with success in one patient. In two patients with abnormal upper gastrointestinal motility and no contractions after diversion, the ileostomy was maintained. Thus constipation resolved in 10 of 12 patients, and six patients avoided colectomy. Diversion of the colon possibly allowed recovery of normal function from chronic stimulant laxative use, and also possibly improved patient selection. Although these results cannot necessarily be transferred to adults, they highlight the potential importance of developing accurate physiologic methods of selecting patients for tailored surgery.

Laparoscopic Colectomy

Improved technology such as ultrasonic dissecting shears has made laparoscopic colectomy feasible. The potential benefits of laparoscopic colorectal resection include less postoperative pain, better cosmesis, improved pulmonary function, earlier return of bowel function, decrease in length of hospital stay, and earlier return to normal activities.[56] Other potential benefits include fewer abdominal adhesions and incisional hernias. These benefits are offset by drawbacks, which include increased costs, complications unique to laparoscopic surgery such as damage to blood vessels or small bowel, loss of ability to perform a thorough laparotomy, and longer operating time.

There has been one retrospective study comparing laparoscopic and open colectomy for slow-transit constipation. Ho et al[57] studied 17 patients having the open procedure and seven patients having the laparoscopic procedure. They found the laparoscopic colectomy group was more satisfied with the cosmetic outcome, but had a longer operation (by a mean of 74 minutes), and had more complications. Blood loss, recovery of ileus, and hospitalization time were the same in the two groups. Two patients in each group developed adhesive small-bowel obstruction, but only the two in the open colectomy group failed conservative treatment and required surgery. Thus, laparoscopy did not confer a significant benefit.

Treatment of Combined Colonic Inertia and Obstructed Defecation

Transit studies and anorectal physiology tests can subdivide severely constipated patients into three groups: colonic inertia causing slow transit, obstructed defecation, and a combination of both. Patients with obstructed defecation may have mechanical outlet obstruction related to the presence of anatomic abnormalities such as a rectocele, or functional outlet obstruction. The principles of treating slow-transit constipation or obstructed defecation alone are generally agreed upon. The optimal treatment of patients with combined colonic inertia and obstructed defecation is controversial. Some advocate preoperative treatment of obstructed defecation, some favor postoperative treatment, some feel that no treatment is required, and others exclude patients with obstructed defecation from colectomy.

Duthie and Bartolo[58] carried out colectomy and IRA in 32 patients with slow colonic transit. These included 15 patients with slow transit as well as nonrelaxing pelvic floor, all of whom were able to evacuate normally after colectomy. The authors suggested that testing these patients in an unnatural environment when there is no desire to defecate was not helpful and resulted in overdiagnosis of anismus. Their results suggested that there was no contraindication to colectomy in combined slow transit and obstructed defecation.

We have observed a poor correlation between preoperative rectal evacuation as demonstrated by proctography and postoperative clinical obstructed defecation.[9] A total of 34 patients undergoing colectomy had preoperative evacuation proctography. Normal preoperative proctography was found in only 10 of 23 patients who had normal postoperative evacuation and four of 11 patients with postoperative evacuation difficulties. Of the 34 patients undergoing proctography, 20 had preoperative obstructed defecation, and 13 of these 20 could defecate normally postoperatively. Of the remaining seven patients, three were improved with postoperative biofeedback. We have not found preoperative pelvic floor retraining with biofeedback to be helpful or indeed necessary in

the majority of patients with obstructed defecation and colonic inertia. Our preferred treatment is to offer biofeedback to those patients with persisting postoperative symptoms of obstructed defecation.

Other studies have shown a poor functional result after subtotal colectomy in patients with untreated obstructed defecation. Kuijpers[59] reported persistent constipation in two of four patients with combined colonic inertia and disordered evacuation compared with a successful outcome in two patients who had preoperative biofeedback. Another study compared 28 patients with slow transit alone, with 33 patients with slow transit and impaired evacuation, and found a significantly higher failure rate in the latter group (11% vs. 39%).[32]

Certain tests of pelvic floor function may have different predictive values of outcome after subtotal colectomy for patients with combined colonic inertia and nonrelaxing pelvic floor. One study from St. Mark's Hospital showed that the ability to expel a balloon was predictive of postoperative pain and laxative requirements after colectomy.[60] However, preoperative evacuation proctogram and paradoxical contraction on straining using puborectalis electromyography were not predictive of symptomatic outcome.

Some authors advocate preoperative biofeedback for patients with combined abnormalities. Nyam et al[18] reported successful postoperative evacuation in all 22 patients with combined abnormalities treated with preoperative biofeedback and then subtotal colectomy. They reported equal functional results and improvement in quality of life in patients with slow-transit constipation and patients with combined slow transit and obstructed defecation. Others have reported less favorable results: Bernini et al[61] found that all 16 patients with combined colonic inertia and obstructed defecation successfully learned to relax the pelvic floor during straining, confirmed on electromyographic studies; seven patients had complete resolution of constipation but six still complained of persisting incomplete evacuation.

Surgical treatment of mechanical outlet obstruction at the same time as colectomy for inertia may improve functional results. Lahr et al[44] advocated pelvic hiatal hernia repair (PHHR) in addition to colectomy in patients with outlet obstruction (due to herniation of the rectum through the hiatus of pelvic diaphragm on defecography) and colonic inertia. Fifty-seven patients underwent total abdominal colectomy and PHHR, whereas 52 patients with colonic inertia alone underwent colectomy. Improvement in symptoms was equivalent in the two groups. Piccirillo et al[16] added rectopexy to total abdominal colectomy in 15 of 54 patients with rectoanal intussusception in addition to colonic inertia. They excluded all patients with puborectalis dysfunction from surgery, and attributed their 94% success rate to a more complete preoperative physiologic assessment.

Small-Bowel Dysmotility

Traditional thinking has been that patients with significant small-bowel dysmotility should be excluded from colectomy because recurrent constipation and abdominal pain are likely to occur. Much of this has been speculative, because accurate means of measuring small-bowel transit have been lacking. Radiopaque marker studies measure whole-gut transit (of which colonic transit time forms a large part) and are not useful to assess the small bowel. Barium studies are helpful only when motility is severely affected, causing megaduodenum and grossly delayed small-bowel transit. Gastric emptying studies are probably similarly helpful only to exclude patients from surgery if emptying is markedly abnormal. Small-bowel transit, assessed in the initial phase of an isotope colon transit study, provides a rough measure of small-bowel motility. All of the ingested isotope should reach the cecum after 6 hours, and failure to do so is an indication of delayed small-bowel transit.[11] Small-bowel transit time can be calculated using the median position of the column of isotope, but this has not been shown to correlate with outcome after colectomy.

Small-bowel manometry is a relatively simple technique and should be more thoroughly investigated in order to determine which parameters of small-bowel manometry can accurately predict significant extracolonic dysmotility that will lead to failure of surgery. Bassotti et al[62] demonstrated that in 21 patients with chronic slow-transit constipation, 71% displayed motor abnormalities of the upper gut. Redmond et al[28] examined the outcome of colectomy in patients with colonic inertia (CI) compared with generalized intestinal dysmotility (GID). Twenty-one patients with CI and 16 patients

with GID were studied. Upper gastrointestinal studies included esophageal, gastric, and small-bowel manometry and electrogastrogram, upper endoscopy, and small-bowel follow-through series. Ninety percent of CI patients improved at a mean follow-up of 7.5 years, with one patient having recurrent constipation and one patient requiring an ileostomy for diarrhea. At 1 year, 12% of GID patients had recurrent constipation but this increased to 80% at 5 years, and ultimately only 13% had a long-term successful outcome. No CI patients complained of abdominal pain or distention by the fifth year, compared with 70% of the GID patients who had abdominal pain and 20% who had distention.

Another study examined patients with slow-transit constipation and small-bowel involvement, and found a high incidence of postoperative small-bowel obstruction (71%).[39] Eighty-six percent of the 21 patients had at least one abnormality of gastrointestinal motility, bladder function, or autonomic function. Symptoms of abdominal pain, bloating, urgency, and straining at defecation continued in the postoperative period. There was also other evidence of smooth-muscle dysfunction in the patients who subsequently developed small-bowel obstruction, with abnormal esophageal motility, delayed gastric emptying, urinary dysfunction, and autonomic dysfunction. The authors concluded that only selected patients with no evidence of smooth muscle dysfunction might be expected to benefit from colectomy.

One small study found that defecation frequency after subtotal colectomy in eight patients was closely related to small-bowel transit time, but another study of 21 patients failed to identify a relationship between small-bowel transit measured by lactulose breath hydrogen test and functional results after colectomy.[41,59] It is clear that additional work is required in this area.

Psychiatric Influences on Functional Results

The presence of a severe psychiatric disorder adversely influences the outcome of surgery for colonic inertia. Constipated patients have been found to have higher depression scores compared with controls, and patients who were improved by surgery could be identified by lower anxiety and depression scores compared with those who were not improved.[63] The authors concluded that good functional outcome after surgery for constipation can be predicted by preoperative psychiatric screening. Kamm et al[31] reported 10 of 44 patients who underwent colectomy had a history of psychiatric illness. Four patients developed serious psychiatric disturbances postoperatively. The authors suggested that patients with psychological disturbances might have the lowest threshold for seeking surgery and also the least ability to tolerate the side effects of surgery.

Several other studies have drawn similar conclusions.[40] Patients with constipation have significantly elevated scores in hypochondriasis, depression, and hysteria scales, manifesting the psychological defense mechanism of somatosization.[64] A significantly higher anxiety and depression score was found in a group of patients undergoing colectomy for constipation compared with a group of other colon resection patients.[39] In this study 19 of 21 such patients had previously used tranquilizers or antidepressants, although the cause-and-effect relationship between psychological disturbances and constipation was unclear. Permanent stoma rates after initial colectomy were significantly higher in patients with psychological disturbances.[32]

Some surgeons now exclude patients with significant preoperative psychiatric disorders from subtotal colectomy.

Conclusion

Elective colectomy for chronic constipation can potentially yield very rewarding results. As has been shown in this chapter, dramatic symptomatic relief including improvement in the frequency of spontaneous bowel movements, decrease in the use of enemas and digitation, and in some cases improvement or resolution of pain or bloating may occur. However, conversely in other patients constipation may persist and abdominal pain may even worsen. It should also be remembered that potential adverse sequelae may result from surgery for a benign condition, including anastomotic leak, small bowel obstruction, and even an ileostomy. The chapter authors and the book editors concur that very stringent investigation including physiological, medical, and psychosocial investigations are required before contemplating this type of

resectional surgery for a functional disorder. Sufficiently motivated patients who have been carefully selected through intensive investigation in a specialist unit may, in appropriate circumstances, be offered this option. It is the book editors' belief that the "ideal" patient is one with reproducible colonic inertia on multiple transit studies with normal gastric emptying and small-bowel function; no evidence of any physiologic, functional, or structural pelvic outlet obstruction; and no associated symptoms like nausea, bloating, abdominal or pelvic pain, or difficult or incomplete evacuation. The patient who understands that all of these symptoms may either persist or develop after surgery and a permanent stoma may be necessary is best prepared to pursue this option.

References

1. Lane WA. Remarks on the results of the operative treatment of chronic constipation. Br Med J 1908;18:126–130.
2. Lane WA. An address on chronic intestinal stasis. Br Med J 1909;12:1408–1411.
3. Bassotti G, Gaburri M, Imbimbo BP, et al. Colonic mass movements in idiopathic chronic constipation. Gut 1988;29:1173–1179.
4. Camilleri M, Zinmeister AR. Towards a relatively inexpensive, noninvasive, accurate test for colonic motility disorders. Gastroenterology 1992;103:36–42.
5. McLean RG, Smart RC, Bruck CE, King DW, Lubowski DZ, Talley NA. Colon transit scintigraphy in health and constipation using oral I-131 cellulose. J Nucl Med 1990;31:985–989.
6. Bharucha AE, Phillips SF. Slow transit constipation. Gastroenterol Clin North Am 2001;30:77–95.
7. Preston DM, Lennard-Jones JE. Pelvic motility and response to intraluminal bisacodyl in slow-transit constipation. Dig Dis Sci 1985;30:289–294.
8. Bassotti G, Chiarioni G, Imbimbo BP, et al. Impaired colonic motor response to cholinergic stimulation in patients with severe chronic idiopathic (slow transit type) constipation. Dig Dis Sci 1993;38:1040–1045.
9. Hinton JM, Lennard-Jones JE, Young AC. A new method of studying gut transit times using radiopaque markers. Gut 1969;10:842–847.
10. Stivland T, Camilleri M, Vassalo M, et al. Scintigraphic measurement of regional gut transit in idiopathic constipation. Gastroenterology 1991;101:107–115.
11. McLean RG, Smart RC, Lubowski DZ, King DW, Barbagallo S, Talley NA. Oral colon transit scintigraphy using indium-111 DTPA: variability in healthy subjects. Int J Colorectal Dis 1992;7:173–176.
12. Dick AC, McCallion WA, Brown S, Boston VE. Antegrade colonic enemas. Br J Surg 1996;83(5):642–643.
13. Malone PS, Ransley PG, Kiely EM. Preliminary report: the antegrade continence enema. Lancet 1990;336:1217–1218.
14. Kenefick NJ, Nicholls RJ, Cohen RG, Kamm MA. Permanent sacral nerve stimulation for treatment of idiopathic constipation. Br J Surg 2002;89(7):882–888.
15. Pemberton JH, Rath DM, Ilstrup DM. Evaluation and surgical treatment of severe chronic constipation. Ann Surg 1991;214:403–413.
16. Piccirillo MF, Reissman P, Wexner SD. Colectomy as treatment for constipation in selected patients. Br J Surg 1995;82:898–901.
17. Platell C, Scache D, Mumme D, Stitz R. A long-term follow-up of patients undergoing colectomy for chronic idiopathic constipation. Aust N Z J Surg 1996;6(8):525–529.
18. Nyam DC, Pemberton JH, Ilstrup DM, Rath DM. Long-term results of surgery for chronic constipation. Dis Colon Rectum 1997;40:273–279.
19. Lubowski DZ, Chen FC, Kennedy ML, King DW. Results of colectomy for severe slow transit constipation. Dis Colon Rectum 1996;39(1):23–29.
20. Klatt ER. Role of subtotal colectomy in the treatment of incapacitating constipation. Am J Surg 1983;145:623–625.
21. Belliveau P, Goldberg SM, Rothenberger DA, Nivatvongs S. Idiopathic acquired megacolon: the value of subtotal colectomy. Dis Colon Rectum 1982;25:118–121.
22. Preston DM, Hawley PR, Lennard-Jones JE, Todd IP. Results of colectomy for severe idiopathic constipation in women (Arbuthnot Lane's disease). Br J Surg 1984;71:547–552.
23. Vasilevsky CA, Nemer FD, Balcos EG, Christenson CE, Goldberg SM. Is subtotal colectomy a viable option in the management of chronic constipation? Dis Colon Rectum 1988;31:679–681.
24. Knowles CH, Scott M, Lunniss PJ. Outcome of colectomy for slow transit constipation. Ann Surg 1999;5:627–638.
25. Webster C, Dayton M. Results after colectomy for colonic inertia: a sixteen-year experience. Am J Surg 2001;182(6):639–644.
26. Pikarsky AJ, Singh JJ, Weiss EG, Nogueras JJ, Wexner SD. Long-term follow-up of patients undergoing colectomy for colonic inertia. Dis Colon Rectum 2001;44(2):179–183.
27. Drossman DA, Sandler RS, McKee DC, Lovitz AJ. Bowel patterns among patients not seeking health care. Gastroenterology 1982;83:529–534.
28. Redmond JM, Gardner WS, Barofsky I, Ratych RE, Goldsborough DC, Schuster MM. Physiological tests to predict long-term outcome of total abdominal colectomy for intractable constipation. Am J Gastroenterol 1995;90(5):748–753.
29. Walsh PV, Peebles-Brown DA, Watkinson G. Colectomy for slow transit constipation. Ann R Coll Surg Engl 1987;69:71–75.
30. Yoshioka K, Keighley MR. Clinical results of colectomy for severe constipation. Br J Surg 1989;76:600–604.
31. Kamm MA, Hawley PR, Lennard-Jones JE. Outcome of colectomy for severe idiopathic constipation. Gut 1988;29:969–973.
32. Hasegawa H, Radley S, Fatah C, Keighley MRB. Long-term results of colorectal resection for slow transit constipation. Colorectal Dis 1999;1:141–145.
33. FitzHarris GP, Garcia-Aguilar J, Parker SC, et al. Quality of life after subtotal colectomy for slow-transit consti-

pation: both quality and quantity count. Dis Colon Rectum 2003;46(4):433–440.
34. Fasth S, Hedlund H, Svanninger G, Oresland T, Hulten D. Functional results after subtotal colectomy and caecorectal anastomosis. Acta Chir Scand 1983;149: 623–627.
35. Fan CW, Wang JY. Subtotal colectomy for colonic inertia. Int Surg 2000;85:309–312.
36. Costalat G, Garrigues JM, Didelot JM, Yousfi A, Boccasanta P. Subtotal colectomy with ceco-rectal anastomosis (Deloyers) for severe idiopathic constipation: an alternative to total colectomy reducing risks of digestive sequelae. Ann Chir 1997;51(3):248–255.
37. Sarli L, Costi R, Sarli D, Roncoroni L. Pilot study if subtotal colectomy with antiperistaltic cecoproctostomy for the treatment of chronic slow-transit constipation. Dis Colon Rectum 2001;44(10):1514–1520.
38. DeGraaf EJ, Gilberts EC, Schouten WR. Role of segmental colonic transit time studies to select patients with slow transit constipation for partial left-sided or subtotal colectomy. Br J Surg 1996:83:648–651.
39. Ghosh S, Papachrysostomou M, Batool M, Eastwood MA. Long-term results of subtotal colectomy and evidence of noncolonic involvement in patients with idiopathic slow-transit constipation. Scand J Gastroenterol 1996;31:1083–1091.
40. Pluta HM, Bowes KL, Jewell LD. Long-term results of total abdominal colectomy for chronic idiopathic constipation: value of preoperative assessment. Dis Colon Rectum 1996;39(2):160–166.
41. Mollen R, Kuijpers H, Claassen AT. Colectomy for slow-transit constipation: preoperative functional evaluation is important but not a guarantee for a successful outcome. Dis Colon Rectum 2001;44(4):577–580.
42. Hughes ESR, McDermott FT, Johnson WR, Polglase AL. Surgery for constipation. Aust NZ J Surg 1981;51(2): 144–148.
43. Nakamura T, Pikarsky AJ, Potenti FM, et al. Are complications of subtotal colectomy with ileorectal anastomosis related to the original disease? Am Surg 2001;67: 417–420.
44. Lahr SJ, Lahr CJ, Srinivasan A, Clerico ET, Limehouse VM, Serbezov IK. Operative management of severe constipation. Am Surg 1999;65:1117–1123.
45. Wexner SD, Daniel N, Jagelman DG. Colectomy for constipation: physiological investigation is the key to success. Dis Colon Rectum 1991;34:851–856.
46. Krevsky B, Maurer AH, Fisher RS. Patterns of colonic transit in chronic idiopathic constipation. Am J Gastroenterol 1989;84:127–132.
47. Lane RHS, Todd IP. Idiopathic megacolon: a review of 42 cases. Br J Surg 1977;64(5):305–310.
48. Kamm MA, Van der Sijp JR, Hawley PR, Phillips RK, Lennard-Jones JE. Left hemicolectomy with rectal excision for severe idiopathic constipation. Int J Colorectal Dis 1991;6:49–51.
49. You YT, Wang JY, Changchien CR, et al. Segmental colectomy in the management of colonic inertia. Am Surg 1998;64:775–777.
50. Lundin E, Karlbom U, Pahlman L, Graf W. Outcome of segmental colonic resection for slow-transit constipation. Br J Surg 2002;89:1270–1274.
51. Hosie KB, Kmiot WA, Keighley MR. Constipation: another indication for restorative proctocolectomy. Br J Surg 1990;77:801–802.
52. Nicholls RJ, Kamm MA. Proctocolectomy with restorative ileoanal reservoir for severe idiopathic constipation. Report of two cases. Dis Colon Rectum 1988;31: 968–969.
53. Christiansen J, Rasmussen OO. Colectomy for severe slow-transit constipation in strictly selected patients. Scand J Gastroenterol 1996;31:770–773.
54. Thakur A, Fonkalsrud EW, Buchmiller T, French S. Surgical treatment of severe colonic inertia with restorative proctocolectomy. Am Surg 2001;67(1):36–40.
55. Villarreal J, Sood M, Zangen T, et al. Colonic diversion for intractable constipation in children: colonic manometry helps guide clinical decisions. J Pediatr Gastroenterol Nutr 2001;33(5):588–591.
56. Luck A, Hensman C, Hewett P. Laparoscopic colectomy for cancer: a review. Aust N Z J Surg 1998;68:318–327.
57. Ho YH, Tan M, Eu KW, Leong A, Seow-Choen F. Laparoscopic-assisted compared with open total colectomy in treating slow transit constipation. Aust N Z J Surg 1997;67(8):562–565.
58. Duthie GS, Bartolo DC. Anismus: the cause of constipation? Results of investigation and treatment. World J Surg 1992;16:831–835.
59. Kuijpers HC. Application of the colorectal laboratory in diagnosis and treatment of functional constipation. Dis Colon Rectum 1990;33:35–39.
60. Van der Sijp JR, Kamm MA, Bartram CI, Lennard-Jones JE. The value of onset and rectal emptying in predicting the outcome of colectomy for severe idiopathic constipation. Int J Colorectal Dis 1992;7(1):35–37.
61. Bernini A, Madoff R, Lowry AC, et al. Should patients with combined colonic inertia and nonrelaxing pelvic floor undergo subtotal colectomy? Dis Colon Rectum 1998;41(11):1363–1366.
62. Bassotti G, Stanghellini V, Chiarioni G, et al. Upper gastrointestinal motor activity in patients with slow-transit constipation. Dig Dis Sci 1996;41:1999–2005.
63. Fisher SE, Breckon K, Andrews HA, Keighley MR. Psychiatric screening for patients with faecal incontinence or chronic constipation referred for surgical treatment. Br J Surg 1989;76:352–355.
64. Heymen S, Wexner SD, Gulledge AD. MMPI assessment of patients with functional bowel disorders. Dis Colon Rectum 1993;36:593–596.
65. Belliveau P, Goldberg SM, Rothenberger DA, Nivatvongs S. Idiopathic acquired megacolon: the value of subtotal colectomy. Dis Colon Rectum 1982;25:118–121.
66. Leon SH, Krishnamurthy S, Schuffler MD. Subtotal colectomy for severe idiopathic constipation: a follow-up of 13 patients. Dig Dis Sci 1987;32:1249–1254.
67. Beck D, Fazio V, Jagelman D. Surgical management of colonic inertia. South Med J 1989;82:305–309.

16

Botulinum Toxin and Other New Pharmacologic Approaches to Constipation

Thanesan Ramalingam and Neil J. Mortensen

Much of the medical treatment of constipation is based on pharmacologic intervention using simple bulking agents and laxatives. The growing acceptance of the use of botulinum toxin in the treatment of anal fissure[1] has highlighted the diverse clinical use of this agent, and has generated further interest in its use in patients with constipation from functional outlet obstruction.[2]

This chapter describes the background relating to the therapeutic use of botulinum toxin, its pharmacologic properties, and its use in patients with disordered defecation. We also describe other new pharmacologic agents used in the treatment of patients with chronic constipation such as serotonin (5-hydroxytryptamine) receptor agonists, colchicines, and neurotrophin-3 agonists.

Botulinum Toxin: Background

Van Ermengem[3] first noted that botulinum toxin, a potent neurotoxin, was produced by the gram-positive bacillus *Clostridium botulinum*. However, it was not until the discovery by Burgen et al[4] in 1949 that the toxin blocked neuromuscular transmission that its potential as a therapeutic tool evolved.

There are seven different types of known botulinum neurotoxin, labeled as type A to G. Although they share a similar chemical structure, the neurotoxin types are antigenically distinct, resulting in variations in their potency. For example, types C and D cause disease in animals (avian botulism), whereas types A, B, E, and F can affect humans, with type A resulting in the most severe clinical effects.[5]

Structurally, the toxin is a protein made up of heavy- and light-chain components held together by a disulfide bond. It is produced as a protoxin with a molecular weight of 150 kd and cleaves into the heavy (100 kd) and light (50 kd) components. The former acts as a carrier that binds to the surface of the target cell (neuron) and allows for the latter to be translocated across the cell membrane. The light-chain component contains zinc-dependent endopeptidases whose action within the cell brings about the toxic effect.[6]

The mechanism of action of botulinum toxin of blocking neurotransmitter release at the cholinergic nerve terminals is thought to take place in three steps. The toxin first binds to receptors on the unmyelinated presynaptic membrane of the neuron, prior to internalization into the cell by endocytosis. The disulfide bond is then cleaved and the light-chain component is translocated into the cytosol. In the final step the light-chain component inhibits neurotransmitter release by the action of zinc-dependent endopeptidases.[7]

Although the process is irreversible, recovery does occur through proximal axonal sprouting and formation of new synaptic contacts. A study by de Paiva and colleagues[8] suggests that regeneration of the original neuromuscular junction does take place eventually.

The first reported clinical use of botulinum toxin (type A) was by Scott[9] in 1981 in successfully treating patients with strabismus. Since then, botulinum toxin has been used in the management of a number of clinical conditions—some with more success than others. Table 16.1 lists some examples of diverse clinical applications of botulinum toxin.

Table 16.1. Examples of the diverse clinical applications of botulinum toxin

Disorders of involuntary muscle activity
Cervical dystonia (torticollis)
Blepharospasm (eyelid apraxia)
Writer's cramp
Hemifacial spasm
Tics
Disorders of localized muscle spasms/pain
Chronic lower back pain
Tension headache
Other disorders of inappropriate muscle overactivity
Strabismus
Nystagmus
Anal fissure
Pelvic floor dysfunction (incl. anismus, vaginismus)
Achalasia
Detrusor-sphincter dyssynergia
Cosmesis
Wrinkles, frown lines

In the United Kingdom preparations of botulinum toxin type A are commercially available in two common forms, namely Botox® and Dysport®. Each freeze-dried vial containing 100 units (U) of botulinum toxin type A is reconstituted with normal saline prior to its use. This unit measurement, the "mouse unit," represents the potency of the agent and is based on the amount of the toxin needed to kill 50% of a group of 20-g Swiss-Webster mice within 3 days of intraperitoneal injection of the toxin. This has led to some confusion, as there appear to be differences in observed potencies between Botox and Dysport in clinical use. It is now generally accepted that for clinical purposes 1 U of Botox is approximately equivalent to 3 or 4 U of Dysport.[10]

The route of administration is by injection directly into the relevant overactive muscle or muscle group and is normally performed without the need for anesthesia. Potentially, the transient nature of its clinical effects confers another advantage of its use over surgery.

Constipation Caused by Dysfunction of the Pelvic Floor Muscles

It is acknowledged that in a proportion of patients with chronic constipation, the symptoms are due to obstructed defecation caused by dysfunction of the pelvic floor musculature.[2] Initially labeled as puborectalis syndrome[11] but also often described as anismus,[12] it is characterized by the failure of the puborectalis muscle to relax or by its paradoxical contraction during efforts to defecate. In the normal course of events the puborectalis muscle and the external anal sphincter relax, allowing the anorectal angle to straighten to accommodate defecation through a patent anal canal.

In patients with chronic constipation and pelvic floor dysfunction, injecting botulinum toxin into the puborectalis muscle weakens or paralyzes the overactive muscle and causes straightening of the anorectal angle to allow easier defecation. It was first used in patients with obstructed defecation in 1988 by Hallan and colleagues.[13] In their study, seven patients with obstructed defecation diagnosed using electromyographic (EMG) studies and dynamic proctography, received botulinum toxin injection to the puborectalis muscle. Taking an empirical dose of 3 ng botulinum toxin (approximately equivalent to 60 U of Botox), four patients derived benefit from the treatment. This finding was based on symptom questionnaires as well as a reduction in the maximum squeeze pressure on anorectal manometry and an increase in the anorectal angle on posttreatment proctography analysis. However, of the remaining three patients, one did not derive any benefit, and two suffered from symptoms of incontinence during the treatment period.

In another study, Joo and colleagues[14] demonstrated some success in using botulinum toxin to treat four patients with obstructed defecation who had failed to respond to conventional biofeedback treatment. They used between 6 and 15 U of botulinum toxin injected into the puborectalis muscle or external anal sphincter under EMG guidance. They found that although all four patients showed both subjective and objective (EMG results) improvement initially, long-term benefits were seen in only two of the four patients after 3 months.

Maria and colleagues,[15] in a study involving three patients with outlet obstruction constipation, injected 30 U of botulinum toxin into the puborectalis muscle as treatment. At 8 weeks following treatment, these patients' symptoms improved as indicated by their reduced laxative or enema use. The authors also showed, using proctography, that there was significant increase in the anorectal angle and a decrease in the anal tone during straining, when compared with pretreatment baseline values.

Ron et al,[16] in one of the larger studies to date, treated with botulinum toxin 25 consecutive patients with a history of constipation and outlet obstruction. The patients were randomly allocated to receive either 10 U of botulinum toxin on each lateral aspect of the puborectalis muscle or 20 U as a single injection to the posterior aspect of the muscle. Over the 1-year follow-up period, 11 patients received at least two treatments with botulinum toxin. There were significant improvements in balloon expulsion tests, manometric relaxation, and straining patterns (on a visual analogue scale) in these patients at 3 months. The authors suggest that the posterior injection site did not confer better results.

Albanese and colleagues[17] observed that injecting botulinum toxin into the puborectalis muscle relieved symptoms of constipation in a patient with Parkinson's disease. They followed up this single case report with a prospective study of 18 Parkinson's disease patients with obstructed defecation, in which the authors injected 100 U of botulinum toxin into the puborectalis muscle of the patients under ultrasound guidance.[18] Two months after treatment they were able to show that there were significant reductions in anal tone during straining and increase in the anorectal angle (measured with dynamic proctography) in these patients when compared with their baseline values.

In some patients with symptoms of obstructed defecation a rectocele, a herniation of the anterior rectal wall into the lumen of the vagina, may be present. Although the etiology of rectocele is unclear, it has been suggested that there may be an association between rectoceles and the paradoxical contraction of the puborectalis during evacuatory efforts.[19]

Maria and colleagues[20] used botulinum toxin to treat 14 female patients with symptoms of obstructed defecation who also had rectoceles; 30 U of botulinum toxin were injected in divided doses into either side of the puborectalis muscle and anteriorly in the external anal sphincter. There was symptomatic improvement in nine patients at 2 months. Furthermore, there were significant decreases in the mean sizes of the rectoceles together with increases in the mean anorectal angles when compared with pretreatment values.

Despite the fact that there seems to be increasing support for the role of botulinum toxin in the treatment of constipated patients with obstructed defecation, there are several aspects regarding its use that need to be highlighted and addressed. First, any beneficial effects of botulinum toxin injections appear to be short-lived. Joo and colleagues[14] found that only 50% of the patients in their study remained well at 3 months. In a study by Shafik and El Sibai,[21] symptomatic improvement in their patients was noted for a mean duration of only 5 months. In the study by Ron et al[16] mentioned earlier, 11 of the 25 patients required at least two treatments with botulinum toxin during the 1-year follow-up period. This diminished clinical response with repeated injections may be due to the development of neutralizing antibodies to the toxin, resulting in immunoresistance.[22]

Second, there does not seem to be any consistency regarding the optimum dose required to reverse the effects of paradoxical puborectalis contraction. As it has been suggested that the effective therapeutic dose should be proportional to the mass of the muscle injected,[23] the lack of a standard therapeutic dose is not surprising. This is further compounded by, as previously mentioned, the lack of dose standardization of botulinum toxin between the commercially available preparations. Additionally, there is also some debate about the preferred site of injection in patients with anismus. Injection of botulinum toxin into the external anal sphincter alone appears to confer symptomatic improvement in some patients with puborectalis syndrome.[14]

Third, although botulinum toxin injections are generally well tolerated, like any other therapeutic agent it is not without side effects. Although its effect diminishes with increasing distance from the injection site, diffusion to nearby muscle or tissues is possible causing muscle weakness.[24] For example, patients receiving botulinum toxin injections for torticollis may develop dysphagia.[5] In relation to the pelvic floor muscles, excessive weakness can result in symptoms of incontinence.[13] Potentially, weakness of distant muscles or generalized muscle weakness is possible by hematologic spread of the toxin, but this is believed to be very rare.[25]

The use of botulinum toxin is not recommended in pregnant or breast-feeding patients, and it should also be used under close supervision in patients with disturbed neuromuscular junction transmission, such as in patients with myasthenia gravis or during treatment with aminoglycosides.[7]

Although the use of botulinum toxin in patients with obstructed defecation seems promising, it would be premature to entirely support its use. Nearly all studies relating to its use in this group of patients involve small patient numbers. Now larger, double-blinded, randomized studies are needed.

Other New Pharmacologic Approaches

Although the use of botulinum toxin appears to have captured the interest of surgeons for its use predominantly in patients with obstructed defecation, among physicians it is the use of serotonin (5-hydroxytryptamine, 5-HT)–modulating drugs in the treatment of patients with functional gastrointestinal disease such as chronic constipation that has generated interest.[26]

Serotonin-Modulating Drugs

The idea that serotonin played a role in peristalsis was first suggested by Bulbring and Crema[27] in 1959, but it is only recently that serotonin (5-HT) mechanisms in the gut are being manipulated.

Nearly 80% of total body serotonin is found in the gastrointestinal tract, and the vast majority of this compound is contained within the granules of the enteroendocrine cells.[28] These cells lie at the base of the crypts and are able to detect changes in the lumen via apical microvilli. Factors that modulate the release of 5-HT from these cells include mechanical stimuli such as luminal pressure changes, bacterial toxins (e.g., cholera toxin), and drugs.[26] Furthermore, receptor-mediated stimulation and inhibition via adrenergic, purinergic, and muscarinic receptors exist. These receptors are thought to act by modulating intracellular calcium, a surge of which is associated with 5-HT release.[29]

With over 21 different receptor subtypes available for 5-HT to bind to and exert an effect, it is not surprising that our knowledge of the mechanism of action of 5-HT is incomplete. In a recent review of 5-HT–modulating drugs for functional gastrointestinal diseases by Spiller,[26] the diverse 5-HT gastrointestinal effects with regard to motility, peristalsis, secretion, and sensation were highlighted.

In relation to the use of 5-HT in patients with slow-transit or functional constipation, therapy has been primarily aimed at modulating the 5-HT_4 receptor. It has been shown that in some of these patients the impaired colonic motility was caused by a decrease in frequency and duration of high-amplitude giant migrating contractions[30] and an associated reduction in the number of mass movements.[31] Studies using 5-HT_4 receptor agonists have shown its prokinetic properties in stimulating the peristaltic response[32] and enhancement of giant migrating colonic contractions in an animal model.[33] Its use in healthy volunteers resulted in increased stool frequency and consistency, with shortened colonic transit times.[34]

In relation to peristalsis, the mechanism of action of 5-HT_4 appears to involve the release of neurotransmitters such as calcitonin gene-related peptide (CGRP), substance P, and vasoactive intestinal peptides (VIPs).[32] Mucosal stimulation releases 5-HT, whose action on 5-HT_4 receptors activates primary afferent neurons within the submucosa to cause a release of CGRP and substance P. This release results in contraction of the circular muscle proximally while the simultaneous release of VIP relaxes the same muscle distally. It seems that these peristaltic effects are blocked by 5-HT_4 (and 5-HT_3) receptor antagonists.[32] In in-vitro animal experiments, a highly selective 5-HT_4 receptor agonist has been shown to facilitate cholinergic and excitatory nonadrenergic, noncholinergic (NANC) neurotransmission to enhance motility.[35]

Cisapride, a 5-HT_4 agonist, was shown to benefit patients with functional constipation.[36] However, the demise of Cisapride use due to its potentially lethal cardiac side effects led to interest in newer 5-HT_4 agonists, such as Tegaserod and prucalopride. Tegaserod has been shown to have effects on visceral sensation and to accelerate colonic transit time. It has therefore been primarily used in irritable bowel syndrome (IBS) patients with constipation.[37] Prucalopride is probably a more potent laxative than Tegaserod. Since its increased potency may cause symptoms of abdominal cramps, its use has been directed toward patients with severe constipation rather than constipated IBS patients.[26]

Prucalopride

Several recent double-blind, randomized clinical studies have shown the benefits of using prucalopride in the treatment of patients with

chronic constipation.[38–40] Emmanuel et al[38] and Sloots et al[39] showed statistically significant improvements in the patients taking 1 mg of prucalopride compared with those on placebo in relation to stool frequency, consistency, and the need to strain. Although there was evidence to suggest improvements in transit times, this did not appear statistically significant when compared to placebo, perhaps supported by the fact that some patients with chronic constipation may have normal colonic transit times.

The study by Coremans et al[40] showed that patients on 4 mg of prucalopride daily had statistically significant improvements in stool consistency when compared to the placebo group. However, they did not show similar improved outcomes for stool frequency and the need to strain.

A range of dosages has been used in these studies, but it seems that a daily dose of 1 or 2 mg is generally well tolerated. Since it has a half-life of 24 hours, a single daily dose has been recommended.

The most frequent adverse effects reported include abdominal cramps, nausea, diarrhea, and flatulence relating to the secretory and prokinetic effect of the drug.

Finally, in relation to the use of 5-HT–modulating drugs in patients with chronic constipation, there has been interest recently in new thiazole derivatives as potent and selective 5-HT_3 receptor agonists for the treatment of constipation.[41] This therapeutic approach is still in its early research stages but has its basis in the knowledge that 5-HT_3 antagonists inhibit colonic motility in healthy humans[42] and help in diarrhea-predominant IBS patients.[43]

Colchicine and Neurotrophin-3

Preliminary studies using other new approaches to treat patients with constipation include the old and the new, such as the use of colchicine[44] and neurotrophin-3 (NT-3)[45] agonists, respectively. The latter agent belongs to the family of protein growth factors, neurotrophins, involved in the growth, development, and function of neurons. A double-blind, randomized study comparing five treatment schedules using NT-3 with placebo showed statistically significant improvements in stool frequency, consistency, and passage in one arm of the treatment group when compared with placebo.[45] This study highlighted the fact that the optimum therapeutic dose of NT-3 is yet to be established, and its route of administration by subcutaneous injection may make its use less desirable.

Colchicine, an alkaloid prepared from the dried seeds and corns of *Colchicum autumnale*, the autumn crocus or meadow saffron, has well-established clinical use in the treatment of patients with acute gout and in patients with familial Mediterranean fever. One of its common side effects, diarrhea, has led to its use in treating patients with refractory constipation.[46] In a small randomized, double-blind study of 16 patients treated with 0.6 mg of colchicine three

Table 16.2. Characteristics of new pharmacologic agents used in the management of patients with constipation

Agent:	Botulinum toxin	Prucalopride	Tegaserod	Colchicine	Neurotrophin-3
Class of drug:	Bacterial neurotoxin (polypeptide)	Aminoguanidine indole	Aminoguanidine indole	Alkaloid	Protein
Mechanism of action:	Neuromuscular blockade (of acetyl choline release)	Selective 5-HT_4 agonist	Selective 5-HT_4 partial agonist	Unknown	Unknown
Proposed indication:	Anismus	Slow-transit constipation	Constipation-predominant irritable bowel syndrome	Refractory constipation	Slow-transit constipation
Proposed therapeutic dose:	N/A Range: 6–100 U	N/A Range: 1–4 mg o.d.	6 mg b.i.d.	N/A 0.6 mg t.i.d.	N/A 9 mg thrice/week
Route of administration:	Intramuscular injection	Oral	Oral	Oral	Subcutaneous injection
Side effects	Fecal incontinence	Headache, nausea, abdominal pain, diarrhea, flatulence	Headache, diarrhea, abdominal pain, flatulence	Diarrhea, nausea, vomiting, abdominal pain	Injection site irritation, nausea, flushing, upper respiratory tract infections, paresthesia

times a day, the treatment group showed statistically significant improvements in bowel movements and colonic transit times compared to the placebo group.[44]

The mechanism of action of colchicine on the gastrointestinal tract is unclear, although it has been suggested that it is involved in prostaglandin synthesis, intestinal secretion, and bowel motility.[47] Its long-term use in patients with familial Mediterranean fever has shown the drug to be relatively free of side effects.[47]

The new pharmacologic approaches described in this chapter aim to benefit patients with chronic constipation by improving either gastrointestinal motility or evacuatory function. Better appreciation of the complex role of pelvic floor muscles in defecation has led to the relatively novel use of botulinum toxin in patients with obstructed defecation. Initial results, although encouraging, are inconclusive, with larger, randomized studies now needed. It would also help to have a more accurate method of assessing the biologic activity (effective therapeutic dose) of botulinum toxin use.

The use of serotonergic drugs, in particular 5-HT_4 receptor agonists, suggests benefit in their use in patients with slow-transit constipation. Nonetheless, evidence of the safety and efficacy of their long-term use is awaited. The use of colchicine and NT-3 in the treatment of patients with chronic constipation is still in the early stages of evaluation. Table 16.2 summarizes the main characteristics of the therapeutic agents discussed in this chapter.

Conclusion

The main thrust of treating patients with chronic constipation remains pharmacologic. Increased use of these agents is appealing because their safety profile is much more acceptable than is the one following colectomy for constipation. Continuing improvements in our knowledge of gastrointestinal motility as well as the physiology of defecation will no doubt help home in on specific pharmacologic targets to benefit these patients.

References

1. Lindsey I, Jones OM, Cunningham C, Mortensen NJ McC. Chronic anal fissure. Br J Surg 2004;91:270–279.
2. Lennard-Jones JE. Constipation. In: Feldman M, Scharschmidt BF, Sleisenger MH, eds. Sleisenger and Fordtran's Gastrointestinal and Liver Disease: Pathophysiology, Diagnosis, Management, 6th ed. Philadelphia: WB Saunders, 1998:174–197.
3. Van Ermengem E. Classics in infectious diseases: a new anaerobic bacillus and its relation to botulism. Originally published as "Ueber einen neuen anaeroben bacillus und seine beziehungen zum botulismus" in Zeitschrift fur Hygiene und Infektionskrankheiten 1897;26:1–56. Rev Infect Dis 1979;1:701–719.
4. Burgen AS, Dickens F, Zatman LJ. The action of botulinum toxin on the neuromuscular junction. J Physiol 1949;109:10–24.
5. Jankovic J, Brin MF. Botulinum toxin: historical perspective and potential new indications. Muscle Nerve 1997;20(suppl 6):S129–145.
6. Schiavo G, Rossetto O, Santucci A, Dasgupta BR, Montecucco C. Botulinum neurotoxins are zinc proteins. J Biol Chem 1992;267:23479–23483.
7. Brin MF. Botulinum toxin: chemistry, pharmacology, toxicity and immunology. Muscle Nerve 1997;20(suppl 6):S146–168.
8. de Paiva A, Meunier FA, Molgo J, Aoki KR, Dolly JO. Functional repair of motor end plates after botulinum toxin type A poisoning: biphasic switch of synaptic activity between nerve sprouts and their terminals. Proc Natl Acad Sci 1999;96:3200–3205.
9. Scott AB. Botulinum toxin injection of the eye muscles to correct strabismus. Trans Am Ophthalmol Soc 1981;79:734–770.
10. Brin MF, Blitzer A. Botulinum toxin: dangerous terminology errors [letter]. J R Soc Med 1993;86:493–494.
11. Wasserman F. Puborectalis syndrome (rectal stenosis due to anorectal spasm). Dis Colon Rectum 1964;7: 87–98.
12. Preston DM, Lennard-Jones JE. Anismus in chronic constipation. Dig Dis Sci 1985;30:413–418.
13. Hallan RJ, Williams NS, Melling J, Waldron DJ, Womack NR, Morrison JF. Treatment of anismus in intractable constipation with botulinum A toxin. Lancet 1988; 338:714–717.
14. Joo S, Agachan F, Wolff B, Nogueras JJ, Wexner SD. Initial North American experience with botulinum toxin type A for treatment of anismus. Dis Colon Rectum 1996;39:1107–1111.
15. Maria G, Brisinda G, Bentivoglio AR, Cassetta E, Albanese A. Botulinum toxin in the treatment of outlet obstruction caused by puborectalis syndrome. Dis Colon Rectum 2000;43:376–380.
16. Ron Y, Avni Y, Lukovetski A, et al. Botulinum toxin type-A in therapy of patients with anismus. Dis Colon Rectum 2001;44:1821–1826.
17. Albanese A, Maria G, Bentivoglio AR, Brisinda G, Cassetta E, Tonali P. Severe constipation in Parkinson's disease relieved by botulinum toxin. Mov Disord 1997;12:764–766.
18. Albanese A, Brisinda G, Bentivoglio AR, Maria G. Treatment of outlet obstruction in constipation in Parkinson's disease with botulinum neurotoxin A. Am J Gastroenterol 2003;98:1439–1440.
19. Johansson, Nilsson BY, Holmström B, Dolk A, Mellgren A. Association between rectocele and paradoxical sphincter response. Dis Colon Rectum 1992;35:503–509.
20. Maria G, Brisinda G, Bentivoglio AR, Albanese A, Sganga G, Castagneto M. Anterior rectocoele due to

obstructed defecation relieved by botulinum toxin. Surgery 2001;129:524–529.
21. Shafik A, El Sibai O. Botulinum toxin in the treatment of nonrelaxing puborectalis syndrome. Dig Surg 1998; 15:347–351.
22. Borodic GE, Johnson E, Goodnough M, Schantz E. Botulinum toxin therapy, immunologic resistance, and problems with available materials. Neurology 1996;46: 26–29.
23. Munchau A, Bhatia KP. Uses of botulinum toxin injection in medicine today. Br Med J 2000;320:161–166.
24. Borodic GE, Ferrante R, Pearce LB, Smith K. Histological assessment of dose related diffusion and muscle fibre response after therapeutic botulinum toxin A injections. Mov Disord 1994;9:31–39.
25. Garner CG, Straube A, Witt TN, Gasser T, Oertel WH. Time course of distant effects of local injections of botulinum toxin. Mov Disord 1993;8:33–37.
26. Spiller R. Serotonergic modulating drugs for functional gastrointestinal diseases. Br J Clin Pharmacol 2002;54: 11–20.
27. Bulbring E, Crema A. The release of 5-hydroxytryptamine in relation to pressure exerted on the intestinal mucosa. J Physiol (Lond) 1959;146:18–28.
28. Gershon MD. The roles played by 5-hydroxytryptamine in the physiology of the bowel. Aliment Pharmacol Ther 1999;13(suppl 2):15–30.
29. Lomax RB, Gallego S, Novalbos J, Garcia AG, Warhurst G. L-type calcium channels in enterochromaffin cells from guinea pig and human duodenal crypts: an in situ study. Gastroenterology 1999;117:1363–1369.
30. Briejer MR, Schuurkes JA, Sarna SK. Idiopathic constipation: too few stools and too little knowledge. Trends Pharmacol Sci 1999;20:1–3.
31. Basotti G, Gaburri M, Imbimbo B, et al. Colonic mass movements in idiopathic chronic constipation. Gut 1988;29:1173–1179.
32. Grider JR, Foxx-Orenstein AE, Jin J-G. 5-Hydroxytryptamine$_4$ receptor agonists initiate the peristaltic reflex in human, rat and guinea pig intestine. Gastroenterology 1998;115:370–380.
33. Briejer MR, Prins NH, Schuurkes JA. Effects of the enterokinetic prucalopride (R093877) on colonic motility in fasted dogs. Neurogastroenterol Motil 2001;13: 465–472.
34. Emmanuel AV, Kamm MA, Roy AJ, Antonelli K. Effect of a novel prokinetic drug, R093877, on gastrointestinal transit in healthy volunteers. Gut 1998;42:511–516.
35. Briejer MR, Meulemens AL, Bosmans J-P, Van Daele P, Schuurkes JA. In vitro pharmacology of the novel enterokinetic, R093877. Gastroenterology 1997;112: A705(abstract).
36. Muller-Lissner SA. Treatment of chronic constipation with cisapride and placebo. Gut 1987;28:1033–1038.
37. Camillieri M. Review article: Tegaserod. Aliment Pharmacol Ther 2001;15:777–789.
38. Emmanuel AV, Roy AJ, Nicholls TJ, Kamm M.A. Prucalopride, a systemic enterokinetic, for the treatment of constipation. Aliment Pharmacol Ther 2002;16:1347–1356.
39. Sloots CEJ, Poen AC, Kerstens R, et al. Effects of prucalopride on colonic transit, anorectal function and bowel habits in patients with chronic constipation. Aliment Pharmacol Ther 2002;16:759–767.
40. Coremans G, Kerstens R, De Pauw M, Stevens M. Prucalopride is effective in patients with severe chronic constipation in whom laxatives fail to provide adequate relief. Digestion 2003;67:82–89.
41. Imanishi N, Iwaoka K, Koshio H, et al. New thiazole derivatives as potent and selective 5-hydroxytriptamine 3 (5-HT$_3$) receptor agonists for the treatment of constipation. Bioorg Med Chem 2003:11:1493–1502.
42. Talley NJ, Phillips SF, Haddad A, et al. GR 38032F (ondansetron), a selective 5HT3 receptor antagonist, slows colonic transit in healthy man. Dig Dis Sci 1990;35:477–480.
43. Camillieri M, Mayer EA, Drossman DA, et al. Improvement in pain and bowel function in female irritable bowel patients with alosetron, a 5-HT$_3$ receptor antagonist. Aliment Pharmacol Ther 1999;13:1149–1159.
44. Verne GN, Davis RH, Robinson ME, et al. Treatment of chronic constipation with colchicine: randomized, double-blind, placebo-controlled, crossover trial. Am J Gastroenterol 2003;98:1112–1116.
45. Parkman HP, Rao SS, Reynolds JC, et al. Neurotrophin-3 improves functional constipation. Am J Gastroenterol 2003;98:1338–1347.
46. Frame PS, Dolan P, Kohli R, et al. Use of colchicine to treat severe constipation in developmentally disabled patients. J Am Board Fam Pract 1998;11:341–346.
47. Levy M, Spino M, Read SE. Colchicine: a state of the art review. Pharmacotherapy 1991;11:196–211.

17

Sacral Nerve Stimulation

Ezio Ganio, Luc Alberto Realis, Giuseppe Clerico, and Mario Trompetto

Although most physicians consider two or fewer evacuations per week as constipation, many patients consider the subjective feeling of incomplete or difficult defecation and include symptoms such as hard feces or the need for digitation, enema suppositories, or the symptoms of tenesmus as part of constipation.

Pelvic causes of abnormal evacuation include rectal aganglionosis, rectal intussusception or complete rectal prolapse, and anterior rectal wall hernia (rectocele), and they may sometimes be cured with surgery. Many patients with rectal constipation lack coordination of the rectum and the anal sphincters (outlet constipation), which is not amenable to simple surgical treatments. While biofeedback, stool softeners, and laxatives help some patients, these agents are often not a satisfactory long-term solution. Moreover some patients with colonic inertia are unresponsive to medical therapy, and the results of a subtotal colectomy are not always predictable.

The application of sacral nerve modulation (SNM) in the field of colorectal surgery has been reported relatively recently and seems to work well in patients with fecal incontinence. When SNM was shown to work in patients with chronic urinary retention it was not surprising that chronic constipation, due to spastic behavior of the pelvic floor or colonic inertia, was explored as an indication to improve defecatory dysfunction by modifying the neural control of the pelvic floor and the proximal bowel.[1]

Technique of Sacral Neuromodulation

Sacral nerve stimulation therapy consists of two stages: peripheral nerve evaluation (the diagnostic stage), and permanent implant (the therapeutic stage). Each step follows specific principles and has specific goals.

Percutaneous nerve evaluation (PNE) of the sacral roots (S2, S3, and S4) is divided into two phases: an acute phase to test the functional relevance and integrity of each sacral spinal nerve to striated anal sphincter function,[2] and a chronic phase of 2 to 3 weeks to assess the therapeutic response to sacral spinal nerve stimulation.

Percutaneous Nerve Evaluation Procedure

With the patient in the prone position, the three sacral foramina S2, S3, and S4 are located using bony landmarks (Fig. 17.1). The sacral foramen S2 is typically found just under the projection of the posterior superior iliac spines and approximately one finger-breadth lateral to the median line. The sciatic notches, which correspond to level S3, are identified. S4 is about 2 cm under foramen S3. The foramina of S3 and S4 are also positioned about one finger-breadth across from the median line.

The acute phase test is performed under local anesthesia using a 20-gauge spinal insulated needle [Medtronic™ (Minneapolis, MN) No. 041828-004] and an external neurostimulator (Medtronic model 3625 screener or Medtronic model 3628 dual screener). The needle is inserted perpendicular to the sacrum, with an angle to the skin of 60 to 80 degrees (Fig. 17.2). After the needle is positioned in the chosen foramen, it is connected to the external neurostimulator. The stimulation parameters used in the acute phase are a pulse width (PW) of 210 μsec, a frequency of 5 to 25 Hz, and an amplitude that results in an increased contraction of the pelvic floor and a deepening and flattening of the

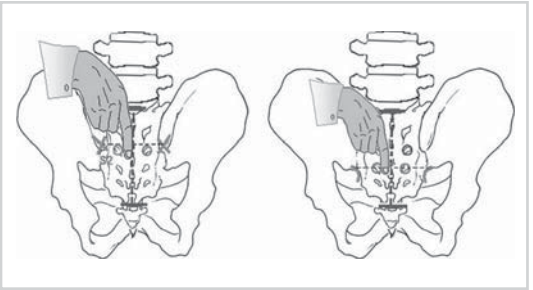


Figure 17.1. The dorsal sacral foramina are positioned approximately 2 cm laterally to the sacral crest. S2 is about 1 cm medially and 1 cm below the posterior superior iliac spine; S3 is positioned on a level with the upper border of the sciatic notch.

buttock muscle. This response usually occurs at between 1 and 6 V; simulation of specific sacral nerves typically results in specific movements of the perineum, anal sphincter, and ipsilateral lower extremity. This test ensures correct lead placement. Stimulation of S2 causes some movement of the perineum and the external sphincter along with a lateral rotation of the leg and contraction of the toes and foot. Stimulation of S3 causes a contraction of the pelvic floor and the external sphincter, the "bellows" contraction, and a plantar flexion of the big toe. Stimulation of S4 causes a contraction of the anus with a clamp-like perineal movement without any leg or foot movement. Vesicle, vaginal (or scrotal), and rectal paresthesia may be perceived by the patient during sacral nerve stimulation.

Temporary Sacral Nerve Stimulation

Once an adequate muscular response is obtained, a temporary stimulator lead (Medtronic model 3065U or model 3057-1) is inserted through the needle, following which the needle is removed. The lead is connected to an external stimulator (screener model 3625) to allow evaluation of the functional responses to the test, both subjectively to continence and objectively using rectoanal manometry. Two to 3 weeks of stimulation is the minimum accepted period for a correct evaluation of the effectiveness of sacral stimulation on constipation. To evaluate the functional results of PNE, patients completed a clinical diary of bowel movements in the 2 weeks preceding, during, and following the PNE.

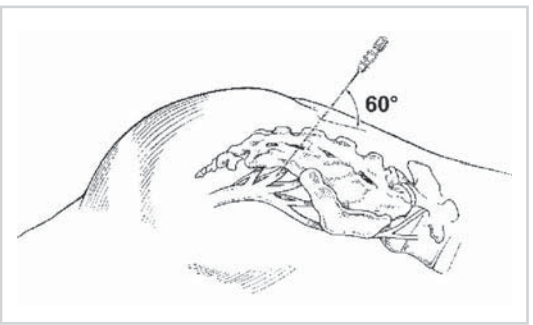


Figure 17.2. The needle is inserted parallel to the foramina axes with an inclination to the skin of 60 to 80 degrees.

Surgical Technique for a Permanent Implant

Surgical technique has recently evolved from the open classical to the newer minimally invasive implant approach.

Classical Open Surgical Technique

Before the incision, the position of the sacral foramen is verified with an isolated needle. Once the sacral foramen is confirmed, an incision is made along the median line above the sacral spinous process, up to the level of the underlying lumbodorsal fascia. The lumbodorsal fascia is cut longitudinally, about one finger-width from the median line. The paraspinous muscles underneath are sharply divided along the length of the fibers. The sacral foramen is checked, and the definitive electrode is inserted (Medtronic model 3080) and anchored to the periosteum using permanent thread or screws.

Each lead is composed of four electrodes that can be individually selected by programming the neurostimulator. Once the tip is anchored, the rest of the lead is tunneled through the subcutaneous tissue to a small incision made on the patient's side. The patient is turned on the side, and a subcutaneous pocket is prepared in the lower quadrant of the abdomen. An extension is used to connect the electrode to the neurostimulator (Medtronic Interstim 3023).

The stimulator (implantable pulse generator, IPG) can be activated the following day using a control unit (Medtronic model 7432), which allows all parameters to be percutaneously set via a radiofrequency (RF) signal. Each

stimulator is programmed in the most effective way to suit the individual patient.

This classical open surgical procedure requires a long operation time (40–70 minutes), and for the IPG abdominal position, some patients complain of displacement or pain at the IPG site. A new modality of buttock placement of the IPG was proposed in 2001 to shorten operative time and reduce complications.[3]

To simplify the technique of implants a less invasive surgical approach using a small paramedian incision was proposed by Chai and Mamo[4]: fluoroscopy is used to localize the sacral foramen before a small paramedian incision is made. The insulated needle used for PNE test and a 14-gauge angiocath are used to direct the permanent lead into the selected sacral foramen without dissection. The lead is then anchored to the lumbodorsal fascia (superficial to the sacral periosteum) using a movable lead anchor system.

Minimally Invasive Technique

A new tined lead, required for percutaneous implant, is now available. After insertion of the needle in the selected sacral foramen and after adequate testing for nerve responses, a metal stylet (directional guide) is inserted through the needle. The needle is removed and an incision is made for access. A dilator is inserted over the guide and advanced into the sacral foramen.

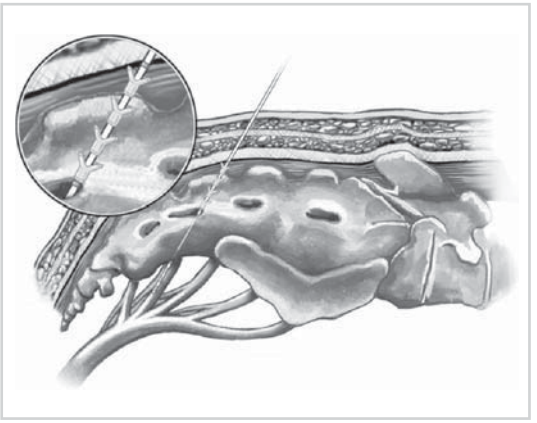


Figure 17.3. Tined lead. Once the position of the chronic tined lead is confirmed under fluoroscopic control, the introducer sheath is removed, thereby deploying the tines and anchoring the lead to the sacral foramina.

Leaving the introducer sheath in place, the tined lead is inserted and advanced under fluoroscopic control (Fig. 17.3). Once the responses of the various electrodes are confirmed, the introducer sheath is removed, thereby deploying the tines and anchoring the lead.[5]

Finally, a temporary and a permanent implant procedure can be combined. Once the permanent lead is implanted, a percutaneous extension is used to connect it to a temporary external stimulator allowing a long period of evaluation (1–2 months) of the effectiveness of sacral neuromodulation. If the response is confirmed, the percutaneous extension is replaced by an implantable extension connected to the IPG. Following the introduction of the minimally invasive technique, the two-stage modality has been recently proposed as an alternative to PNE.

Indications and Patient Evaluation

The lack of knowledge of the mechanism of action makes it difficult to give precise indications for eligible patients, and until now the possibilities of SNM have been evaluated both in patients with colonic slow transit and in patients with difficult evacuation.

It is a shared belief that the indication for neuromodulation is severe constipation not amenable to standard drugs or biofeedback therapy or a failed conventional surgical management. The integrity of the nervous supply must be considered. Patients with complete spinal cord lesion or peripheral nervous lesions such as spina bifida or iatrogenic nerve lesion are not candidates for sacral neuromodulation.[6,7]

The initial assessment includes a complete clinical history and physical examination. Before applying the stimulator, patients undergo a radiopaque marker transit study and anorectal physiologic evaluation. This evaluation includes defecography and rectoanal manovolumetry.[6] Rectoanal manovolumetric evaluation includes the sphincter parameters of maximum resting pressure and maximum squeeze pressure, rectoanal inhibitory reflex threshold, urge to defecate expressed as volume and distention pressure, maximum rectal volume at 1 minute of distention with 40 cm of H_2O, the contraction response to rapid distention with 30 cm of H_2O, and rectal compliance (Δ volume/Δ pressure). Manometric evaluation is performed before

Table 17.1. Straining index

	Time*	Squeeze	Evacuation manual
Occasional	1	5	3
>1/month	2	6	3
>1/week	3	7	6
Daily	4	8	6

Note: Add the number of failed attempts at evacuating per day.
* Time necessary to empty the bowels:

Less than 5 minutes	0
5–10 minutes	1
>10–20 minutes	2
>20–30 minutes	3
>30 minutes	4

stimulation, during the acute stimulation phase, and on the last day of PNE testing. It is repeated again at 1- and 4-month follow-up visits in patients with permanent implants. However, anal manometry is not a specific examination to select eligible patients, but it could help to better understand the mechanisms of sacral stimulation.

To establish baseline function, patients complete a 14-day bowel symptom diary prior to PNE. The same diary is used during the PNE and in the 2 weeks following PNE. The evaluation of the bowel symptom diary is the only parameter that currently allows selecting the patients for definitive implant. The number of evacuations per week, squeeze pressures, number of unsuccessful visits to the toilet, the time necessary to empty the bowel, and the necessity of manual help are the considered parameters. From these parameters we calculate an index of difficulty to evacuation or straining index from ranging 0 to >20 (Table 17.1). Usually a PNE is considered positive if there was a complete cessation of, or reduction of, more than 50% in the difficulty of evacuation combined with a reduction in the Cleveland Clinic–Florida Constipation Score[8] (Table 17.2) of more than 50% together with a rapid return to pre-PNE conditions when stimulation is turned off.

After permanent sacral implant, patients are evaluated for functional disorders with clinical examination and anorectal manometry, and all patients complete a 14-day bowel symptom diary prior to each scheduled follow-up visit at 3 and 6 months and then every 6 months after the implant.

Table 17.2. Cleveland Clinic Florida Constipation scoring system (minimum score 0; maximum score 30)

Item	Score
Frequency of bowel movements	
1–2 times per 1–2 days	0
2 times per week	1
Once per week	2
Less than once per week	3
Less than once per month	4
Difficulty: painful evacuation effort	
Never	0
Rarely	1
Sometimes	2
Usually	3
Always	4
Completeness: feeling incomplete evacuation	
Never	0
Rarely	1
Sometimes	2
Usually	3
Always	4
Pain: abdominal pain	
Never	0
Rarely	1
Sometimes	2
Usually	3
Always	4
Time: minutes in lavatory per attempt	
Less than 5	0
5–10	1
>10–20	2
>20–30	3
>30	4
Assistance: type of assistance	
Without assistance	0
Stimulative laxatives	1
Digital assistance or enema	2
Failure: unsuccessful attempts for evacuation per 24 hours	
Never	0
1–3	1
>3–6	2
>6–9	3
>9	4
History: duration of constipation (year)	
0	0
1–5	1
>5–10	2
>10–20	3
>20	4

Clinical Trial Results

The short-term clinical and physiologic effect of continuous sacral nerve stimulation in 12 patients (mean age 50.2 years) with rectal constipation was first described in 2001. In the 10 patients who completed the minimum stimulation period, the mean number of voluntary bowel movements per week [weekly bowel

Table 17.3. Results of 10 patients who completed the minimum stimulation period after SNS for rectal constipation

			Evacuation in 14 days		Unsuccessful evacuation in 14 days		Difficult evacuation (number)		Time necessary to evacuate		Treatment		Use of urinary catheter	
Gender	Age	Anamnesis	Baseline	PNE	Baseline	PNE	Baseline	PNE	Baseline	PNE	Baseline	PNE	Baseline	PNE
F	31	—	7	7	70	0	7	0	10	5				
F	27	Hemorrhoidectomy	21	14	14	4	21	3	10	3	Suppository			
F	33	Rectopexy	14	14	18	0	10	6	15	5	Suppository			
F	75	Myelitis	28	4	14	0	14	4	20	30			Yes	No
F	63	—	7	4	14	0	3	0	5	5				
F	44	—	2	7	14	0	2	0	20	10	Enema	Enema		
F	44	Myelitis	3	3	28	28	3	3	10	10				
F	61	Hysterectomy, gastric resection of complete spinal lesion	2	2			2	2	10	10	Enema	Enema	Yes	Yes
M	62	Hemorrhoidectomy	4	6	84	28	4		20	10				
F	33	Hysterectomy	7	3	7	0	4	1	5	5	Enema			

PNE, percutaneous nerve stimulation

movements (WBM)] decreased, during sacral nerve stimulation, from 9.5 WBM to 6.4 WBM ($p = .2$), as did the difficulty of evacuation (from 7 to 2.1, $p < .01$). The number of unsuccessful visits to the toilet decreased from 29.2 (range 7–24) to 6.7 (0–28) per week ($p = .01$) and the time necessary to evacuate decreased from 12.5 (5–20) to 9.3 (5–30) minutes per bowel movement ($p = .4$) (Table 17.3).[9]

The improvement in symptoms disappears in all patients after the removal of the electrodes. The only statistically significant changes noted during manometric evaluation were an increase in amplitude of maximum squeeze pressure during sacral nerve stimulation ($p = .009$) and a reduction in the rectal volume for the urge threshold ($p = .004$). Rectal compliance did not significantly change during stimulation.

We have also presented the results of nine patients implanted out of 25 short-term tests (mean age 49.8 years), or patients complaining of outlet constipation with normal[5] or prolonged colon transit time.[4] The stimulatory electrodes were positioned in the S3 foramen in all patients; there were no early or late electrode displacements. An infection at the IPG implant site necessitated the temporary removal of the pulse generator in one patient. One patient complained of pain at implant site when the IPG case was used as an anode (unipolar impulse), and no adverse changes in bladder function were recorded.[10]

The clinical diary was used to evaluate SNM results. In one patient the results did not reproduce the PNE test. The Cleveland Clinic–Florida Incontinence score decreased from 12.3 (range 8–15) before the SNM to 3.7 after 3 months (range 0–14) ($p = .02$) and to 2.9 at the last follow-up (8.5 months (range 3–16) ($p < .01$) (Table 17.4).

The mean number of voluntary bowel movements per week increased from 6.6 (range 2–14) to 11.7 (range 5–14) at 3 months' follow-up ($p = .05$, 44% increase). Considering the subgroup of patients with slow transit time, the mean number of voluntary bowel movements per week increased from 2.25 (range 1–4) to 11 per 2 weeks (range 5–14), a 61% increase. All patients were using laxatives before SNM, but only one continued to use an enema to complete evacuation and all nine recovered a normal desire to evacuate.

The number of unsuccessful attempts per week to evacuate decreased from the preoperative frequency of 22.5 to 2.1 at 3 months'

Table 17.4. Cleveland Clinic Florida constipation score in nine implanted patients

		Constipation Score			
	Age	Baseline	3 months	6 months	12 months
Mean	50.7	12.3	3.7	4.5	1.7
Median	53	12.0	3.0	3.5	0.0
Std. dev.	16.7	2.1	5.0	5.1	2.9
Min.	30	8	0	0	0
Max.	73	15	14	14	5
Patients	9	9	8	8	3
P			.02	.01	NS

NS, nonsignificant.

follow-up (p = .05, 90% reduction), as did the difficulty to empty the rectum, which decreased from 27.2 episodes per week before sacral neuromodulation to 0.6 at 3 months' follow-up (p = .02, 98% reduction). The time necessary to evacuate decreased from 21.7 to 6.3 minutes (p = .1, 71% reduction) per bowel movement at 3 months' follow-up (Table 17.4).

In two patients, the sacral neuromodulation device was temporary deactivated, in one patient because of a desire to become pregnant and in the other patient because of an infection at the IPG site. During the 2 months when the stimulation system was deactivated the former patient (patient 1) reported difficulty in evacuation of gas and solid feces along with the need for an enema to commence defecation. Subsequent to reactivation of the IPG, spontaneous evacuation for gas and feces restarted and spontaneous rectal stimulation reappeared. In the latter (patient 5), with a solitary rectal ulcer syndrome, the sacral stimulation led to a dramatic normalization of evacuations and to disappearance of the endoscopic features of solitary ulcer. With the removal of the IPG, clinical and endoscopic signs of the rectal ulcer syndrome reappeared within 3 days. Following the IPG reimplant 2 months later, a rapid clinical and endoscopic normalization was again observed. Anal pressure showed no statistically significant modification. The volume requested for the first sensation to evacuate along with the urge to evacuate were both lower than they were before SNM.

The short-term effects of sacral nerve stimulation in eight patients (median age 47 years) with slow-transit constipation were presented by Malouf et al[11] in 2001. Two patients had cessation or marked diminution of symptoms, including normalization of bowel frequency. Colonic transit did not return to normal in any patient. Rectal sensory threshold to distention was decreased during stimulation. The conclusions were that percutaneous temporary sacral nerve stimulation symptomatically improved a minority of patients with resistant idiopathic slow-transit constipation; sensory function was altered by stimulation.

In 2002, the same group published the results of temporary and then permanent stimulation in four women with idiopathic constipation, resistant to maximal therapy, with symptoms for 8 to 32 years.[12] A marked improvement was reported in all patients with temporary, and in three patients with permanent stimulation. With a median follow-up of 8 (range 1–11) months, bowel frequency increased from one to six to six to 28 evacuations per 3 weeks. Improvement occurred, at longest-follow-up, in the median (range) evacuation score (4 versus 1), time with abdominal pain (98% versus 12%), time with bloating (100% versus 12%), Cleveland Clinic Florida Constipation Score (21 versus 9), analogue score (22 versus 80), and quality of life. Maximum anal resting and squeeze pressures increased. Rectal sensation was altered. Transit time normalized in one patient. The authors concluded that permanent sacral nerve stimulation can be used to treat patients with resistant idiopathic constipation.

Medium-term results of a substantial series of 17 patients with a permanent implant, 10 for rectal constipation and seven for slow-transit constipation, and a mean follow-up of 15.6 (range 8–37) months, confirmed the results of the temporary stimulation in 13 patients (eight and five, respectively). The Cleveland Clinic Florida Constipation Score improved from 12.7 to 1.5 in the rectal constipation subgroup (p = .04), and from 15.2 to 6.3 (p = .001) in the slow-transit constipation subgroup. Improvement occurred in median evacuation time (16 versus 5 minutes). The mean number of bowel movements per week increased from 4.3 to 27 in patients with rectal constipation and from one to eight in patients with slow-transit constipation, and the number of unsuccessful attempts to evacuate decreased from 22.5 to 0.1 at 12 months' follow-up (p = .03). Improvement in colon motility was observed in three patients with slow-transit constipation. Again, the more meaningful manometric change was a reduction in the volume threshold for rectal sensations rather than any influence on the sphincter function. Furthermore, although the experience in severe constipation is still limited, similar results have been reported by urologists, and sacral nerve stimulation seems to be effective for both fecal incontinence and rectal constipation.

Mechanism of Action

Debate as to the mechanism of action for sacral stimulation is still ongoing. Action on the striated sphincters and a facilitation of voluntary contraction have been suggested and attributed to direct alpha motor fiber stimulation.[13] Several studies have tried to show an improvement of the

external anal sphincter during neuromodulation, but the results are controversial. However, according to observations by Fowler et al,[14] studies on the latencies of the pelvic floor contraction during peripheral nerve evaluation show that the muscle response is reflexly mediated with a latency ranging from 41 to 57 msec instead of the 4 to 5 msec observed with sacral root magnetic depolarization.[15,16] As concerning where these reflexes originate, the observation that it is possible to record a sphincteric contraction in patients with a spinal cord injury (SCI) suggests a segmental level within the sacral spinal cord without the necessity of preserved spinobulbar spinal loops. The finding that neuromodulation is working in nonneurogenic patients but is less successful in complete SCI patients could give evidence that preserved spinobulbar spinal loops,[16] not necessary for the reflexive pelvic floor and anal sphincter contractions, contribute to the positive effects of neuromodulation. These observations refute the importance of the external sphincter contraction as a mechanism of action during sacral neuromodulation and support our actual and previous findings that showed no significant impact of sacral stimulation on the external sphincter contraction.[16–18]

The trend toward an improvement in rectal sensitivity with a reduction in the threshold of perception of rectal distention and urge sensation is of particular interest. These observations imply special attention to afferent fiber stimulation and medulla synaptic integrity, both for the sensitive and sphincteric motility during chronic sacral neuromodulation, and confirm the canine animal experiments of Tanagho and Schmidt,[19] in which stimulation of the intact dorsal component (afferent) of S2 produced responses in the bladder and sphincter that were similar to those induced by stimulation of the intact nerve.

Three types of fibers are generally recognized in the sensory subclass of nerve fibers: Aβ fibers, the largest fibers, mediate the sensations of touch and mild pressure, as well as the sensation of position of joints and vibration. Aδ fibers, smaller than Aβ fibers, mediate the sensation of cold and the first components of the sensation of pain. C fibers, the slowest and smallest, mediate the sensation of warmth and the main component of the sensation of pain. In addition, C fibers subserve most of the autonomic peripheral functions.

Some experimental animal studies seem to confirm the hypothesis that neuromodulation has an effect on the central nervous system via afferent sensory fibres. A double-blind randomized study with spinally transected rats has evaluated the role of neuromodulation on C-afferent fibers that form the afferent arc of the pathologic reflex responsible of bladder hyperreflexia after spinal cord trauma. T10 spinal transection developed bladder hyperreflexia after 3 weeks, associated with an increase in the neuropeptide content (substance P, neurokinin A, and calcitonin gene-related peptide, CGRP) in L6 dorsal root ganglions. The electric stimulation of S1 reduces the increase of neuropeptide in L6 and abolished bladder hyperreflexia, suggesting that the blockade of C-afferent fibers is one of the mechanisms of action of sacral neuromodulation.[20]

An interesting contribution to the comprehension of the mechanism of action of the SNM comes from Hamdy et al,[21] who showed that the anal sphincter contraction induced by magnetic cortical stimulation was facilitated when this stimulation was preceded by repetitive stimulation of the pudendal or sacral nerve, suggesting that repetitive stimulation of a sacral nerve could cause sensorimotor interactions with better control of the sphincter function.

Finally, Hirabayashi et al[22] compared the colorectal motility during spontaneous defecation and during sacral nerve stimulation under general anesthesia in adult mongrel dogs. Sacral nerve stimulation elicited a contractile movement propagated from the distal colon to the rectum, a relaxation response in the rectum, and an internal anal sphincter relaxation response similar to those that occurred during spontaneous defecation, suggesting that sacral nerve stimulation may control the lower colonic and rectal movements.

The Future

Sacral nerve stimulation is still under evaluation. In particular, we need to better understand the modulating effect of sacral nerve afferent pathways stimulation on the rectosphincteric and colonic complex. Attention must be directed toward colonic motility and to the functional mechanisms as the cause of constipation to characterize a subgroup of constipated patients suitable for this therapy. In some patients we have observed a change of left colon motility rhythm, and this finding could suggest a possible extension of the indications to patients with

constipation from colonic inertia. Additionally we have observed a dramatic improvement of the clinical, proctoscopic, and histologic picture in a patient with solitary rectal ulcer syndrome, suggesting a possible neuroplastic effect of SNS on the rectal mucosa. These few successes are only at the beginning of the exploration of the possible effects of SNS on colonic function. In light of the very promising preliminary results, the future of sacral nerve stimulation is indeed very optimistic.

References

1. Bosch JLHR. Emerging indications for sacral nerve stimulation. In: Jonas U, Grunewald V, eds. New Perspectives in Sacral Nerve Stimulation. Martin Dunitz, London 2002:223–224.
2. Matzel KE, Stadelmaier U, Hohenfellner M, Gall FP. Electrical stimulation of sacral spinal nerves for treatment of faecal incontinence. Lancet 1995;346: 1124–1127.
3. Scheepens WA, Weil EH, van Koeveringe GA, et al. Buttock placement of the implantable pulse generator: a new implantation technique for sacral neuromodulation—a multicenter study. Eur Urol 2001;40(4):434–438.
4. Chai TC, Mamo GJ. Modified techniques of S3 foramen localization and lead implantation in S3 neuromodulation. Urology 2001;58(5):786–790.
5. Spinelli M, Giardiello G, Arduini A, van den Hombergh U. New percutaneous technique of sacral nerve stimulation has high initial success rate: preliminary results. Eur Urol 2003;43(1):70–74.
6. Ganio E, Luc AR, Clerico G, Trompetto M. Sacral nerve stimulation for treatment of fecal incontinence: a novel approach for intractable fecal incontinence. Dis Colon Rectum 2001;44(5):619–629.
7. Ganio E, Ratto C, Masin A, et al. Neuromodulation for fecal incontinence: outcome in 16 patients with definitive implant. The initial Italian Sacral Neurostimulation Group (GINS) experience. Dis Colon Rectum 2001;44(7):965–970.
8. Agachan F, Chen T, Pfeifer J, Reissman P, Wexner SD. A constipation scoring system to simplify evaluation and management of constipated patients. Dis Colon Rectum 1996;39(6):681–685.
9. Ganio E, Masin A, Ratto C, et al. Short-term sacral nerve stimulation for functional anorectal and urinary disturbances: results in 40 patients: evaluation of a new option for anorectal functional disorders. Dis Colon Rectum 2001;44(9):1261–1267.
10. Ganio E, Masin A, Ratto C, Basile M, Realis Luc A, Lise G, Doglietto GB, Gidaro S, Giardiello G, De Seta F. Sacral nerve modulation for chronic outlet constipation. American Society of Colon and Rectal Surgeons Meeting, San Diego, 2001.
11. Malouf AJ, Wiesel PH, Nicholls T, Nicholls RJ, Kamm MA. Short-term effects of sacral nerve stimulation for idiopathic slow transit constipation. World J Surg 2002;26(2):166–170.
12. Kenefick NJ, Nicholls RJ, Cohen RG, Kamm MA. Permanent sacral nerve stimulation for treatment of idiopathic constipation. Br J Surg 2002;89(7):882–888.
13. Matzel KE. Sacral neurostimulation: principles and its role in the treatment of fecal incontinence. Proceedings of the 6th Biennial International Meeting of Coloproctology, 2000:101–103.
14. Fowler CJ, Swinn MJ, Goodwin RJ, Oliver S, Craggs M. Studies of the latency of pelvic floor contraction during peripheral nerve evaluation show the muscle response is reflexy mediated. J Urol 2000;163(3): 881–883.
15. Vaizey CJ, Kamm MA, Turner IC, Nicholls RJ, Woloszko J. Effects of short-term sacral nerve stimulation on anal and rectal function in patients with anal incontinence. Gut 1999;44:407–412.
16. Schurch B, Reilly I, Reitz A, Curt A. Electrophysiological recordings during the peripheral nerve evaluation (PNE) test in complete spinal cord injury patients. World J Urol 2003;20(6):319–322.
17. Ganio E, Ratto C, Masin A, et al. Neuromodulation for fecal incontinence: outcome in 16 patients with definitive implant. The initial Italian Sacral Neurostimulation Group (GINS) experience. Dis Colon Rectum 2001;44:965–970.
18. Ganio E, Realis Luc A, Ratto C, et al. Sacral nerve modulation for fecal incontinence. Functional results and assessment of the quality of life. Acts from 13th Annual Colorectal Disease, Fort Lauderdale, FL, Febraury 14–16, 2002.
19. Tanagho EA, Schmidt RA. Electrical stimulation in the clinical management of the neurogenic bladder. J Urol 1988;140:1331–1339.
20. Chan CLH, Facer P, Davis JB, et al. Sensory fibres expressing capsaicin receptor TRPV1 in patients with rectal hypersensitivity and faecal urgency. Lancet 2003;361:385–391.
21. Hamdy S, Enck P, Aziz Q, et al. Spinal and pudendal nerve modulation of human corticoanal motor pathways. Am J Physiol 1998;274:G419–G423.
22. Hirabayashi T, Matsufuji H, Yokoyama J, et al. Colorectal motility induction by sacral nerve electrostimulation in a canine model: implications for colonic pacing. Dis Colon Rectum 2003;46(6):809–817.

18

Surgical Treatment of Rectocele: Colorectal Approaches

Guillermo O. Rosato and Carlos M. Lumi

The rectum and the vagina have a common embryologic origin with close anatomic affinity. They originate from the cloaca that is divided by the urorectal septum into a ventral (urogenital) and a dorsal (rectal) portion. From an anatomic point of view, a layer of strong connective-type tissue has been identified between the rectum and vagina known as the rectovaginal septum or the rectovaginal fascia. This layer, located immediately beneath the vaginal mucosa, could be considered part of the vaginal wall and acts as a supportive structure for the perineal body that prevents the rectum from bulging into the vagina. Rectoceles represent a defect in this layer that allows the rectum to bulge into the vagina anteriorly due to the higher pressure on the rectal side.

The true cause of anterior rectocele is unclear. Childbirth is a known risk factor due to the stretching and distention of the pelvic floor and tearing of the rectovaginal fascia. Prolonged straining during defecation in chronic constipation or in nonrelaxing puborectalis syndrome may also lead to the formation of a rectocele. Both of these events promote widening of the genital hiatus, perineal muscle laxity, and pelvic organ descent, which may subsequently lead to pudendal neuropathy. Postmenopausal status and hysterectomy are also proven to be predisposing factors of rectocele.

The rectovaginal septum tends to debilitate with age and parturition.[1–3] Additionally, a debilitated anterior rectal submucosal layer may play a role in rectocele formation, as described by Block[4] and Janssen and van Dijke.[5] However, it is still unknown whether this weakening is the cause of rectocele or the result of a persistent anterior rectal wall stretching into the vagina.

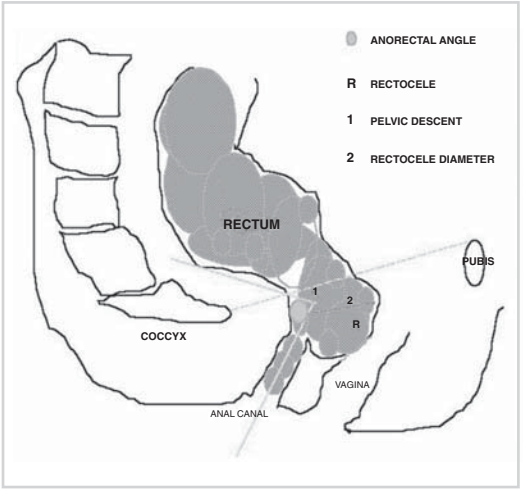
Anterior rectocele is a frequent finding in females, with an incidence ranging from 39% to 72%.[6] Furthermore, rectocele may coexist with other anal or perineal pathologies such as sigmoidocele, enterocele, hysterocele, cystocele, rectal prolapse, hemorrhoids, and anal fissure. Olsen et al[7] noted that 76% of woman with documented pelvic organ prolapse had concomitant rectocele. Moreover, Freimanis et al[8] and Shorvon et al[9] found a 60% and 76% incidence of rectoceles, respectively, in dynamic proctography of asymptomatic females.

Rectoceles may cause mild-to-severe anorectal symptoms and are usually associated with a sensation of incomplete evacuation, the need for prolonged straining, and the need for some form of rectal/vaginal digitation for rectal evacuation. These patients may also experience perineal pressure as well as the sensation of a pouch at the vagina, dyspareunia, or some degree of anal incontinence.

A diagnosis of rectocele is made by taking an adequate history and performing a thorough physical examination. Digital rectal examination is usually performed with the patient in the left lateral position. If any doubt remains, examination can be performed with the patient in the supine position and then asked to bear down in order to further elucidate whether any associated disorders such as a cystocele, descending uterus, enterocele, or sigmoidocele is present. Digital examination also allows the physician to evaluate the height and size of the rectocele and rule out abnormal puborectalis function during the straining effort.

Rectosigmoidoscopy is used to evaluate rectal intussusception and exclude the presence of rectal masses that may mimic these symptoms.

Defecography has allowed visualization of the dynamics of rectal evacuation and has contributed to confirming the presence of a rectocele. Moreover, the functional impairment as well as the anatomic aberration can be appreciated. This is performed by introducing a radiopaque paste (100–200 cc) into a clean rectum by means of a plastic syringe. An additional 20 to 50 cc of liquid radiopaque contrast can be added in order to delineate details with a double-contrast technique.[10–12] Spot x-rays are obtained for the rest (R), squeeze (S), and push (P) phases on which measurements of the anorectal angle (ARA), pelvic descent (PD), and rectocele diameter can be accomplished (Fig. 18.1). The rectocele diameter is defined as the distance between the extended line of the anal canal axis and the tip of the rectocele.[13,14]



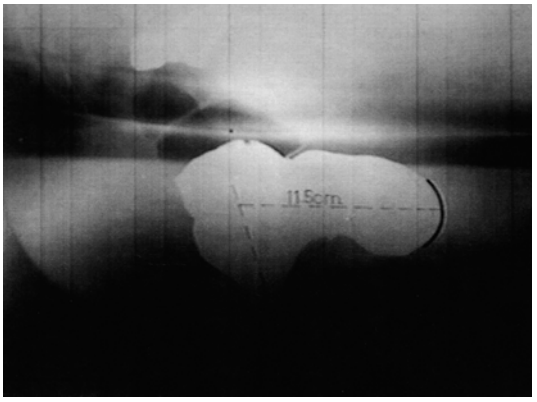


Figure 18.1. Rest (R), squeeze (S), and push (P) phases on which measurements of the anorectal angle (ARA), pelvic descent (PD), and rectocele diameter can be accomplished.

Rectoceles may present at one or more of three levels and are known as high, middle, and low rectoceles (Fig. 18.2). High rectoceles are usually due to a stretching or disruption of the upper third of the rectovaginal septum, cardinal, or uterosacral ligaments. This type of rectocele is frequently associated with enteroceles of varying degrees that may need simultaneous surgical correction. The middle level rectocele is by far the most frequent and is caused by the loss of pelvic floor support and further influenced by parturition. Middle rectoceles are located just over the anal sphincter complex, extending upward 3 to 7 cm, whereas low rectoceles are usually the consequence of perineal body defects due to an inadequately repaired major obstetrical injury or overdistention during childbirth.[15]

Johansson et al[16] and Mellgren et al[17] pointed out the possibility that some rectoceles may be the result of a paradoxical sphincter response (paradoxical puborectalis contraction) leading to an outlet obstruction and subsequently disappointing surgical results. To rule out this possibility, concentric needle electromyography should be performed to evaluate the recruitment of motor unit potentials (MUPs)[18] during an evacuatory effort; generally MUP recruitment should be equal to or less than at rest. If MUP recruitment is increased compared to rest, a paradoxical muscle response can be suspected and preoperative biofeedback therapy is advisable. Mimura et al[19] and Johansson et al[16] have suggested that biofeedback should be taken into account to ensure better surgical results. Response to medical therapy leads to symptomatic relief in only a minor percentage of patients with paradoxical puborectalis response and rectocele.

It has been reported that patients with rectocele may present with anal incontinence as the predominant symptom.[20] This association may be due to the coexistence of other pelvic floor muscle deficiencies and pudendal neuropathy. Thus, the complaint of concomitant incontinence justifies a more in-depth physiologic evaluation including manometry, neurophysiology of the pelvic floor, and endoanal ultrasonography, besides defecography, in order to assess the anal sphincter functionality and anatomic conformation. If any anatomic defect is confirmed, it may be correctable at the time of the rectocele repair.

Rectoceles may also be classified according to size—small <2 cm, medium 2 to 4 cm, or large

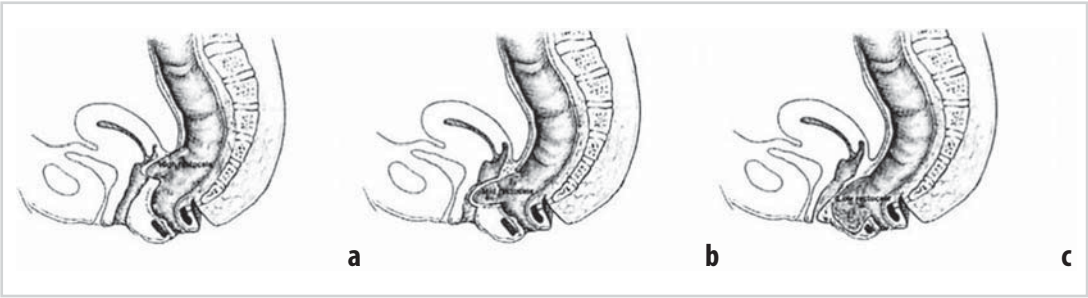


Figure 18.2. Rectoceles are known as high (a), middle (b), and low (c).

Table 18.1. Criteria of patient selection for surgery

1. Rectocele >4 cm in diameter as measured by defecography
2. Non- or partial emptying of rectocele during push in defecography
3. Rectal or vaginal symptoms for longer than 12 months
4. Persistence of symptoms for at least 4 weeks despite increased fiber intake of up to 35 g/day
5. Need for rectal/vaginal digitation to facilitate rectal evacuation

>4 cm—or degree—type I, protruding into the upper vagina; type II, protruding up into the introitus; and type III, protruding beyond the introitus. Once the diagnosis has been confirmed, a high-fiber diet (25–35 g/day) and ingestion of 2 to 3 L of nonalcoholic fluids per 24 hours is recommended as initial conservative treatment. If symptom control does not occur after 4 weeks, despite these initial conservative measures, surgery is suggested (Table 18.1).

Surgical Approaches

There are a variety of surgical techniques and approaches described for the management of a symptomatic rectocele including transvaginal, transanal, transperineal, and combination of these with or without the use of a mesh. As well, some surgeons prefer transanal approaches with linear or circular stapling devices. All these procedures correct herniated defects and restore normal anatomy.

To date, there are insufficient data and postoperative randomized trials from which any meaningful comparative conclusions can be drawn. Gynecologists usually prefer the transvaginal approach, while colorectal surgeons adhere either to transanal, transperineal, or a combination of transvaginal or transanal and transperineal approaches.

Surgical Technique

The transvaginal approach proceeds to open the posterior vaginal wall, identifying the rectovaginal septum and separating the anterior rectal wall by lateral blunt dissection to expose the levator muscle. The levator muscle is then plicated in the midline by several sutures. Care is taken to avoid perforating the rectum while placing the sutures. To exclude the rectal wall from the suture line, a finger can be introduced into the rectum. The redundant vaginal wall is excised and closed with a running absorbable suture material. In some instances, simultaneous hemorrhoidectomy is undertaken.[16,21,22]

The most frequent postoperative complications associated with the transvaginal approach include pain and sexual dysfunction.[21–23] This surgical option should be considered when a concomitant vaginal hysterectomy is planned or in the presence of an anovaginal fistula.

Comparative results have been summarized in Table 18.2. In Mark's[24] experience, the vaginal approach was insufficient to treat symptomatic rectoceles, and he was the first surgeon to note the importance of the rectal side of rectoceles and the need to correct this deficiency. During transanal repair, simple techniques such as the "obliterative suture" described by Block,[4] stapling procedures described by Bresler et al,[25] such as linear stapling, or the STARR (stapled transanal rectal resection) procedure using a circular stapler, can be utilized.[26] Other transanal repair alternatives described by Sarles et al[28,29]

Table 18.2. Results of various series

Author	n	Technique	Results	%	Complications (%)
Sullivan et al (1968)[30]	151	Transrectal	Excellent/good	79.5	12.5
Khubchandani et al (1983)[31]	59	Transrectal	Excellent/good	79.6	35.5
Sehapayak (1985)[33]	355	Transrectal	Excellent/good	84.5	5.6
Arnold et al (1990)[23]	35	Transrectal	Excellent/good	80	34.2
Sarles et al (1991)[29]	39	Transrectal	Excellent/good	95	n/s
Janssen et al (1994)[5]	76	Transrectal	Excellent/good	92 (87)*	2.6
Khubchandani (1997)[32]	123	Transrectal	Excellent/good	82	3
Boccasanta (2001)[27]	90	Transrectal	Excellent/good	90	30
Redding (1964)[42]	20	Transvaginal	Excellent/good	100	5
Pitchford (1967)[21]	44	Transvaginal	Excellent/good	n/s	0
Arnold et al (1990)[23]	29	Transvaginal	Excellent/good	80	31
Mellgren et al (1995)[22]	25	Transvaginal	Excellent/good	88	20
Watson (1996) (w/Marlex)[39]	9	Transperineal	Excellent/good	80	n/s
Trompetto (1998)[40]	102	Transperineal	Excellent/good	85	15
Misici (1998) (w/Marlex)[35]	44	Transperineal	Excellent/good	n/s	n/s
Rosato (2004)[43]	52	Transperineal	Excellent/good	96.2	3.8

* After 1 year follow-up; n/s, not stated.

and Sullivan et al[30] and variations of this technique have been applied by Khubchandani et al[31,32] and Sehapayak.[33] All of these techniques tend to plicate the rectal muscle layer on a vertical or transverse fashion, after opening the rectal mucosa, also known as a Delorme's type plication. The redundant rectal mucosa is resected to prevent anterior mucosal prolapse or tenesmus.[28–33]

Some studies have concluded that the transanal approach would be contraindicated in patients who present with combined fecal incontinence and rectocele due to its deleterious effects on internal sphincter function and resting anal pressures.[34] Complications associated with transanal techniques include bleeding, rectovaginal fistula, fecal impaction, delayed healing due to mucosa retraction, and dyspareunia. Stapled procedures have been followed by stenosis after linear stapling and vaginal tear after the STARR procedure.[25,26]

The transperineal approach to rectocele repair is another surgical option (Figures 18.3–18.9).[35–38] Some surgeons have utilized prosthetic mesh between the rectum and the vagina in order to reinforce the rectovaginal septum,[35,39,40] while others[41] resect the redundant vaginal wall and reinforce the plasty by plicating the puborectalis muscle (Figs. 18.3 to 18.9).

Preoperative mechanical bowel preparation and prophylactic antibiotics are given to all patients. Patients are placed in the prone jackknife position with the buttocks taped apart. The

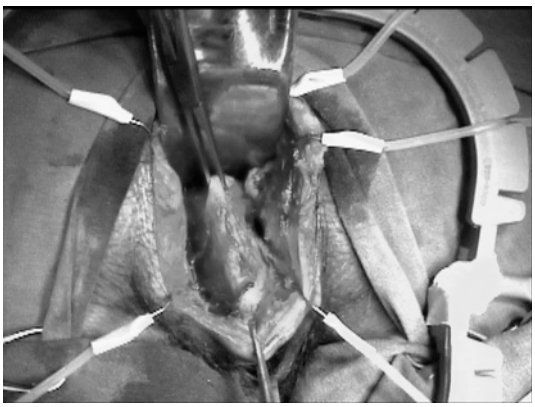


Figure 18.3. Vaginal wall exposed.

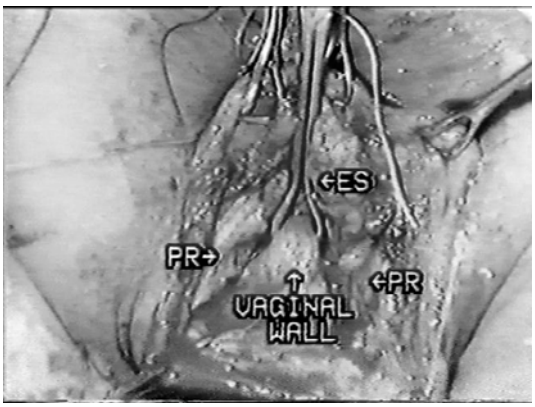


Figure 18.4. External sphincter (ES), puborectalis (PR), and vaginal wall.

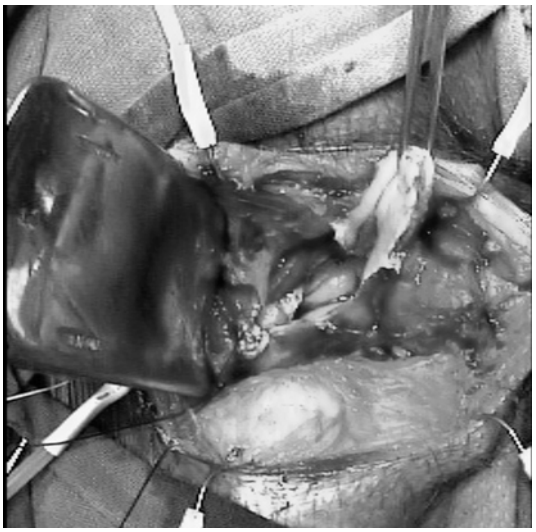


Figure 18.5. Vaginal wall resected.

size and location of the rectovaginal defect is confirmed by manual palpation. An incision at the perineal area (elliptical or U-shape) is created. Electrocautery and blunt dissection allows entry into the rectovaginal space. A high dissection is carried out to the level of the vaginal cupola. If the vaginal wall will be resected, a trapezoid strip of posterior vaginal wall is sectioned. Reconstruction is carried out by plicating the levator muscle using two to three

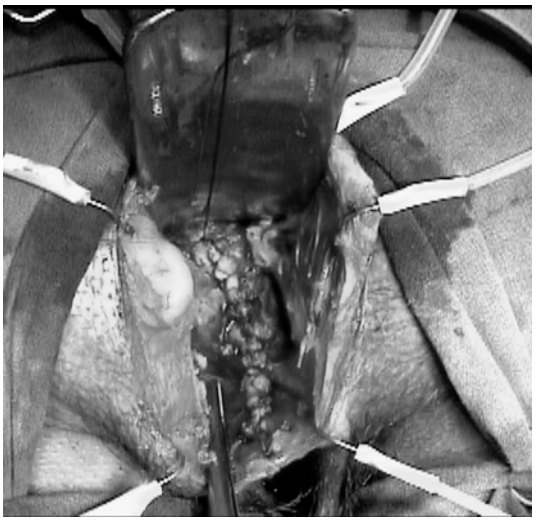


Figure 18.6. Vaginal wall sutured.

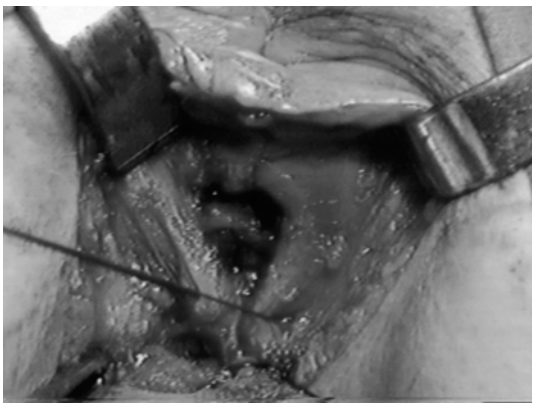


Figure 18.7. Puborectalis plication.

running 3.0 polyglactin sutures. Thorough hemostasis is undertaken prior to completely closing the skin, with no drains left in place. Concomitant sphincter repair can be accomplished as well other procedures such as hemorrhoidectomy, rectovaginal fistulas, or fissures.

Complications associated with the transperineal approach include rectovaginal fistula, dyspareunia, and anterior mucosal prolapse. The

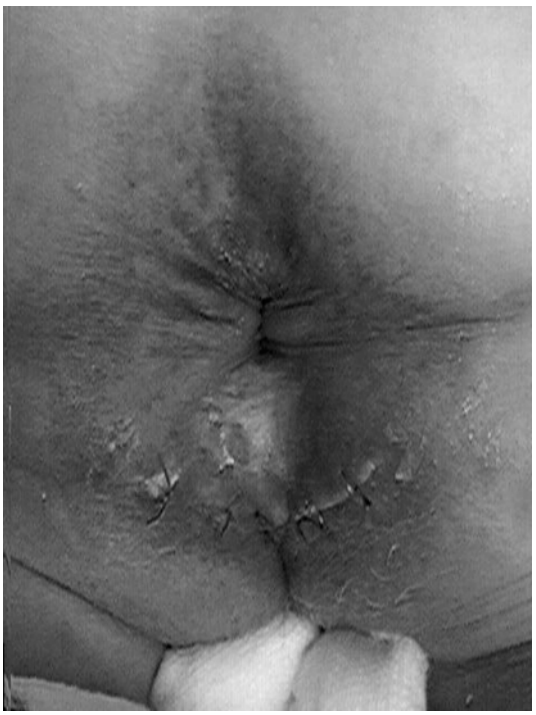


Figure 18.8. Skin incision.

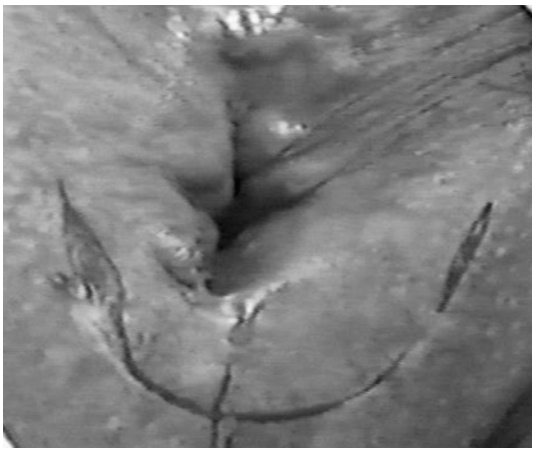


Figure 18.9. Wound closure, 1 week postoperatively.

mucosal prolapse, if present, can be successfully treated with rubber banding.

References

1. Khun RJ, Hollyyok VE. Observations on the anatomy of the rectovaginal pouch and septum. Obstet Gynecol 1982;59(4):445–447.
2. Czerniuk E, Rapisarda JA. Anatomia proctologica. Buenos Aires: Eudeba, 1985:17–21.
3. Segal JL, Karram MM. Evaluation and management of rectoceles. Curr Opin Urol 2002;12:345–352.
4. Block IR. Transrectal repair of rectocele using obliterative suture. Dis Colon Rectum 1986;29:707–711.
5. Janssen LWM, van Dijke CF. Selection criteria for anterior rectal wall repair in symptomatic rectocele and anterior rectal wall prolapse. Dis Colon Rectum 1994;37:100–1107.
6. Siproudhis L, Dautreme S, Ropert A, et al. Dyschezia and rectocele—a marriage of convenience? Physiologic evaluation of the rectocele in a group of 52 women complaining of difficulty in evacuation. Dis Colon Rectum 1993;36:1030–1036.
7. Olsen AL, Smith VJ, Bergstrom JO et al. Epidemiology of surgically managed pelvic organ prolapse and urinary incontinence. Clin Obstet Gynecol 1993;36: 976–983.
8. Freimanis MG, Wald A, Caruana B, et al. Evacuation proctography in normal volunteers. Invest Radiol 1991;26:581–585.
9. Shorvon PJ, McHugh S, Diamant NE, et al. Defecography in normal volunteeres: results and implications. Gut 1989;30:1737–1749.
10. Rosato GO. Techniques of physiology assessment. In: Colorectal Disease in 1992. Cleveland Clinic Foundation, Cleveland Clinic–Florida, 1992:283–297.
11. Bartram CI, Mahieu PHG. Evacuation proctography and anal endosonography. In: Henry MM, Swash M, eds. Coloproctology and the Pelvic Floor, 2nd ed. New York: Butterworth-Heinemann, 1992;149–156.
12. Jorge JMN, Wexner SD, Marchetti F, Rosato GO, Sullivan M, Jagelman DG. How reliable are currently available methods of measuring the anorectal angle? Dis Colon Rectum 1992;35:332–338.
13. Yoshioka K, Matsui Y, Yamada O, et al. Physiologic and anatomic assessment of patients with rectocele. Dis Colon Rectum 1991;34:704–708.
14. Lu RH. Rectocele: analysis of 239 cases. Second Military Medical College, Shangai. Ching Hua Wai Ko Tsa Chih 1990;28(2):102–104,127.
15. Lucas JD, Landy LB. The gynecologist's approach to anterior rectoceles. Semin Colon Rectal Surg 1992;3(2): 138–143.
16. Johansson C, Nilsson BY, Holmström B, Dolk A, Mellgren A. Association between rectocele and paradoxical sphincter response. Dis Colon Rectum 1992;35:503–509.
17. Mellgren A, Lopez A, Schultz I, Anzen B. Rectocele is associated with paradoxical anal sphincter reaction. Int J Colorectal Dis 1998;13(1):13–16.
18. Rosato GO, Lumi CM, Miguel AM. Anal sphincter electromyography and pudendal nerve terminal motor latency assessment. Semin Colon Rectal Surg 1992;3(2):68–74.
19. Mimura TE, Roy AJ, Storie JB, Kamm MA. Treatment of impaired defecation associated with rectocele by behavioural retraining (biofeedback). Dis Colon Rectum 2000;43:1267–1272.
20. Ayabaca SM, Zbar AP, Pescatori M. Anal continence after rectocele repair. Dis Colon Rectum 2002;45:63–69.
21. Pitchford CA. Rectocele: a cause of anorectal pathologic changes in women. Dis Colon Rectum 1967;10:464–466.
22. Mellgren A, Anzen B, Nilsson B-Y, et al. Results of rectocele repair: a prospective study. Dis Colon Rectum 1995;38:7–13.
23. Arnold MW, Stewart WRC. Aguilar PS. Rectocele repair: four years' experience. Dis Colon Rectum 1990;33:684–687.
24. Marks M. The rectal side of rectocele. Dis Colon Rectum 1967;10:387–388.
25. Bresler L, Rauch P, Denis B, Grillot M, et al. Traitement des rectocèles sus—lévatoriennes par voie endorectale. J Chir 1993;130(6–7):304–308.
26. Altomare DF, Rinaldi M, Veglia A, et al. Combined perineal and endorectal repair of rectocele by circular stapler. A novel surgical technique. Dis Colon Rectum 2002;45:1549–1552.
27. Boccasanta P, Venturi M, Calabro G, et al. Which surgical approach for rectocele? A multicentric report from Italian Coloproctologists. Tech Coloproctol 2001;5(3): 149–156.
28. Sarles JC, Arnaud A, Selezneff I, Olivier S. Endorectal repair of rectocele. Int J Colorectal Dis 1989;4(3): 167–171.
29. Sarles JC, Ninou S, Arnaud A. Rectoceles. Diagnosis and treatment. Chirurgie 1991;8:618–623.
30. Sullivan ES, Leaverton GH, Hardwick CE. Transrectal perineal repair: an adjunct to improved function after anorectal surgery. Dis Colon Rectum 1968;11:106–114.
31. Khubchandani IT, Sheets JA, Stasik JJ, Hakki AR. Endorectal repair of rectocele. Dis Colon Rectum 1983;26:792–796.
32. Khubchandani IT, Clancy JP III, Rosen I, et al. Endorectal repair of rectocele revisited. Br J Surg 1997;84:89–91.

33. Sehapayak S. Transrectal repair of rectocele: anextended armamentarium of colorectal surgeon. A report of 355 cases. Dis Colon Rectum 1985;28:422–433.
34. Ho YH, Ang M, Nyam D, Tan M, Seow-Choen F. Transanal approach to rectocele repair may compromise anal sphincter pressures. Dis Colon Rectum 1998,41:354–358.
35. Misici R, Primo Feitosa JN. Transperineal treatment of recurrent anterior rectocele using marlex mesh. Annals of the 5th Biennial Course International Meeting of Coloproctology, Ivrea, Italy, March 1998.
36. Rosato GO, Lumi CM, Gualdrini U. Perineal approach to rectocele repair: a new technique for an old problem. International Society of University Colon and Rectal Surgeons, XVth Biennial Congress, Abstract Book, 1994.
37. Rosato GO. Rectocele repair. International Symposium of Colorectal Disease, Fort Lauderdale, Florida, 1996.
38. Rosato GO. Anterior rectocele: perineal approach to rectocele repair. Osp Ital Chir 2001;7:570–572.
39. Watson SJ, Loder PB, Halligan S, Bartram CI, Kamm MA, Phillips RK. Transperineal repair of symptomatic rectocele with Marlex mesh: a clinical, physiological and radiologic assessment of treatment. J Am Coll Surg 1996;183:257–261.
40. Trompetto M. Rectocele repair: when and how? International Symposium of Colorectal Disease, Fort Lauderdale, Florida, 1998.
41. Rosato GO. Rectocele and perineal hernias. In: Wexner SD, Beck DE, eds. Fundamentals of Anorectal Surgery, 2nd ed. London: WB Saunders, 1998:87–197.
42. Redding MD. The relaxed perineum and anorectal disease. Dis Colon Rectum 1965;8:279.
43. Rosato GO. Patologia del Piso Pelviano—Constipacion cronica cirugia en el sindrome de obstruccion del tracto de salida (SOTS)—VI Curso Internacional de Coloproctologia 2005 "Dr Alfonso Marcelo Fraise". www.coloproctologia.com.ar—2005.

19

Surgical Treatment of Rectocele: Gynecologic Approaches

G. Willy Davila

Herniation of the rectum or posterior vaginal wall into the vaginal canal, resulting in a vaginal bulge, is commonly termed a rectocele. Women may complain of perineal and vaginal pressure, obstructive defecation, constipation, and the need to splint or digitally reduce the vagina in order to effectuate a bowel movement. These anatomic defects arise from a superior, inferior, or lateral tear or central stretching of the rectovaginal fascia. If the weakness is present below the levator musculature, it is termed a rectocoele. If the weakness occurs above the levator muscles, it is more likely an enterocele. Very commonly, both anatomic defects coexist. Although anatomic cure rates with surgery are high, there are conflicting reports with regard to functional outcome, postoperative defecatory symptoms, and sexual dysfunction including dyspareunia.

Marked differences exist between the management approaches followed by urogynecologists and colorectal surgeons. Rectocele repair, or posterior colporrhaphy, represents one of the most commonly performed gynecologic pelvic reconstructive procedures. In a recent survey, 100% of gynecologists surveyed managed rectoceles, whereas 68% of colorectal surgeons manage them.[1–3] There are a large number of gynecologic indications for rectocele repair (Table 19.1).

The restoration of normal anatomy to the posterior vaginal wall is referred to as an enterocele repair if it involves the upper posterior vaginal wall, and as a posterior repair or colporrhaphy if the lower wall is involved. Although sometimes used interchangeably with the term *rectocele repair*, these two operations may have varying treatment goals. A rectocele repair focuses on correcting a hernia of the anterior rectal wall into the vaginal canal secondary to a weakened or torn rectovaginal septum, whereas a posterior colporrhaphy corrects a rectal bulge and normalizes vaginal caliber by restoring structural integrity to the posterior vaginal wall and introitus.

Evaluation

Unlike surgery to treat urinary stress or fecal incontinence, for which a patient usually undergoes careful preoperative evaluation, the gynecologic preoperative evaluation of a symptomatic posterior vaginal bulge typically includes only a history and physical examination. Gynecologists have not adopted the performance of defecography or other evaluation techniques for the evaluation of this anatomic defect. Although 80% of colorectal surgeons use defecography, only 6% of gynecologists use it.[1–3] In addition, differentiation between enterocele and rectocele components of posterior vaginal wall prolapse is typically performed on a clinical and intraoperative basis, rather than radiographically. It is unclear at this time whether surgical therapy outcomes are negatively impacted by the lack of preoperative evaluation beyond a history and physical exam. Most gynecologists consider repair of the rectocele to be commonly necessary during routine pelvic reconstructive procedures, and it is associated with low morbidity for their patients.

Table 19.1. Gynecologic indications for rectocele repair

Obstructive defecation symptoms
Lower pelvic pressure and heaviness
Prolapse of posterior vaginal wall
Pelvic relaxation with enlarged vaginal hiatus

Physical Examination

The typical physical finding in a woman with a symptomatic enterocele or rectocele is a lower posterior vaginal wall bulge. An enterocele is identified as a bulge of the superior posterior vaginal wall between the vaginal apex and the levator plate. It may extend superiorly to weaken the support of the vaginal apex, leading to vaginal vault prolapse. In an isolated rectocele, the bulge extends from the edge of the levator plate to the perineal body (Fig. 19.1). As a rectocele enlarges, the perineal body may further distend and loosen its bulk, leading to an evident perineocele and an enlarged vaginal hiatus. Enteroceles and rectoceles frequently coexist. The physical examination should include not only a vaginal exam but also a rectal exam, as a perineocele may not be evident on vaginal examination. Perioneoceles can be identified primarily upon digital rectal examination, where an absence of fibromuscular tissue in the perineal body is found along with a low anterior rectocele.

Classification Schemes

The traditional Baden-Walker system uses the midvaginal plane as a landmark, and anatomic defects are graded from 0 to 4. Grade 0 is normal while a grade 4 extends beyond the hymen. In the recently adopted Pelvic Organ Prolapse Quantification (POP-Q) system, two points along the posterior vaginal wall are identified (Ap: 3 cm proximal to the hymen; and Bp: the most dependent part), and their distances from the hymen are measured in centimeters with maximum Valsalva effort (Fig. 19.2). The more traditional approach has a surgical focus, whereas the newer POP-Q simply identifies the location of specific vaginal points.

Additional factors that should be evaluated during the physical exam include associated pelvic support defects such as vaginal vault prolapse or cystocele, pelvic neuromuscular function, and vaginal mucosal estrogenation. All pelvic floor anatomic defects should be repaired during a reconstructive surgical procedure even if minimally symptomatic, as untreated anatomical defects of the anterior and apical vagina may enlarge after repair of the posterior vaginal wall. Thus, preoperative identification of specific individual defects is crucial. Appropriate levator contraction strength is a key factor in enhancing the long-term success rate of pelvic reconstructive surgery. Regular Kegel exercises should be rec-

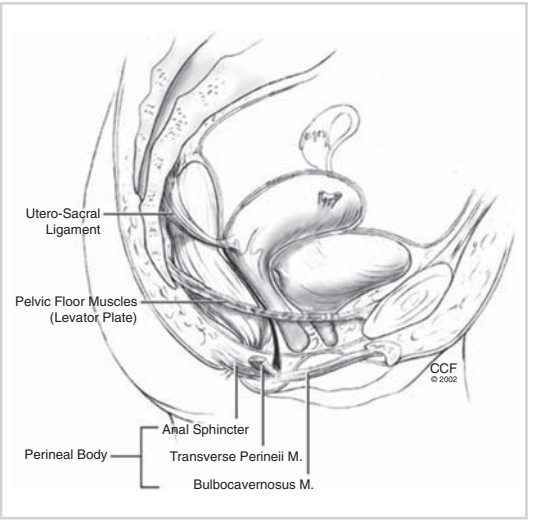


Figure 19.1. Lateral view of pelvis. Rectoceles typically develop between the levator plate and the perineal body due to weakness of the rectovaginal septum endopelvic fascia. Reprinted with permission of the Cleveland Clinic Foundation.

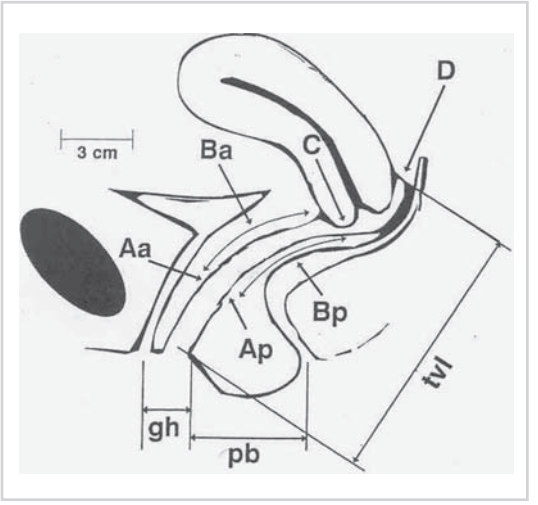


Figure 19.2 POP-Q classification of prolapse severity; points Ap and Bp mark the posterior vaginal wall. Other points include anterior vaginal wall (Aa, Ba), vaginal depth (D), cervix (C), total vaginal length (TVL), genital hiaturs (gh), and perineal body (pb).

ommended following pelvic reconstructive procedures. Biofeedback therapy may be necessary to instruct patients how to adequately isolate and contract their pelvic floor muscles. Poorly estrogenized thin vaginal mucosa should be treated with local estrogen prior to surgical therapy, as well as postoperatively to enhance mucosal strength.

Anatomy

Defects in the integrity and attachments of the posterior vaginal wall and rectovaginal septum may result in herniation of the posterior wall into the vaginal lumen through these defects. The normal posterior vagina is lined by squamous epithelium that overlies the lamina propria, a layer of loose connective tissue. A fibromuscular layer of tissue composed of smooth muscle, collagen, and elastin underlies this lamina propria, and is referred to as the rectovaginal fascia. This is an extension of the endopelvic fascia that surrounds and supports all of the pelvic organs, and contains blood vessels, lymphatics, and nerves that supply and innervate the pelvic organs.

Denonvilliers originally described a dense tissue layer in men between the bladder and the rectum and named it the rectovesical septum.[4] Many clinicians refer to this layer as Denonvilliers' fascia. The layer of tissue between the vagina and the rectum was felt to be analogous to the rectovesical septum and became known as Denonvilliers' fascia in the female, or the rectovaginal septum.[4] Others described the rectovaginal fascia as a support mechanism of the pelvic organs, and were successful in identifying this layer during surgical and autopsy dissections.[4–6]

The normal vagina is stabilized and supported on three levels. Superiorly, the vaginal apical endopelvic fascia is attached to the cardinal-uterosacral ligament complex (level I). Laterally, the endopelvic fascia is connected to the arcus tendineus fasciae pelvis (level II). Inferiorly, the lower posterior vagina connects to the perineal body (level III).[7] The endopelvic fascia extends between the vaginal apex and the perineal body, comprising the rectovaginal septum (Fig. 19.3). An enterocele or rectocele results from a stretching or actual separation or tear of the rectovaginal fascia, leading to a bulging of the posterior vaginal wall noted on examination during a Valsalva maneuver. Trauma from vaginal childbirth

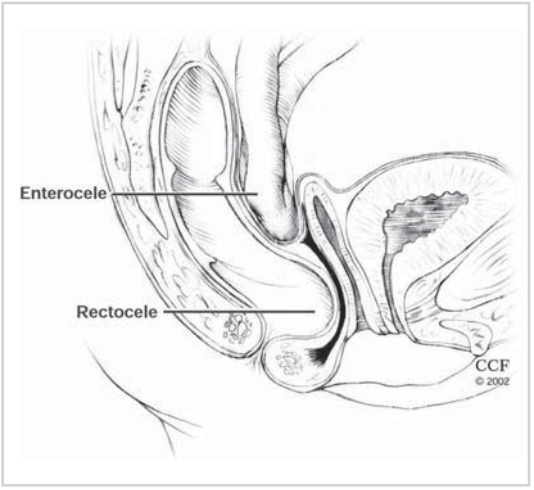


Figure 19.3 Schematic representation of the rectovaginal septum including its attachment to the vaginal apex superiorly and perineal body inferiorly. Reprinted with permission of the Cleveland Clinic Foundation.

commonly leads to transverse defects above the usual location of the connection to the perineal body (Fig. 19.4).[4,8] In addition, patients may present with lateral, midline, or high transverse fascial defects. Separation of the rectovaginal septum fascia from the vaginal cuff results in the development of an enterocele as a hernia sac without fascial lining and filled with intraperitoneal contents. The levator plate extends from the pubic bone to the sacrum/coccyx and provides support for the change in vaginal axis from vertical to horizontal along the midvagina. A rectocele typically develops at, or below, the levator plate, along the vertical vagina.

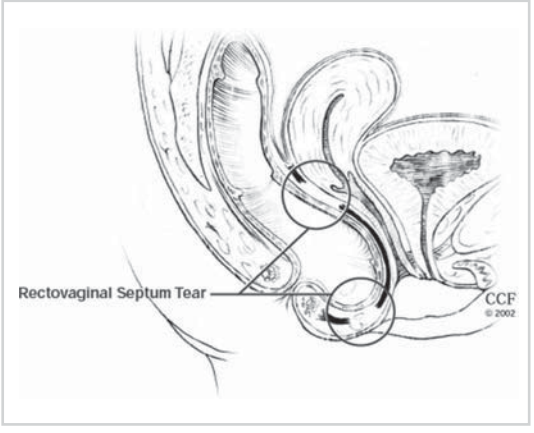


Figure 19.4 Fascial tears of the rectovaginal septum can occur superiorly or inferiorly at sites of attachment to a central tendon. Reprinted with permission of the Cleveland Clinic Foundation.

Symptoms

Symptoms of a rectocele typically entail pelvic/perineal pressure or bulge with an associated need to digitally reduce or splint the posterior vaginal bulge or the perineum in order to either initiate or complete a bowel movement. Accumulation of stool within the rectocele reservoir leads to increasing degrees of perineal pressure and obstructive defecation. In the absence of digital reduction, women will note incomplete emptying, which leads to a high degree of frustration and a vicious cycle of increasing pelvic pressure, need for stronger Valsalva efforts, enlargement of the rectocele bulge, and increasing perineal pressure. Rectal digitation is not commonly self-reported by patients with a symptomatic rectocele unless asked by their physicians.

An enlarging enterocele or rectocele will widen the levator hiatus and increase the vaginal caliber.[9] In addition, women with increasing degrees of prolapse have progressively larger genital hiatuses.[10] This may lead to sexual difficulties including symptoms of vaginal looseness and decreased sensation during intercourse. Whether this is due to the enlargement of the vaginal introitus and levator hiatus, or coexistent damage to the pudendal nerve supply to the pelvic floor musculature, is unclear. Decreased sexual sensation and vaginal looseness are increasingly reported symptoms that are also surgically addressed by a posterior colporrhaphy and perineoplasty. A large enterocele or rectocele may extend beyond the hymenal ring. Once exteriorized, the patient is at risk for vaginal mucosal erosion and ulceration.

Surgery to Correct a Rectocele

Since gynecologic indications for rectocele repair extend beyond the presence of a symptomatic nonemptying rectocoele, the goals of rectocele repair procedures also vary (Table 19.2).

Table 19.2. Goals of gynecologic rectocele repair

Reestablish the following:
Endopelvic fascial integrity from apex to perineum
Levator plate integrity
Anterior rectal wall support
Normal vaginal caliber and length
Integrity of perineal body

Although less than half of colorectal surgeons approach a rectocele repair vaginally, 95% to 100% of gynecologists repair rectoceles vaginally.[1–3] The vaginal approach to rectocele repair allows for correction of vaginal as well as rectal symptomatic dysfunction.

Posterior Colporrhaphy Technique

Posterior colporrhaphy is commonly performed in conjunction with a perineoplasty to address a rectocele or relaxed perineum and widened genital hiatus. Preoperatively, the severity of the rectocele is assessed, and the desired final vaginal caliber is determined. Allis clamps are placed on the hymen remnants bilaterally and approximated in the midline such that the resultant vagina should loosely admit two to three fingers. The skin is infiltrated with a dilute epinephrine solution. A triangular incision over the perineal body is made between the Allis clamps, and sharp dissection is then performed to separate the posterior vagina from the underlying rectovaginal fascia. A midline incision is made along the length of the vagina to a site above the superior edge of the rectocele.

The dissection is carried laterally to the lateral vaginal sulcus and medial margins of the puborectalis muscles (Fig. 19.5). The rectovaginal fascia with or without the underlying levator ani muscles is then plicated with interrupted sutures while depressing the anterior rectal wall (Fig. 19.6). The plication is begun at the level of the levator muscles. Typically, absorbable sutures (No. 1 Vycril) are placed along the length of the

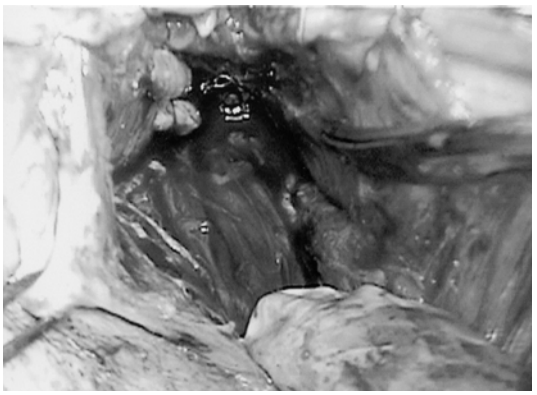


Figure 19.5 Surgical dissection is carried to the lateral vaginal sulcus in order to identify the fascia, which will be plicated for correction of posterior vaginal wall weakness.

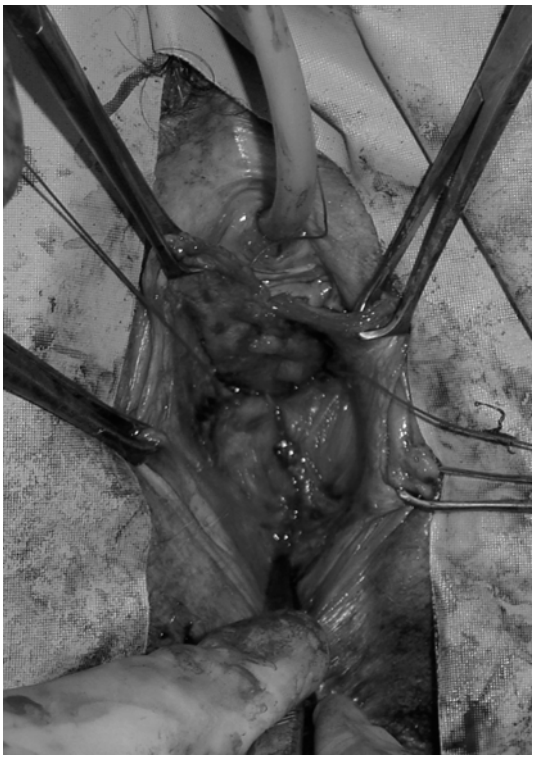


Figure 19.6 Multiple interrupted sutures are used to approximate the endopelvic fascia overlying the levator muscles in the midline.

rectocele until plication to the level of the perineal body is complete. In the presence of a large rectocele, multiple suture layers may be necessary to restore adequate support to the anterior rectal wall. Excess vaginal mucosa is carefully trimmed and then reapproximated. A concomitant perineoplasty may be performed by plicating the bulbocavernosus and transverse perineal muscles. This reinforces the perineal body and provides enhanced support to the corrected rectocele.

Discrete Fascial Defect Repair Technique

Discrete tears or breaks in the rectovaginal fascia or rectovaginal septum may contribute to the formation of rectoceles (Fig. 19.4).[4] The intent of the discrete facial defect repair of rectoceles is to identify the fascial tears and reapproximate the edges. The surgical dissection is similar to the traditional posterior colporrhaphy, whereby the vaginal mucosa is dissected off the underlying rectovaginal fascia to the lateral border of the levator muscles. Instead of plicating the fascia and levator muscles in the midline, however, any fascial tears are identified and repaired with interrupted permanent sutures. We have identified most posterior vaginal fascial defects to be superior transverse separations off the vaginal apex—and lead to the frequent coexistence of enteroceles and rectoceles. Richardson[4] describes pushing anteriorly with a finger in the rectum in order to identify areas of rectal muscularis that are not covered by the rectovaginal septum. Thereby, the surgeon can locate fascial defects, and identify and then reapproximate the fascial margins. A perineoplasty may be necessary if a widened vaginal hiatus is present.

Results of Surgical Repair

The posterior colporrhaphy has been the traditional approach to rectocele repair by gynecologists. Although commonly performed, it has been described as "among the most misunderstood and poorly performed" gynecologic surgeries.[11] Although many authors have reported satisfactory anatomic results, conflicting effects on bowel and sexual function postoperatively have been noted. Several authors have reported sexual dysfunction rates of up to 50% of women reporting dyspareunia or apareunia after posterior colporrhaphy.[12]

As noted, there are conflicting reports with regard to functional outcome after posterior colporrhaphy. Importantly, many authors suggest that the significant rate of postoperative dyspareunia may be due to the plication of the levator ani muscles, and has led to the popularization of the discrete fascial defect repair. Several authors have reported a similar anatomic cure rate with this surgery, along with significant improvement in quality of life measures. Unlike the traditional posterior colporrhaphy, all these series report less postoperative dyspareunia. The authors noted significant improvement in splinting, vaginal pressure, and stooling difficulties. However, rates of fecal incontinence and constipation were unchanged postoperatively.

These studies show promising anatomic and functional results; however, long-term prospective studies are warranted. Thus far, the incidence of postoperative dyspareunia with the discrete fascial defect repair is less than with the traditional posterior colporrhaphy. Although

the above authors positively present the results of this approach to rectocele repair, other authors report skepticism about the ability to demonstrate and repair discrete fascial tears.

Other Techniques and Results

The use of synthetic mesh placed abdominally from the perineal body to the vaginal vault to correct a rectocele at the time of abdominal sacrocolpopexy for vaginal vault prolapse has been reported.[13] The mesh is attached to the anterior longitudinal ligament overlying the sacral promontory in a tension-free fashion. The authors treated 29 patients and noted continued bowel symptoms including constipation and incomplete defecation. Others have noted a similar persistence or increase in bowel symptoms in 39% of patients who underwent this type of surgery.[14]

Adopting the principles of hernia repair used by general surgeons, reconstructive pelvic surgeons have reported reinforcement of pelvic organ prolapse repairs with synthetic and biologic prostheses. Synthetic mesh such as polypropylene is widely used for anti-incontinence surgery and abdominal sacrocolpopexy to repair vaginal vault prolapse. Although high success rates have been reported, erosion of the mesh and infection has been associated with these repairs.[15] Autologous grafts and allograft prostheses, including fascia lata, rectus sheath, and dermal grafts, have been employed. Few complications have been associated with these grafts, and they appear to have a comparable success rate to synthetic materials. Xenograft material, including bovine pericardium and porcine dermis and small intestinal mucosa, has also been used to reinforce these repairs; however, there are no reports on complications and success rates in the literature.

Few studies have reported on the use of graft materials to reinforce posterior compartment defects. Sand et al[16] reported on 132 women undergoing either standard rectocele repairs or rectocele repairs reinforced with Polyglactin 910 mesh (an absorbable mesh), and found no difference in recurrence rates between the two groups. Small observational studies on the use of Marlex mesh for rectocele repair have not reported erosion or recurrence.

Laparoscopic rectocele repair involves opening the rectovaginal space and dissecting inferiorly to the perineal body. The perineal body is sutured to the rectovaginal septum, and rectovaginal fascial defects are identified and closed. The advantages are reported to be better visualization, and more rapid recovery, with decreased pain and shorter hospitalization. Disadvantages include difficulty with laparoscopic suturing, increased operating time and expense, and an extended time necessary to master the laparoscopic surgical techniques.[17]

Rectocele operations performed transanally versus transvaginally have been compared.[18] Complications occurred equally in the two groups of patients. In all, 54% had postoperative constipation, and 34% had gas and liquid or solid stool incontinence. Sexual dysfunction was reported in 22%. The only significant difference was that the patients receiving transvaginal repair had more persistent pain.

Discussion

Gynecologic indications for rectocele repair are more numerous compared to traditional colorectal indications because gynecologists primarily address vaginal symptoms when repairing a rectocele. Obstructive defecation symptoms are only some of the accepted indications. Preoperative evaluation typically includes only clinical assessment gained from the history and physical exam, and gynecologists rarely depend on defecography to plan a reconstructive procedure for rectocele. Overall, surgical correction success rates are quite high when using a vaginal approach for rectocele correction. Vaginal dissection results in better visualization and access to the endopelvic fascia and levator musculature, which allows for a more firm anatomic correction. Re-creation of a strong perineal body enhances the longevity of pelvic reconstructive procedures, especially rectocele repairs. In addition, maintaining rectal mucosal integrity appears to reduce the risk of postoperative infection and fistula formation. More comprehensive data collection is necessary to better understand the effect of various surgical techniques on vaginal, sexual, and defecatory symptoms.

References

1. Kapoor D, Davila GW, Rosenthal RJ, Ghoniem GM. Voiding and sexual dysfunction in morbidly obese

women using validated symptom inventories and quality of life questionnaires: A case control study. Int Urogynecol J 2001;12:S53.
2. Mizrahi N, Kapoor D, Nogueras JJ, Weiss EG, Wexner SD, Davila GW. A gynecologic perspective of posterior compartment defects. Colorect Dis 2002;4(suppl.):H68.
3. Davila GW, Ghoniem GM, Kapoor DS, Contreras-Ortiz O. Pelvic floor dysfunction management practice patterns: a survey of members of the international urogynecological association. Int Urogynecol J 2002;13:319–325.
4. Richardson AC. The rectovaginal septum revisited: its relationship to rectocele and its importance in rectocele repair. Clin Obstet Gynecol 1993;36:976–983.
5. Uhlenhuth E, Wolfe WM, Smith EM, Middleton EB. The rectogenital septum. Surg Gynecol Obstet 1948;86:148–163.
6. Milley PS, Nichols DH. A correlative investigation of the human rectovaginal septum. Anat Rec 1969;163:443–452.
7. Delancey JOL. Anatomic aspects of vaginal eversion after hysterectomy. Am J Obstet Gynecol 1992;166: 1717–1724.
8. Shull BL, Bachofen CG. Enterocele and rectocele. In: Walters MD, Karram MM, eds. Urogynecology and Reconstructive Pelvic Surgery, 2nd ed. St. Louis: Mosby, 1999:221–234.
9. Kahn MA, Stanton SL. Techniques of rectocele repair and their effects of bowel function. Int Urogynecol J 1998;9:37–47.
10. Delancey JOL, Hurd WW. Size of the urogential hiatus in the levator ani muscles in normal women and women with pelvic organ prolapse. Obstet Gynecol 1998;91:364–368.
11. Nichols DH. Posterior colporrhaphy and perineorrhaphy: separate and distinct operations. Am J Obstet Gynecol 1991;164:714–721.
12. Francis WJ, Jeffcoate TN. Dyspareunia following vaginal operations. J Obstet Gynaecol Br Emp 1961;68:1–10.
13. Fox SD, Stanton SL. Vault prolapse and rectocele: assessment of repair using sacrocolpopexy with mesh interposition. Br J Obstet Gynaecol 2000;107:1371–1375.
14. Taylor GM, Ballard P, Jarvis GJ. Vault prolapse and rectocele: assessment of repair using sacrocolpopexy with mesh interposition. Br J Obstet Gynaecol 2001;8:775–776.
15. Iglesia CB, Fenner DE, Brubaker L. The use of mesh in gynecologic surgery. Int Urogynecol J 1997;8:105–115.
16. Sand PK, Koduri S, Lobel RW. Prospective randomized trial of Polyglactin 910 mesh to prevent recurrences of cystoceles and rectoceles. Am J Obstet Gynecol 2001; 184:1357–1364.
17. Paraiso MFR, Falcone T, Walters MD. Laparoscopic surgery for enterocele, vaginal apex prolapse and rectocele. Int Urogynecol J 1999;10:223–229.
18. Arnold MW, Stewart WRC, Aguilar PS. Rectocele: four years' experience. Dis Colon Rectum 1990;33:684–687.

20

Perineal Procedures for Rectal Prolapse

Richard E. Karulf and Karim Alavi

Constipation and rectal prolapse frequently coexist. Estimates of preoperative constipation range from 30% to 67% in prospective studies.[1] It is not clear whether constipation results in rectal prolapse, or prolapse results in constipation due to a functional outlet obstruction. Many patients report improvement in bowel function after surgery for rectal prolapse. Conversely, some patients with normal bowel function prior to surgery for rectal prolapse complain of constipation after surgery. Nevertheless, perineal procedures are often performed for patients with constipation and rectal prolapse.

Perineal Approaches

Not all patients are able to withstand the stress of an abdominal procedure. In fact, the conditions that may predispose patients to rectal prolapse, such as increased age, malnutrition, and pulmonary disease, may prohibit performing an abdominal approach to repair this problem. Perineal approaches offer an alternative form of treatment that generally places the patient under less stress in the operative period and may be better tolerated.

Evaluation

The importance of preoperative evaluation prior to embarking of any form of surgical intervention for rectal prolapse cannot be overemphasized. Three specific areas are assessed before perineal surgery for patients with constipation and rectal prolapse. First, many of the patients specifically referred for perineal procedures for rectal prolapse are sent because of their high risk for abdominal surgery. A careful evaluation of the patient's medical history and risk factors for surgery must be performed.

Second, because patients with prolapse can manifest a wide range of dysfunction from incontinence to constipation, the understanding of the pelvic floor physiology of each individual is essential. A common battery of tests may include electromyography, anal manometry, and defecography. Paradoxical puborectalis contraction is often found during preoperative evaluation with defecography. In one series, 12 of 61 patients (20%) with rectal prolapse had nonrelaxing puborectalis prior to surgery, and the association with constipation was significant.[2] Although some authors have noted a good correlation between electromyography (EMG) and defecography in identifying paradoxical puborectalis,[3] others have found a poor correlation.

Third, it is important to evaluate the colon for sources of constipation. Endoscopic examination of the colon is an important part of the workup, specifically in the elderly, to identify pathologic sources of rectal prolapse (requiring a different form of intervention) and synchronous pathology. A colon transit study is also indicated to identify patients with colonic dysmotility as a primary cause of constipation. In a series comparing abdominal rectopexy with and without sigmoid resection, 54% of patients in both groups had prolonged transit studies before surgery.[4] It was noted in this study, after surgery, that patients with resection had a lower incidence of constipation than patients without resection. It was concluded that angulation of

the bowel or kinking due to redundant sigmoid colon could be the original cause of the constipation before surgery and was unrelieved after surgery.

Anal Encirclement Procedure

In 1891, Thiersch initially described encirclement of the anus with silver wire for treatment of incontinence and rectal prolapse.[5,6] It was hoped that the wire would produce an area of fibrosis around the anus that would act as a passive support for the pelvic floor (Fig. 20.1). Unfortunately, not only did the wire fail to provoke the desired fibrosis, but it also produced unwanted complications, including ulceration, erosion, breakage, and fecal impaction.

Surgeons have attempted to modify the encirclement technique by using other materials including fascia, tendon, nylon, polypropylene mesh, Mersilene®, and Teflon®. These materials have shown less of a tendency to break and have had fewer complications than were noted with the silver wire.

The disadvantage of encirclement procedures is that, in most cases, the ring is placed in the subcutaneous space and does not support the levators. As a result, this technique does not cure prolapse; it merely hides it away from view and should be regarded as a palliative procedure. The advantage of encirclement procedures is that they can be performed under local or spinal anesthesia and they have minimal impact on even the poorest risk patient. The disadvantage is that if the rectum prolapses through the ring, it may incarcerate necessitating an emergency operation.

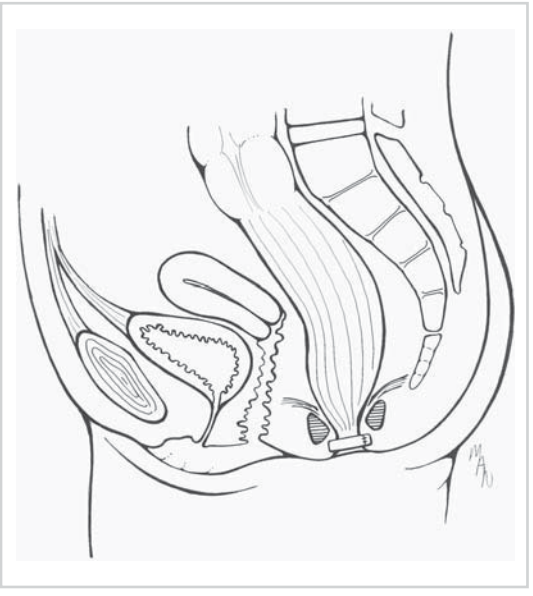


Figure 20.1. Anal encirclement. Also known as the Thiersch procedure, this operation has been performed with the use of many types of material. Note that the ring is placed in the subcutaneous (perianal) tissue and offers no support to the levators. (From Karulf RE, Madoff RD, Goldberg SM. Rectal prolapse. Curr Probl Surg 2001;38:771–832, with permission from Elsevier.)

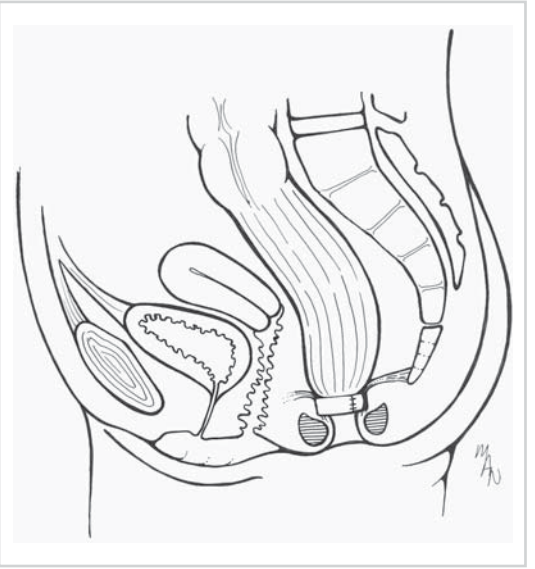


Figure 20.2. Notaras variation of the Thiersch procedure. The ring of foreign material is placed around the anorectal musculature at the level of the puborectalis muscle, thus supporting both the anorectal angle and the anal canal. (From Karulf RE, Madoff RD, Goldberg SM. Rectal prolapse. Curr Probl Surg 2001;38:771–832, with permission from Elsevier.)

Notaras[7] described one interesting variation of the Thiersch anal encirclement procedure (Fig. 20.2). In this variation, a ribbon of polypropylene mesh is placed around the rectum at the level of the puborectalis. The goal of this procedure is to support both the anorectal angle and the anal canal. Due to the more extensive dissection that was required with this technique, general anesthesia is often required. Limited information is available about recurrence rates with this technique.

One other unusual technique used an Angelchik prosthesis to encircle the distal rectum; this device was at one point in time popular for the treatment of esophageal reflux.[8] The technique is no longer performed, because the device was withdrawn from the market when

it fell into disfavor due to complications. The device was placed above the levators in a series of eight elderly patients with rectal prolapse. With the exception of this one nuance, it was similar to other encirclement procedures. Results showed one death on postoperative day 10 due to a stroke, and one patient with pelvic sepsis in whom the prosthesis was removed. There were no reports of recurrence, morbidity, or mortality in the six remaining patients.

Another version of anal encirclement is the Gant-Miwa procedure, which has been described in Japan. In this procedure, an absorbable suture is used to create dozens of tags of mucosa and submucosa on the surface of the prolapsed rectum. The rectum is then returned to its normal anatomic position and a nonabsorbable purse-string suture is placed around the anus. A recent review of this procedure lists low complication and recurrence rates, although it is not widely practiced outside of Japan.[9]

Perineal Rectosigmoidectomy

Although first performed by Mickulicz[10] in 1889 and later advocated by Miles[11] in 1933 and Gabriel[12] in 1948, the perineal rectosigmoidectomy is most commonly associated with Altemeier (Fig. 20.3). In 1971, Altemeier et al[13] reported the results of a one-stage procedure with 106 patients over a 19-year period. There were no postoperative deaths and only three recurrences in their series. Their results were especially impressive considering the patients were older (average age: 62 years) than the patients in most series of the time, and the majority of the patients had documented psychiatric disease (52%).

The technique of the perineal rectosigmoidectomy is thought to be difficult to conceptualize. With the rectum prolapsed, there are two full-thickness layers of the bowel wall. The outer layer is distal and attaches to the anal canal, while the inner layer is in continuity with the proximal bowel. An incision is made through the outer layer, 2 to 4 cm above the dentate line, which straightens the rectum and sigmoid colon. With traction on the bowel, the mesorectum is divided with suture ligation of the vessels. A surprising amount of proximal rectum and sigmoid colon can be prepared for resection with this technique. When, in the judgment of the surgeon, sufficient bowel has been devascularized, the inner layer of bowel is transected and a hand-sewn or stapled anastomosis is created between the two cut ends of bowel. As originally described, Altemeier opened the peritoneal cul-de-sac and obliterated what he considered to be a sliding hernia sac. He also reefed the

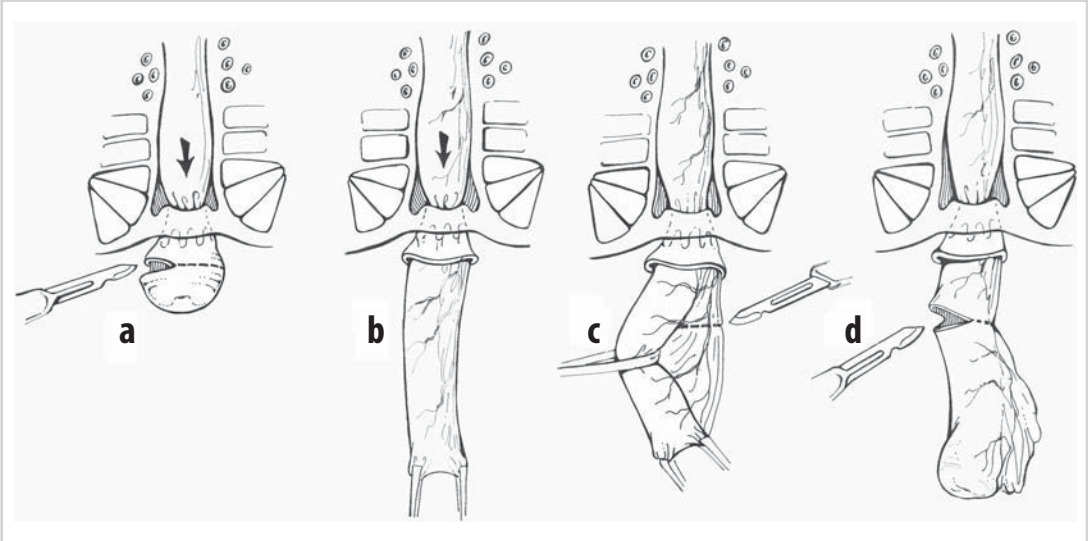


Figure 20.3. Perineal rectosigmoidectomy. With the rectum prolapsed, the outer rectal tube is incised circularly (a) and unfolded (b). The mesorectum is serially ligated and divided (c). When all redundancy has been removed, the inner tube is divided, which completes the resection (d). From Karulf RE, Madoff RD, Goldberg SM. Rectal prolapse. Curr Probl Surg 2001;38:771–832, with permission from Elsevier.

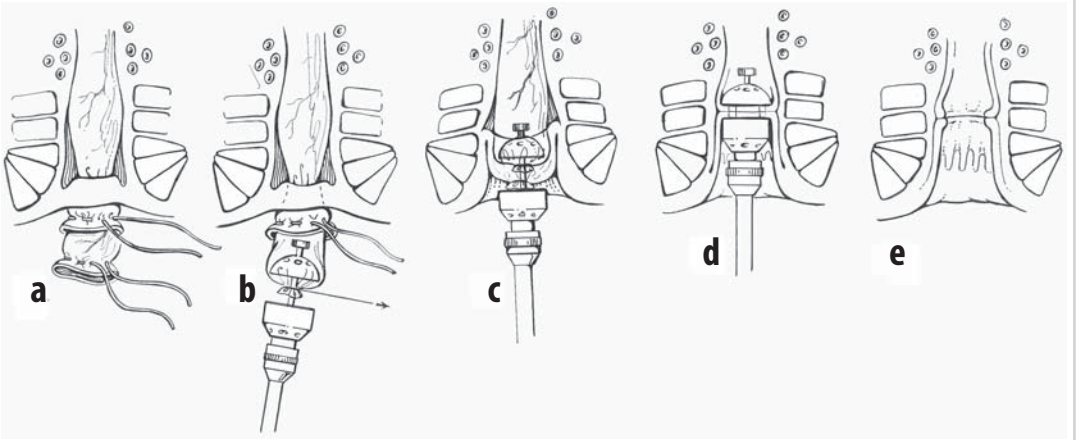


Figure 20.4. Variation of Altemeier's technique. The anastomosis may be performed with an intraluminal stapling device (a–e). From Karulf RE, Madoff RD, Goldberg SM. Rectal prolapse. Curr Probl Surg 2001;38:771–832, with permission from Elsevier.

puborectalis together anterior to the rectum and performed a sutured anastomosis. Other surgeons often omit these two additional technical points due to lack of proven benefit.

One variation on Altemeier's technique employs an intraluminal stapling device to create the anastomosis (Fig. 20.4).[14] Bennett and Geelhoed[15] reviewed the subject and advocated the use of a stapler in creating the anastomosis, for three reasons. First, it simplifies the anastomosis. Second, there can be a more extensive resection, since the anastomosis is completed inside the anus. Third, in their opinion, the narrowing that is seen after stapled anastomosis may prevent the later need for sphincter plication. However, superior functional results have never been documented with stapled compared to hand-sewn anastomosis for this procedure.

Because of its minimally invasive nature, perineal rectosigmoidectomy has been suggested as an alternative for elderly or high-risk patients. A series at the University of Minnesota reviewed the results of perineal rectosigmoidectomy in 114 patients of a median age of 78 years.[16] There were no deaths and a 12% complication rate; hospital stay averaged 4 days. Only 11 of the 104 patients (11%) who were available for follow-up developed recurrent full-thickness rectal prolapse. In a second series from Arizona, 72 patients over age 70 were treated with perineal excision of rectal prolapse.[17] In this series, nine of the 72 patients presented with acute incarcerated rectal prolapse. Two anastomotic leaks were noted, both in the acutely incarcerated group, both of which required a diverting colostomy. The length of stay averaged 7 days. In a follow-up of 6 months to 9 years (average 48 months), there were no deaths, and eight complications were noted (11%). Four of the 72 patients, had recurrent full-thickness rectal prolapse (5.6%) and another four had prolapse limited to the mucosa. These studies provide evidence that even in elderly or high-risk patients, rectal prolapse can be treated with perineal rectosigmoidectomy with minimal morbidity.

Other authors have reported their results with the Altemeier procedure with less encouraging results. A high rate of recurrence (58%) was reported in the St. Mark's series, with half of these in the first 3 years.[18] Other authors report a recurrence rate as high as 60% with perineal rectosigmoidectomy.[19] It is not clear why these early reports are at odds with reports in recent years. It is clear that the recurrence rate is linked to the length of follow-up, and more recent reports have emphasized the use of this technique in older and high-risk patients. It is possible that if the early reports had a greater percentage of younger patients, the recurrence rates could be unfavorably skewed.

In addition, these reports from 50 years ago used a technique in which the colorectal anastomosis was hand sewn well outside of the anal canal. The anastomosis was then reduced through the sphincters. By allowing this amount of redundancy, the patients were leaving the

operating room with an inadequate resection. More recent articles have described creating the anastomosis closer to the sphincter complex and allowing more tension on the repair. These small technical points and the difference in patient selection may account for the difference in recurrence rates.

One interesting finding, noted in both the University of Minnesota and the Arizona series, was an improvement in continence after surgery. In the Minnesota series, 67 of the 104 patients were incontinent to solid or liquid stool prior to surgery; 56 of these individuals underwent rectosigmoidectomy as a sole procedure and 26 (46%) regained full control. The remaining 11 patients had levatoroplasty at the time of rectosigmoidectomy and 10 improved (91%) with seven becoming fully continent (64%). In the Arizona series, 54 of 72 patients were incontinent to feces and all patients were incontinent to flatus prior to surgery. Following surgery, which included perineal excision of the rectum and posterior levator approximation to re-create the anorectal angle, 48 patients (67%) had regained continence of both flatus and feces. A study at the Cleveland Clinic Florida analyzed 20 consecutive elderly patients of a mean age of 82 years who underwent perineal rectosigmoidectomy for full-thickness rectal prolapse.[20] Detailed functional assessment and physiologic testing were performed before and after surgery. There was one death, one major complication, and no recurrences in an average of 26 months of follow-up. Before surgery, six of 10 patients had prolonged pudendal nerve terminal motor latency (PNTML) values (longer than 2.5 msec). Continence scores improved, on an average, from 14.5 before surgery to 8.4 after surgery. It is interesting to note that continence scores improved in four of the six patients with evidence of at least unilateral neuropathy. This finding suggests that a prolonged PNTML may not be an accurate predictor of postoperative continence. The low recurrence rate was undoubtedly due to the very short follow-up, as a subsequent series of 61 patients from Cleveland Clinic Florida reported a recurrence rate of 12.5%.[21]

Mucosal Sleeve Procedure

Unlike many other operations for prolapse that were performed at the beginning of the 20th century, the mucosal sleeve resection, originally described by Delorme[22] in 1900, is still performed today (Fig. 20.5). The procedure includes a stripping of the mucosa of the prolapsed rectum and sutured plication of the remnant bare muscle, collapsing the wall like an accordion. The mucosa is then reapproximated to seal the anastomosis.

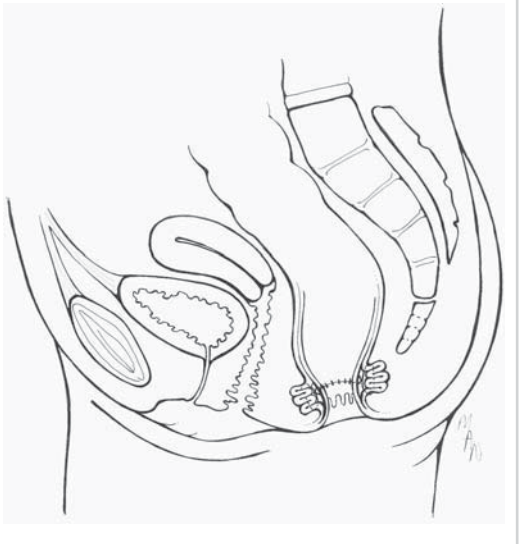


Figure 20.5. Resection of mucosal sleeve and plication of the rectal wall (Delorme procedure). This operation involves a total mucosal stripping of the prolapsed segment and its plication in an accordion-like fashion by a series of stitches. From Karulf RE, Madoff RD, Goldberg SM. Rectal prolapse. Curr Probl Surg 2001;38:771–832, with permission from Elsevier.

The main advantage of the Delorme procedure is its minimal physiologic impact. The lack of an abdominal incision and avoidance of the peritoneal cavity are key factors. It can be performed under local anesthesia, if needed, on even the highest risk patients. It is ideal for a low or a small prolapse. Frail or elderly patients with a limited life expectancy, who have a symptomatic rectal prolapse, are best suited to this procedure.

There are many disadvantages of the mucosal sleeve procedure. The procedure requires a dissection of the mucosa from the muscle wall. More importantly, the procedure does not fix the rectum to the sacrum or repair the pelvic floor, and the pleated muscle at the anal verge provides a false sense of security when considering the potential for recurrence. Even in favorable series, the recurrence rate for mucosal sleeve resection is higher than the rate for most contemporary

abdominal procedures or rectosigmoidectomy. While a focus on patient selection may improve the results,[23] selection criteria alone are not the answer. Patients who are seeking a durable repair for rectal prolapse should look elsewhere for a solution.

Perineal Rectopexy

The earliest versions of this procedure were described by Lockhart-Mummery in 1910. Packing the retrorectal space with gauze was found to have a prohibitively high recurrence rate. Inserting a Mersilene mesh high in the retrorectal space and suturing the edges to the sides of the rectum modified the technique to improve the recurrence rate.[24] Mobilization of the rectum and placement of mesh was performed through a posterior perineal approach, occasionally removing the coccyx to improve exposure (Fig. 20.6). In a series of 22 women with a mean age of 75 years undergoing this procedure, there were no deaths or significant morbidity and only one recurrence.

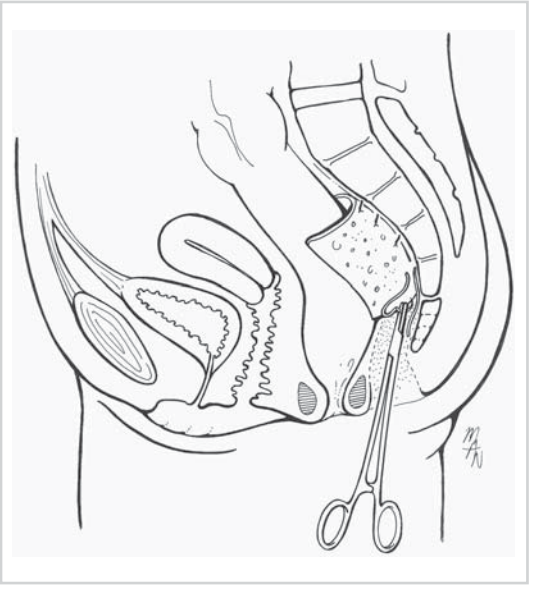


Figure 20.6. Perineal rectopexy. Through a posterior perineal incision, the rectum is widely mobilized. A patch of Mersilene mesh is sewn to the sacrum. The sides of the rectum will then be sutured to its edges. From Karulf RE, Madoff RD, Goldberg SM. Rectal prolapse. Curr Probl Surg 2001; 38:771–832, with permission from Elsevier.

After Surgery

Patients who had no difficulty with defecation prior to surgical management of rectal prolapse have developed constipation after surgery. In fact, the development of constipation is the single most common problem after fixation rectopexy.[25] The cause of the constipation after perineal procedures is not clear. Two theories dominate the discussion: decreased rectal compliance and dysmotility.

Decreased Compliance

Compliance is a measure of the elasticity of tissues. Scarring of the rectum during mucosal sleeve resections[26] and mesh rectopexy[27] may reduce compliance and therefore make passage of stool more difficult for some patients. Decreased compliance is also noted with perineal rectosigmoidectomy when a compliant rectum is replaced with a less distensible sigmoid colon.[28]

One note regarding compliance warrants mention. Attempts have been made to apply the concept of compliance to discussions of the physiology of defecation. However reasonable this is in theory, practical application is difficult because, in the absence of a Hartmann pouch, the rectum is an open-ended tube. As a result, direct measurements of compliance are not possible with current technology. Measurements using air- or fluid-filled condoms will, at best, approximate the compliance of the rectum.

Abnormal Motility

In a review, 12 patients complaining of constipation after Orr-Loygue rectopexy were compared with 12 patients with full-thickness rectal prolapse and 10 healthy volunteers.[29] The rectopexy group was similar to the other two groups in terms of demographics and preoperative function. However, the rectopexy group had lower weekly stool frequency and a higher prevalence of abdominal pain. The authors also reported prolonged global, right, and left colonic transit times in the rectopexy group, but similar rectosigmoid transit times and manometric parameters of the anal sphincter in all three groups. They suggested that the obstruction was

functional, rather than anatomic, and that the source of the denervation may have been incidental injury of the autonomic parasympathetic innervation of the left colon and rectum. They concluded that constipation following rectopexy seems to be related to acquired sigmoid motility disturbances above the rectopexy, rather than to anorectal emptying.

Conclusion

There is a strong association between rectal prolapse and constipation. Perineal procedures to correct the prolapse may improve preexisting constipation. Modern series show that perineal rectosigmoidectomy for correction of rectal prolapse can be performed in even high-risk patients with a low recurrence rate and minimal morbidity.

References

1. Madoff RD, Mellgren A. One hundred years of rectal prolapse surgery. Dis Colon Rectum 1999;42:441–450.
2. Agachan F, Pfeifer J, Wexner SD. Defecography and proctography. Results of 744 patients. Dis Colon Rectum 1996;39:899–905.
3. Kuijpers HC, Bleijenberg G. Assessment and treatment of obstructed defecation. Ann Med 1990;22:405–411.
4. McKee RF, Lauder JC, Poon FW, Aitchison MA, Finlay IG. A prospective randomized study of abdominal rectopexy with and without sigmoidectomy in rectal prolapse. Surg Gynecol Obstet 1992;174:145–148.
5. Gabriel WB. Thiersch's operation for anal incontinence. Proc R Soc Med 1948;41:467–468.
6. Gabriel WB. Thiersch's operation for anal incontinence and minor degrees of rectal prolapse. Am J Surg 1953;86:583–590.
7. Notaras MJ. The use of mersilene mesh in rectal prolapse repair. Proc R Soc Med 1973;66:684–686.
8. Ladha A, Lee P, Berger P. Use of Angelchik anti-reflux prosthesis for repair of total rectal prolapse in elderly patients. Dis Colon Rectum 1985;28:5–7.
9. Yamana T, Iwadare J. Mucosal plication (Gant-Miwa procedure) with anal encircling for rectal prolapse—a review of the Japanese experience. Dis Colon Rectum 2003;46(suppl):S94–99.
10. Mickulicz J. Zur operativen behandlung dis prolapsus recti et coli invaginati. Arch Klin Surg 1889;38:74–97.
11. Miles WE. Rectosigmoidectomy as a method of treatment for procidentia recti. Proc R Soc Med 1933;26:1445.
12. Gabriel WB. The Principles and Practices of Rectal Surgery, 4th ed. Springfield, IL: Charles C Thomas, 1948.
13. Altemeier WA, Culbertson WR, Schowengerdt C, Hunt J. Nineteen years' experience with the one-stage perineal repair of rectal prolapse. Ann Surg 1971;173: 993–1006.
14. Vermeulen FD, Nivatvongs S, Fang DT, Balcos EG, Goldberg SM. A technique for perineal rectosigmoidectomy using autosuture devices. Surg Gynecol Obstet 1983;156:84–86.
15. Bennett BH, Geelhoed GW. A stapler modification of the Altemeier procedure for rectal prolapse. Experimental and clinical evaluation. Am Surg 1985;51: 116–120.
16. Williams JG, Rothenberger DA, Madoff RD, Goldberg SM. Treatment of rectal prolapse in the elderly by perineal rectosigmoidectomy. Dis Colon Rectum 1992;35: 830–834.
17. Ramanujam PS, Venkatesh KS, Fietz MJ. Perineal excision of rectal procidentia in elderly high-risk patients. A ten-year experience. Dis Colon Rectum 1994;37: 1027–1030.
18. Porter NH. Collective results of operations for rectal prolapse. Proc R Soc Assoc Med 1962;55:1087–1091.
19. Hughes ESR. In discussion on rectal prolapse. J R Soc Med 1949;42:1007–1011.
20. Johansen OB, Wexner SD, Daniel N, Nogueras JJ, Jagelman DG. Perineal rectosigmoidectomy in the elderly. Dis Colon Rectum 1993;36:767–772.
21. Agachan F, Reissman P, Pfeifer J, Weiss EG, Nogueras JJ, Wexner SD. Comparison of 3 perineal procedures for the treatment of rectal prolapse. South Med J 1997; 90(9):925–932.
22. Delorme R. Sur le traitement des prolapssu du rectum totaux pour l'excision de la musqueuse rectale ou rectocolique. Bull Mem Soc Chir Paris 1900;26:498–499.
23. Sielezneff I, Malouf A, Cesari J, Brunet C, Sarles JC, Sastre B. Selection criteria for internal rectal prolapse repair by Delorme's transrectal excision. Dis Colon Rectum 1999;42:367–373.
24. Wyatt AP. Perineal rectopexy for rectal prolapse. Br J Surg 1981;68:717–719.
25. Gordon PH, Hoexter B. Complications of the Ripstein procedure. Dis Colon Rectum 1978;21:277–280.
26. Plusa SM, Charig JA, Balaji V, Watts A, Thompson MR. Physiological changes after Delorme's procedure for full-thickness rectal prolapse. Br J Surg 1995;82:1475–1478.
27. Duthie GS, Bartolo DC. Abdominal rectopexy for rectal prolapse: a comparison of techniques. Br J Surg 1992; 79:107–113.
28. Farouk R, Duthie GS. The evaluation and treatment of patients with rectal prolapse. Ann Chir Gynaecol 1997;86:279–284.
29. Siproudhis L, Ropert A, Gosselin A, et al. Constipation after rectopexy for rectal prolapse. Where is the obstruction? Dig Dis Sci 1993;38:1801–1808.

21

Constipation and Rectal Prolapse

Michael R.B. Keighley

There are many excellent reviews of the surgical treatment of rectal prolapse, but there are few that have specifically addressed the issue of constipation in rectal prolapse patients.

It is worth remembering that almost every patient with a rectal prolapse has some abnormality of bowel function. Whether the abnormality of bowel function is the cause of the prolapse or whether the functional bowel abnormality is a consequence of the prolapse is difficult to say.

Constipation in Rectal Prolapse

Etiology

Rectal prolapse is considered by most authorities to be a true intussusception of the rectum through the pelvic floor and sphincters. Videoproctographic studies clearly demonstrate the apex of a rectal prolapse descending through the ampulla of the rectum and through the puborectalis swing to appear inside the anal canal and subsequently on the perineum as a rectal prolapse.

Intussusception

It is unknown whether an intussusception subsequently develops into a full-thickness rectal prolapse. Studies on the long-term natural history of intussusception indicate that some patients do ultimately develop full-thickness rectal prolapse.

Intussusception is commonly associated with chronic straining due to a feeling of incomplete evacuation of the rectum, causing straining and in time possibly the development of a full-thickness rectal prolapse.

There is no doubt that intussusception is commonly associated with obstructed defecation, purely on the basis of mechanics. Thus, the intussusception fills the lumen of the rectum and prevents normal evacuation. It is quite likely that there are some patients who have a primary problem of colonic inertia and impaired rectal emptying who, as a result of straining, develop an incomplete intussusception, which exacerbates the constipation. Hence, it is likely that a small proportion of patients with rectal prolapse have a primary abnormality of colonic transit and rectal emptying, leading to an intussusception, which subsequently forms into a full-thickness rectal prolapse.

Schultz and colleagues[1] compared the results of Marlex rectopexy in 46 patients with a full-thickness rectal prolapse to 29 with an intussusception. A much higher proportion of patients with intussusception developed deteriorating constipation compared with the prolaspe group (Table 21.1).

Associated Constipation

A careful history in patients with rectal prolapse indicates that between 30% and 45% of women suffering from full-thickness rectal prolapse have constipation.[2–8] Often there is a history of incomplete rectal evacuation. It is more common, however, to elicit a history of fecal incontinence in patients with rectal prolapse, as approximately 70% of women with a full-thickness rectal prolapse suffer bowel

Table 21.1. Functional results of rectopexy: comparing prolapse with incomplete intussusception[1]

	Rectal prolapse ($n = 46$)	Incomplete intussusception ($n = 29$)
Rectal emptying		
Improved	17	4
Unchanged	21	12
Deteriorated	8	13
Bowel incontinence		
Improved	20	7
Unchanged	16	8
Deteriorated	10	4

incontinence, with urgency, imperfect control of flatus, soiling, and poor bowel control, particularly if there is associated straining.[4,9–13]

Investigation in Rectal Prolapse Patients

Investigation in patients who have full-thickness rectal prolapse can be notoriously difficult. Colonic transit marker studies may be performed to assess the presence of colonic inertia, but they should probably be repeated, as a single study may be unreliable. Between 30% and 50% of women with full-thickness rectal prolapse have associated impaired colonic transit[14]; this incidence may be even higher in men.

Videoproctography is remarkably difficult to interpret in patients with rectal prolapse. There is nearly always an intussusception, and a full-thickness rectal prolapse can usually be demonstrated. The presence of the intussusception or the prolapse may mask underlying impaired rectal evacuation. Thus, interpretation of videoproctography as a means of identifying the proportion of prolapse patients who also have impaired rectal emptying may be difficult.[15]

History

A good clinical history is probably the most important single investigation. Patients will tell you whether or not they have to strain to evacuate. Patients will also be able to identify if they have infrequent evacuation with relatively normal emptying. If a patient has a history of chronic laxative use with difficulty evacuating, concomitant colectomy may be seriously considered.[16] In patients with laxative dependence, constipation is often worsened following abdominal rectopexy.[13] Thus, if colonic inertia is identified, a subtotal colectomy with ileoproctostomy may be indicated. Similarly, finding a symptomatic third-degree sigmoidocele with otherwise normal colonic transit may warrant a synchronous sigmoid colectomy.

A word of warning is needed with respect to resection rectopexy. Fixation of the prolapse and coexisting resection of the sigmoid may control the prolapse and normalize constipation, but if an excessively long left-sided colonic resection is performed, there may be a risk of precipitating incontinence. Most rectal prolapse patients have a patulous anus associated with low resting and squeeze pressures.[4] There is a fine line between postoperative continence with some constipation and incontinence but control of the prolapse with elimination of constipation. Thus, resection rectopexy should be reserved for patients with a clear history of preoperative constipation where there have been no factors that may have weakened the sphincter. Moreover, clinical examination, anal manometry, and anal ultrasonography should all reveal satisfactory findings.

Thus, the thrust of preoperative investigations in rectal prolapse patients is not only to determine colonic transit and impaired rectal evacuation, but also to assess whether the sphincters are strong enough to withstand the consequences of a colonic resection. Although this is an important warning note, the data seemed to indicate that resection rectopexy has no deleterious effect on either resting or squeeze anal canal pressure compared with rectopexy alone. Furthermore, the incidence of persistent incontinence is no greater after resection rectopexy compared with resection rectopexy alone (Table 21.2). In fact, the incidence of postoperative constipation is superior after resection rectopexy as compared to rectopexy alone.[17,18] Two prospective randomized studies revealed superior function after resection rectopexy as compared to rectopexy alone. Specifically, Luukkonen and coworkers[17] prospectively randomized 30 patients between abdominal rectopexy and sigmoid resection versus rectopexy alone. While constipation

Table 21.2. Functional outcome: rectopexy versus resection rectopexy[13]

	Constipation		Incontinence	
	Preop	Postop	Preop	Postop
Rectopexy ($n = 129$)	47 (36)	42 (33)	48 (37)	25 (19)
Resection rectopexy ($n = 18$)	12 (67)	2 (11)	5 (28)	3 (17)

Values in parentheses are percentages.

disappeared in three patients after resection rectopexy and in two other patients after rectopexy alone, it became considerably worse in five additional patients who had rectopexy alone, one of whom required a colectomy. The authors noted that although surgery did not significantly change colonic transit times and did seem to increase operative morbidity, sigmoid colectomy did diminish postoperative constipation specifically, causing less obstruction.

In a similar study, McKee and associates[18] prospectively randomized 18 patients with full-thickness rectal prolapse to rectopexy with or without sigmoid colectomy. Using postoperative colonic transit studies, the authors noted that after rectopexy alone there was a statistically significantly higher number of patients who developed postoperative marker delay as compared to patients after sigmoid colectomy with rectopexy. Anorectal physiologic investigation may have helped provide some answers to this difference, in that patients following rectopexy alone had a significantly higher rectal compliance than did patients after resection rectopexy. The authors have hypothesized that the redundant sigmoid colon may have delayed passage of the intestinal contents and caused kinking at the junction of the sigmoid and rectum.

Risk Factors for Constipation

The principal risk factor for constipation after rectopexy for rectal prolapse is young age.[19] Young patients have a high rate of recurrence, and the majority have been constipated for most of their lives. In the majority of these young people rectal prolapse is secondary to a long history of chronic straining.

Thus, young people with a rectal prolapse should be thoroughly investigated. In this group, not only should there be an assessment of colonic transit, but it would be wise to assess small-bowel transit and even gastric emptying as well, as some of these patients have a panenteric myopathy or neuropathy. These are a group of patients in whom electromyography (EMG) assessment of puborectalis activity during straining might identify patients with anismus in whom results are likely to be poor. Panenteric inertia may preclude any resection and pelvic outlet obstruction may be amenable to biofeedback or botulinum toxin injection.

Other risk factors for postoperative constipation are (1) patients with gross perineal descent, (2) patients who admit to a history of straining, and (3) patients with a coexisting solitary rectal ulcer.

Advice Regarding Primary Treatment for Prolapse in Patients with a History of Constipation or Impaired Evacuation Without Colonic Inertia or Megacolon

Resection rectopexy may be strongly recommended in most of these patients. All the evidence points to the fact that resection rectopexy has a lower incidence of postoperative constipation compared with rectopexy alone.

The literature suggests that the rectopexy should be sutured and that a foreign material should be avoided. The incidence of constipation is much higher if Marlex or Ivalon or other foreign materials are used for fixation of the rectum (Table 21.3).

Table 21.3. Continence and constipation after rectopexy and alternative procedures

Reference	Operation	Same	Improved	Worse	New Onset
Kimm et al (1999) ($n = 44$)[6]	Resection rectopexy	45	52	NS	NS
Aitola et al (1999) ($n = 50$)[7]	Rectopexy	16	8	6	22
Sayfan et al (1990) ($n = 57$)[5]	Rectopexy	40	24	NS	24
Lechaux et al (2001) ($n = 35$)[8]	Resection rectopexy	6	47	3	0
Holmstrom et al (1986) ($n = 108$)[9]	Ripstein 27 (foreign material)	NS	NS	43	NS
Klaaborg et al (1985) ($n = 23$)[11]	Roscoe Graham (suture)	27	NS	NS	30
Watts et al (1985) ($n = 138$)[2]	Ivalon rectopexy + sigmoid colectomy	35	56	9	0
Mann and Hoffman 1988 ($n = 66$)[3]	Ivalon rectopexy alone	29	NS	NS	47
Yoshioka et al (1989) ($n = 135$)[4]	Ivalon rectopexy alone	24	0	22	18
Sayfan et al (1990) ($n = 13$)[5]	Sutured and sigmoid colectomy	8	31	0	0

NS, not stated.

Table 21.4. Randomized trial of sponge versus sutured rectopexy (no resections)[20]

	Ivalon sponge ($n = 31$)	Sutured alone ($n = 32$)
Hospital stay (days)	14 (8–52)	14 (8–50)
Mortality	0	0
Complications	6 (19%)	3 (9%)
Recurrent prolapse	1 (3%)	1 (3%)
Late postoperative incontinence	6/10	2/10
Postop constipation	15 (48%)	10 (31%)

Anterior rectopexy (Ripstein procedure) would also be contraindicated in patients with a history of constipation. The incidence of constipation after anterior rectopexy, even without stenosis, is very high, and there is a risk of mechanical stricturing as well.

A randomized controlled trial comparing Ivalon rectopexy with sutured rectopexy reported a lower incidence of constipation when the foreign body was avoided (Table 21.4).[20]

Perhaps the most difficult question to answer is how much colon to remove. Usually in resection rectopexy the sigmoid is removed so that the large bowel is straight between the descending colon and the rectum, with some bowstringing as a consequence of the rectopexy. Some data would support a subtotal colectomy in a patient with colonic inertia where anal sphincter anatomy and function are satisfactory and where there is no history of incontinence.

Constipation After Rectopexy in Patients Who Have Had No Apparent Constipation Beforehand

The other major consideration in rectal prolapse surgery is the risk of rendering patients constipated after the operation.

Factors that seem to increase the risk of constipation for the first time after rectopexy are age under 40, the use of mesh, anterior rectopexy, avoidance of resection, and the use of an open operation as opposed to laparoscopic rectopexy and division of the lateral stalks.[22]

The problem with postoperative constipation after rectopexy is that it is very difficult to predict who will become constipated and thus in whom concomitant resection would be justified.

To help avoid disappointed patients, it is crucially important to warn patients that rectopexy might conceivably precipitate or exacerbate constipation. Similarly, they should have these same expectations about new or preexisting fecal incontinence.

Laparoscopic Rectopexy

All the evidence suggests that open rectopexy, particularly with mesh, has a 20% to 40% risk of causing constipation. Recent data suggest that the incidence of constipation is probably reduced by laparoscopic rectopexy, even without a resection, and that the number who develop constipation for the first time is also small (Table 21.5).[21–25]

Treatment Implications

Warning About Risk

The key messages are that patients having a rectopexy, even if they do not suffer from any preoperative constipation, should be warned about the risks of postoperative constipation. Furthermore, the majority of these patients should be offered a resection rectopexy on the grounds that this does not in any way increase the risk of incontinence while reducing the incidence

Table 21.5. Laparoscopic rectopexy

						Constipation		
	No.	Mortality	Recurrence	Hospital stay (days)	Resection	Before	After	New onset
Bruch et al (1999)[22]	72*	0	0	15 (6–47)	40	37	8	4
Stevenson et al (1998)[21]	34	1	0	5 (3–66)	30	14	5	2
Boccasanta et al (1999)[25]	10	0	1	7 (5–12)	0	1	1	0
Heah et al (2000)[23]	25	0	0	7 (3–23)	0	9	9	2
Solomon et al (2002)[24]	20	0	0	4 (3–6)	0	Visual analogue scale only		

* 22% rendered incontinent or incontinence worse after operation.

of postoperative constipation. Division of the lateral stalks will reduce the incidence of postoperative recurrence at the expense of increasing the incidence of postoperative constipation. A prospective randomized study was undertaken including 26 patients with full-thickness rectal prolapse.[26] Fourteen patients had rectopexy with and 12 without division of the lateral ligaments. Incontinence improved in both groups of patients; however, the authors note that division of the lateral ligaments statistically significantly increased the number of patient with postoperative constipation. While three patients had preoperative constipation, 10 patients suffered postoperative constipation in this latter group. Although mean anal canal pressures were higher after surgery in all patients in the study, sensory thresholds significantly increased in those in whom the ligaments had been divided but not in those in whom they had been preserved. However, these benefits of preservation of the lateral stalk were at the expense of an increased rate of recurrence, as prolapse recurred in six patients in whom the stalks were not divided, but did not recur in any of the 12 patients in whom the ligaments were divided. Therefore, there seems to be a balance between improved function but a worsened outcome relative to recurrence when the ligaments were divided. Conversely, there was a low rate of recurrence, although at the expense of a higher rate of constipation when the ligaments are divided. Surgeons should consider these variables and discuss them with the patient prior to surgery for rectal prolapse.

Laparoscopic Procedures

To date, the results of laparoscopic rectopexy and resection rectopexy seem to be associated with less constipation than open rectopexy alone. Thus, laparoscopic treatment should be encouraged, provided the recurrence rates remain low.

All patients who develop postoperative constipation should be investigated by colonic transit studies and probably also by small-bowel transit studies, videoproctography, and anal manometry and contrast enema. These studies should help identify both physiologic and anatomic causes of constipation.

If the original operation was rectopexy alone, then subsequent sigmoid resection might be contemplated as a secondary procedure. Conversely, sigmoid colectomy alone is unlikely to resolve the problems of persistent constipation, and a high proportion of these individuals require a subtotal colectomy and ileorectal anastomosis. Thus, the majority of patients with constipation after a previous rectopexy, after appropriate counseling and investigation, are likely to be offered some form of subtotal colectomy, provided that their sphincter anatomy and function are satisfactory and provided that the preoperative tests do not indicate a high risk of incontinence.

References

1. Schultz I, Mellgren A, Dolk A, Johansson C, Holmstrom B. Long-term results and functional outcome after Ripstein rectopexy. Dis Colon Rectum 2000;43:35–43.
2. Watts JD, Rothenberger DA, Buls JG, Goldberg SM, Nivatvongs S. The management of procidentia: 30 years experience. Dis Colon Rectum 1985;28:96–102.
3. Mann CV, Hoffman C. Complete rectal prolapse: the anatomical and functional results of treatment by an extended abdominal rectopexy. Br J Surg 1988;75:34–37.
4. Yoshioka K, Hyland G, Keighley MRB. Anorectal function after abdominal rectopexy: parameters of predictive value in identifying return of continence. Br J Surg 1989;76:64–68.
5. Sayfan J, Pinho M, Alexander-Williams J, Keighley MRB. Sutured posterior abdominal rectopexy with sigmoidectomy compared with Marlex rectopexy for rectal prolapse. Br J Surg 1990;77:143–145.
6. Kimm DS, Tsang CBS, Wong WD, Lowry AC, Goldberg SM, Madoff RD. Complete rectal prolapse. Evolution of management and results. Dis Colon Rectum 1999;42:460–469.
7. Aitola PT, Hiltunen K-M, Matikainen MJ. Functional results of operative treatment of rectal prolapsae over an 11 year period. Dis Colon Rectum 1999;42:655–660.
8. Lechaux JP, Atienza P, Goasguen N, Lechaux D, Bars I. Prosthetic rectopexy to the pelvic floor and sigmoidectomy for rectal prolapse. Am J Surg 2001;182:465–469.
9. Holmstrom B, Broden G, Dolk A. Results of the Ripstein operation in the treatment of rectal prolapse and internal rectal procidentia. Dis Colon Rectum 1986;29:845–848.
10. Mortensen NJ McC, Vellacott KD, Wilson MG. Lahaut's operation for rectal prolapse. Ann R Coll Surg Engl 1984;66:17–18.
11. Klaaborg KE, Qvist N, Kongburg O. Rectal prolapse and anal incontinence treated with a modified Roscoe Graham operation. Dis Colon Rectum 1985;28:582–584.
12. Schlinkert RT, Beart RW, Wolf BG, Pemberton JH. Anterior resection for complete rectal prolapse. Dis Colon Rectum 1985;28:409–412.
13. Tjandra JJ, Fazio VW, Church JM, Milsom JW, Oakley JR, Lavery IC. Ripstein procedure is an effective treatment

for rectal prolapse without constipation. Dis Colon Rectum 1993;36:501–507.
14. Preston DM, Lennard-Jones JE. Does failure of bisacodyl induced colonic peristalsis indicate intrinsic nerve damage? Gut 1983;23:A891.
15. Shorvon PJ, McHugh S, Diamant NE, Somers S, Stevenson GW. Defecography in normal volunteers: results and implications. Gut 1989;30:1737–1749.
16. Huber FT, Stein H, Siewert JR. Functional results after treatment of rectal prolapse with rectopexy and sigmoid resection. World J Surg 1995;19:138–143.
17. Luukkonen P, Mikkonen U, Jarvinen H. Abdominal rectopexy with sigmoidecctomy vs rectopexy alone for rectal prolapse: a prospective randomized study. Int J Colorectal Dis 1992;7:219–222.
18. McKee RF, Lauder JC, Poon FW, Aitchison MA, Finlay IG. A prospective randomized study of abdominal rectopexy with and without sigmoidectomy in rectal prolapse. Surg Gynecol Obstet 1992;174:145–148.
19. Boulos PB, Stryker SJ, Nicholls RJ. The long term results of polyvinyl alcohol (Ivalon) sponge for rectal prolapse in young patients. Br J Surg 1984;71:213–214.
20. Novell JR, Osborne MJ, Winslet MC, Lewis AAM. Prospective randomized trial of Ivalon sponge versus sutured rectopexy for full-thickness rectal prolapse. Br J Surg 1994;81:904–906.
21. Stevenson ARL, Stitz RW, Lumley JW. Laparoscopic-assisted resection-rectopexy for rectal prolapse: early and medium follow up. Dis Colon Rectum 1998; 41:46–54.
22. Bruch H-P, Herold A, Schiedeck T, Schwandner O. Laparoscopic surgery for rectal prolapse and outlet obstruction. Dis Colon Rectum 1999;42:1189–1195.
23. Heah SM, Hartley JE, Hurley J, Duthie GS, Monson JRT. Laparoscopic suture rectopexy without resection is effective treatment for full-thickness rectal prolapse. Dis Colon Rectum 2000;43:638–643.
24. Solomon MJ, Young CJ, Eyers AA, Roberts RA. Randomized clinical trial of laparoscopic versus open abdominal rectopexy for rectal prolapse. Br J Surg 2000;89:35–39.
25. Boccasanta P, Venturi M, Reitano MC, et al. Laparotomic vs. laparoscopic rectopexy in complete rectal prolapse. Dig Surg 1999;16:415–419.
26. Speakman CTM, Madden MV, Nicholls RJ, Kamm MA. Lateral ligament division during rectopexy causes constipation but prevents recurrence: results of a prospective randomized study. Br J Surg 1991;78:1431–1433.

22

Laparoscopic Surgery for Rectal Prolapse

Ara Darzi and Yaron Munz

Rectal prolapse is regarded as a combined anatomic and functional disorder. This condition is usually accompanied by constipation or incontinence, thus requiring different treatment approaches.

Full-thickness rectal prolapse (FTRP) may be approached transabdominally, by rectopexy, by colonic resection, or by a combination of the two, or perineally, either by a Delorme's procedure or a perineal rectosigmoidectomy. Methods described for rectopexy entail a variety of slings, sutures, and even special screws, which are applied in different ways. All of these variations are amenable for the conventional open technique or the minimally invasive approach. The minimally invasive approach offers less postoperative pain, better cosmetic results, and shorter hospital stay, thus making it more appealing.[1] It is well recognized that performing laparoscopic colorectal surgery requires training and has a considerable learning curve. The advent of technology and the emergence of surgical robotics such as the Da Vinci telemanipulator, equipped with stereoptic vision and working tips with seven degrees of freedom, provide surgeons with dexterity enhancement and a shorter learning curve (Fig. 22.1). Thus, colorectal procedures (among others) can now be safely performed with results that are comparable to the conventional laparoscopic technique, using skills acquired in a much shorter period of time.[2]

This chapter summarizes the current data available on surgical management of full-thickness rectal prolapse, highlighting the basic steps in each of the major laparoscopic procedures. This review is intended to provide an idea of the minimally invasive or the laparoscopic approach and its use in patients with rectal prolapse.

Preoperative Investigations and Management

Preoperative investigations are important to ensure that patients receive the appropriate treatment or procedure. Flexible sigmoidoscopy or colonoscopy is necessary to exclude any possibility of a malignant or benign lesion that may act as a lead point for intussusception. In addition, other conditions such as solitary rectal ulcer, suggestive of internal rectal prolapse, should be excluded.

Prolonged constipation prior to rectal prolapse is suggestive of colonic inertia, thus mandating a combined approach of resection with rectopexy.[3–5] In patients with suspected incontinence, anal ultrasonography, manometry, and pudendal nerve latency tests should be performed prior to the procedure. It is suggested that these patients would benefit mostly from a suture rectopexy without the addition of bowel resection.[6] These tests may be of some predictive value and serve as a point of reference in monitoring postoperative improvement. Also, they may dictate the preference of one method over the other.

The objectives of the surgical treatment are to eliminate the rectal prolapse and improve any condition associated with it; thus it is up to the surgeon to decide what should be the most appropriate course of investigation and surgical management.

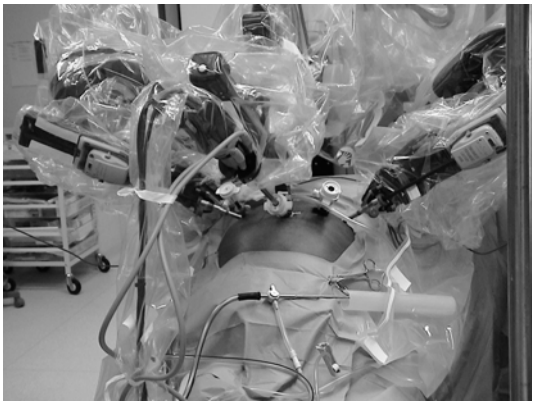


Figure 22.1. Port positioning for robotic-assisted laparoscopic suture rectopexy. The patient is placed in the lithotomy Trendelenburg position to accommodate the robotic slave-cart. Ports are placed similarly to the conventional laparoscopic procedure. The surgeon is seated at the master console, equipped with stereoptic vision and working tips with seven degrees of freedom of motion. (Courtesy of St. Mary's Hospital, London, UK, 2002.)

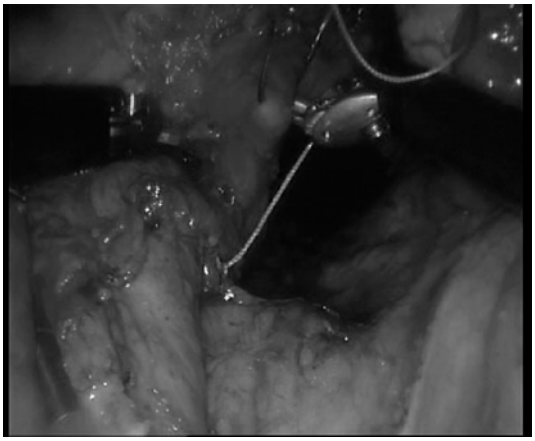


Figure 22.2. Robotic-assisted suturing of the mesorectum to the sacral promontorium. Stereoscopic vision together with powerful magnification and wrist-like working tips provide the surgeon with marked enhancement of dexterity, making intracorporeal suturing and knot tying as easy as if it were performed by hand. Two sutures only are placed fixing the posterior rectum to the sacrum. (Courtesy of St. Mary's Hospital, London, UK, 2002.)

Laparoscopic Suture Rectopexy

The laparoscopic approach provides improved visibility and magnification within the confines of the pelvic space, where important structures such as the ureters and the hypogastric nerves run. In the posterior approach (most commonly practiced) the posterior part of the rectum is fixed to the sacral promontory.

The patient is placed in the supine position and anesthetized. Then the procedure is begun. Initially a 10-mm port is inserted at the umbilicus, and pneumoperitoneum is achieved. Then, two additional working ports are positioned, a 10-mm port on the right and slightly caudal to the umbilicus and a 5-mm port to the left of the umbilicus. Before the dissection is carried out, any organ that may come in the way is pulled out of the pelvis and if needed tacked in to the abdominal wall. Dissection begins at the right side medially to the right ureter. Once the peritoneum is cut, gas infiltrates into the retrorectal space, thus simplifying the dissection, and providing an avascular plane. Dissection is continued down to the pelvic floor, dividing the lateral stalks while avoiding contact with the sacral nerves. Dissection is continued anteriorly and posteriorly to the rectum and is completed on the left side. Now the rectum is fully mobilized down to the pelvic floor, and once it is retracted out of the pelvis, nonabsorbable sutures are inserted at both sides of the posterior third of the rectal circumference fixing it to the sacral promontory. No more than two stitches are needed and the procedure is completed (Fig. 22.2). This procedure is relatively simple to perform and can often be successfully undertaken even in the hands of the noncolorectal specialist surgeon. Relatively good postoperative functional results are in favor of this procedure as long as careful patient selection is applied.[7]

Laparoscopic Anterior Resection

The idea behind this approach is that resection of redundant bowel reduces postoperative constipation while fibrosis associated with the healing process of the anastomosis will fix the bowel to the sacrum. However, this approach is subjected to higher morbidity due to an increased risk for anastomotic leakage (2–12%). Technically, this procedure is more demanding when attempted laparoscopically.

The patient is positioned in the modified Lloyd Davis position with the legs slightly flexed.

Port positioning is the same as previously mentioned, and additional ports are placed in the right side to allow the use of endo-staplers and other instruments such as the harmonic scalpel.

Once the redundant bowel is identified, dissection is started from left lateral toward the center, avoiding damage to the left ureter. The mesentery of the sigmoid colon is then divided using the harmonic scalpel, and the blood vessels are stapled or sealed by the LigaSure device (Valleylub, Boulder, Co). The distal end of the resection is set at the level of the rectosigmoid junction or lower, if needed. The bottom end is then divided using an endo-stapler, and thus the majority of the procedure is completed. Next, the dissected bowel is delivered out of the abdomen through a small left lower abdominal incision and the resection is completed. The anvil of the end-to-end anastomotic stapler is placed and secured in the proximal end, and the bowel is returned to the abdominal cavity. The abdominal wound is closed and pneumoperitoneum is reestablished.

Before reuniting the bowel ends, attention is paid to ensuring a tension-free anastomosis. The EEA stapler is then transanally introduced and the anastomosis is performed. The procedure is completed after the anastomosis is tested for airtightness. Although relatively standard, anterior resection is generally regarded as insufficient as a stand-alone procedure, and most surgeons would advocate completion with a rectopexy of some sort.[8]

Laparoscopic Rectopexy and Sigmoid Resection

The combined procedure follows the principle of providing remedial surgical treatment for each of the disorders/malfunctions in the proposed mechanism of full-thickness rectal prolapse. This procedure entails full mobilization of the rectum without division of the lateral stalks and followed by a posterior rectopexy, fixing the rectum to the sacral promontory.

Before the resection of the redundant large bowel, the endopelvic fascia is anteriorly sutured to the rectum, thereby obliterating the pouch of Douglas. Resection of large bowel can include just a redundant sigmoid loop or be extended to as much as a subtotal colectomy in cases of proven colonic inertia. From the technical point of view this procedure is not much different from the procedures mentioned above and can be carried out safely using the laparoscopic approach.[9–11]

Postoperative Outcome

Evaluation of the postoperative outcome of surgical treatment for rectal prolapse is based not only on morbidity and recurrence rates but also on functional outcome.[12] There are a large variety of surgical solutions for this disorder, suggesting that no single solution can provide 100% of success.

At the moment there are not enough data to support or refute any of the procedures; thus we have to make our decisions regarding the preferred type of procedure based on clinical and laboratory evidence, combined with results from the current literature.[13] It is believed that postoperative constipation is attributed primarily to the preoperative condition of the patient, the type of rectopexy chosen, whether or not the lateral stalks were divided, and whether or not the procedure included bowel resection.[14]

A prolonged history of constipation prior to the operation would suggest colonic inertia, possibly mandating bowel resection in combination or without rectopexy. Conversely there are not enough data to support preservation of the lateral stalks, although there is a sound theoretical basis to support it. When addressing incontinence in these patients, there is a 50% to 75% postoperative improvement.[15] It is generally accepted that in patients suffering from significant incontinence, rectopexy without resection should be preferred. If continence is not improved postoperatively there are a range of treatments that can be offered to the patients such as biofeedback and sphincter repairs.

Addressing recurrence rates after the different procedures mentioned above reveals a confusing pattern. Apparently, more physiologically appropriate solutions are characterized by a relatively higher recurrence rate compared to less physiologically suitable procedures with lower recurrence rates. Suture rectopexy with lateral stalks division is associated with a 2% to 6% recurrence rate, whereas when the lateral stalks are preserved the recurrence rate rises to 10%. Resection procedures are characterized by even higher recurrence rates, up to 12%, and are also subjected to the risk of anastomotic leakage.

Conclusion

After carefully reviewing the current literature it is clear that at present there are not enough data to accept an ideal approach for the surgical treatment of full-thickness rectal prolapse. There is a need for longitudinal, structured, and standardized studies and randomized clinical trials comparing the different methods of surgery, thus putting to the test theoretical mechanisms suggested as the cause of this disorder. Conversely, there are enough data to support the use of the minimally invasive approach in appropriately selected patients. This method provides the surgeon with means that enhance vision and therefore accuracy. There is no doubt that mastering the skills required for laparoscopic colorectal surgery may take years; however, once surgeons have completed their learning phase, the advantages to patients as well as to health care services are tremendous.[16,17] As all the abdominal procedures included in the surgical armamentarium for rectal prolapse are amenable for the laparoscopic approach, these should become the methods of choice, performed in centers of excellence around the world, thus providing the best of care combined with the highest level of patient safety.

It is clear that sound clinical judgment and strict criteria for patient selection are the key factors for success in any surgical procedure, as it is in the case of rectal prolapse. Therefore, it was not the intention of the authors to recommend or dismiss any of the suggested procedures, but rather to provide readers with sufficient data for selection of the most appropriate procedure for their patients.

References

1. Rose J, Schneider C, Scheidbach H, et al. Laparoscopic treatment of rectal prolapse: experience gained in a prospective multicenter study. Langenbecks Arch Surg 2002;387:130–137.
2. Munz Y, Moorthy K, Kodchanndka R, et al. Robotic assisted suture rectopexy. Am J Surg 2004;187(1):88–92.
3. Berman IR, Manning DH, Harris MS. Streamlining the management of defecation disorders. Dis Colon Rectum 1990;33:778–785.
4. Madbouly KM, Senagore AJ, Delaney CP, Duepree HJ, Brady KM, Fazio VW. Clinically based management of rectal prolapse. Surg Endosc 2003;17:99–103.
5. Benoist S, Taffinder N, Gould S, Chang A, Darzi A. Functional results two years after laparoscopic rectopexy. Am J Surg 2001;182:168–173.
6. Briel JW, Schouten WR, Boerma MO. Long-term results of suture rectopexy in patients with fecal incontinence associated with incomplete rectal prolapse. Dis Colon Rectum 1997;40:1228–1232.
7. Heah SM, Hartley JE, Hurley J, Duthie GS, Monson JR. Laparoscopic suture rectopexy without resection is effective treatment for full-thickness rectal prolapse. Dis Colon Rectum 2000;43:638–643.
8. Ignjatovic D, Bergamaschi R. Preserving the superior rectal artery in laparoscopic [correction of laparoscopis] anterior resection for complete rectal prolapse. Acta Chir Iugosl 2002;49:25–26.
9. Baker R, Senagore AJ, Luchtefeld MA. Laparoscopic-assisted vs. open resection. Rectopexy offers excellent results. Dis Colon Rectum 1995;38:199–201.
10. Bachoo P, Brazzelli M, Grant A. Surgery for complete rectal prolapse in adults. Cochrane Database Syst Rev 2000;CD001758.
11. Bruch HP, Herold A, Schiedeck T, Schwandner O. Laparoscopic surgery for rectal prolapse and outlet obstruction. Dis Colon Rectum 1999;42:1189–1194.
12. Aitola PT, Hiltunen KM, Matikainen MJ. Functional results of operative treatment of rectal prolapse over an 11-year period: emphasis on transabdominal approach. Dis Colon Rectum 1999;42:655–660.
13. Douard R, Frileux P, Brunel M, Attal E, Tiret E, Parc R. Functional results after the Orr-Loygue transabdominal rectopexy for complete rectal prolapse. Dis Colon Rectum 2003;46:1089–1096.
14. Mollen RM, Kuijpers JH, van Hoek F. Effects of rectal mobilization and lateral ligaments division on colonic and anorectal function. Dis Colon Rectum 2000;43:1283–1287.
15. Zittel TT, Manncke K, Haug S, et al. Functional results after laparoscopic rectopexy for rectal prolapse. J Gastrointest Surg 2000;4:632–641.
16. Marusch F, Gastinger I, Schneider C, et al. Experience as a factor influencing the indications for laparoscopic colorectal surgery and the results. Surg Endosc 2001;15:116–120.
17. Schlachta CM, Mamazza J, Seshadri PA, Cadeddu M, Gregoire R, Poulin EC. Defining a learning curve for laparoscopic colorectal resections. Dis Colon Rectum 2001;44:217–222.

23

Antegrade Continent Colonic Conduit

Marc A. Gladman, S. Mark Scott, and Norman S. Williams

The successful treatment of intractable constipation remains challenging. Standard conservative therapies such as oral laxatives, suppositories, retrograde enema techniques, and bowel retraining programs incorporating biofeedback techniques may fail to achieve adequate bowel emptying and resolution of symptoms in some patients, who may therefore seek a surgical solution. Although surgery has a role in the management of selected patients with severe constipation, some procedures have suboptimal long-term success rates.[1,2] Nevertheless, antegrade colonic irrigation, in which water or saline, with or without added aperients, is instilled via a catheter introduced into the proximal colon, may, in highly selected cases, provide an alternative method to improve rectal evacuation. This technique also promotes continence by ensuring regular bowel emptying, and thus is particularly useful in constipated patients with associated fecal (overflow) incontinence. This chapter outlines the evolution of methods of antegrade colonic irrigation for the treatment of constipation, and focuses on the relatively new procedure of the continent colonic conduit (CCC).[3]

Evolution of Antegrade Colonic Irrigation

Retrograde irrigation has been used successfully in the treatment of constipation for many years, particularly in patients with an inability to effectively evacuate rectal contents.[4] However, such methods may not reliably accomplish complete emptying in certain patients, and can lead to complications, including perforation[5–8]; this significant problem has prompted the search for alternative "washout" techniques.

The observed effectiveness of antegrade cleansing to prepare the bowel for surgery[9] and colonoscopy[10] encouraged the use of whole-gut irrigation for the treatment of constipation in elderly patients.[11] However, this technique, consisting of the delivery of copious volumes of isotonic saline via a nasogastric tube, is impractical for patients with constipation, and may be associated with significant absorption of fluid, causing electrolyte disturbances and intravascular expansion.[12]

Antegrade irrigation of the entire colon (as opposed to retrograde washout of the distal colon/rectum only, as with standard enemata) is frequently performed intraoperatively during emergency large-bowel surgery, and has been shown to be an effective method of ensuring successful colonic emptying.[13,14] Irrigation is traditionally undertaken via tubes inserted by way of a cecostomy or appendicostomy.[14,15] Using this principle, Malone et al[16] attempted to devise a method by which children with chronic fecal soiling (e.g., secondary to congenital abnormalities) could efficiently empty their lower bowel through regular fluid irrigation via a catheter inserted through an appendicostomy into the proximal colon. In 1990, they reported their experience with administration of antegrade washouts to prevent soiling in children with myelodysplasia. Use of this technique was subsequently extended to include the management of pediatric patients with intractable constipation,[17] because complete emptying of the colon may be expected to relieve such symptoms. The

Malone antegrade continence enema (ACE or MACE) involves the creation of an appendicostomy in the right iliac fossa using the Mitrofanoff principle[18] to provide a nonrefluxing channel that may be intermittently catheterized to perform the antegrade washout.[16] The appendicostomy is usually created during open surgery, although it may be laparoscopically constructed.[19]

In specialist centers, the ACE procedure has become an established treatment for children with fecal incontinence and constipation, and the literature suggests success rates of 60% to 79%.[20–24] The commonest overall cause for failure has been "washout failure," resulting in nonpassage of enema within 1 to 2 hours following administration.[22] However, complications affect up to 71% of patients. Stomal complications are most commonly encountered, with stenosis affecting 30%, and reflux affecting 7% of patients.[23] Pain or cramping during administration of enema has also been frequently observed (58%), and the repeated use of phosphate enemas can lead to phosphate toxicity.[21]

Following the success of the ACE procedure in pediatric patients with neurogenic and structural abnormalities of the hindgut, appendicostomy, allowing antegrade enema administration, was performed in adult patients with severe idiopathic constipation.[25,26] Hill et al[25] performed this procedure in six women with confirmed slow-transit constipation, three of whom had associated outlet obstruction. All patients were able to evacuate the colon within 1 hour of irrigation, and reported resolution or improvement of symptoms, although 50% of the women suffered with stomal stenosis.[25] Overall, however, this procedure may be somewhat less successful in adults compared to pediatric patients; success rates are reported as being 50% to 75% in adults with intractable constipation resulting from different etiologies.[27–29] Long-term problems are similar to those issues encountered with pediatric patients, and include pain or chills during administration of the enema, appendiceal stenosis and reflux of colonic contents, and irrigation fluid into the ileum.[27–30] Psychological morbidity has also been reported.[27]

Alternative procedures have been devised to achieve antegrade colonic irrigation when the appendix is absent. The Monti procedure, involving the formation of a segment of transversely tubularized ileum,[31] and ileocecostomy[32,33] have been performed as an alternative to appendicostomy to enable administration of antegrade enemas. Although there appears to be no difference in terms of success, or stomal complication rates between the two techniques,[34] if the appendix is present, its preferential use as the conduit has been advised, since it is not associated with the additional morbidity or operative time of a bowel anastomosis.

Other modifications have involved the insertion of skin-level devices in an attempt to reduce the morbidity of the standard procedure. Percutaneous or open placement of cecostomy tubes[35,36] and cecostomy buttons have been used.[37,38] More recently, particularly in relation to the management of obstructed defecation, percutaneous irrigation tubes, located endoscopically, have been inserted into the sigmoid colon in small numbers of patients, with reasonable success.[39,40] However, such devices have a finite life span, may become dislodged, and often get infected, resulting in troublesome superficial infections.[36,38]

The Continent Colonic Conduit

Rationale

The high risk and nature of the complications of the ACE, frequently necessitating repeat operation,[41] coupled with the fact that the appendix may be of too narrow a caliber to permit successful antegrade irrigation in adults, or absent due to surgical excision (as in up to 50% of women with constipation)[42] and a desire to avoid the infective complications and short life span of skin devices, led us to develop a new procedure—the continent colonic conduit.[3] This procedure involves the construction of a valved conduit using the colon through which the distal colon and rectum can be irrigated from above. The colonic conduit provides a channel leading from the skin to the colonic lumen that is capable of accommodating a 24-French (F) rectal catheter, unlike the appendiceal lumen, which only accepts much narrower catheters. A large-diameter catheter is preferable to generate the flow required to produce rectal evacuation in adults.[43]

When the technique was initially devised, conduits were placed in the sigmoid colon. This site was chosen so that the fluid did not have to travel the entire length of the colon, allowing the use of smaller volumes, and avoidance of abdominal pain and cramps.[44] It was also hoped that

distention of the distal colon would stimulate a more prompt and forceful contraction, and thus a faster evacuation.[39] More recently, conduits have been constructed in the transverse colon as this placement achieves superior results.[45] This maneuver still obviates the need to irrigate the entire colon, which we believe is unnecessary.[46] Indeed, radiologic studies in healthy volunteers have shown that it is only the descending colon and rectum that empty to any significant degree during defecation,[47–49] although concurrent mass movement of proximal colonic contents may occur.[48–50] Irrigation, therefore, of the transverse colon in patients with chronic constipation, in whom normal propulsive/expulsive movement within the left colon may be lost,[48,51,52] may potentially restore a more "physiologic" defecatory mechanism.

Patient Selection

The management of constipation is often complex, and antegrade enemas are indicated particularly for patients with structural (such as rectal agenesis)[53] and neuropathic abnormalities of the hindgut, and idiopathic constipation (particularly those individuals with obstructed defecation).[54] However, in common with other surgical procedures, the continent colonic conduit has its own inherent risks and complications. Therefore, it should be reserved for patients with intractable symptoms with severely impaired quality of life who have failed maximum medical and behavioral (bowel retraining/biofeedback) therapy, and who are desperate to avoid a permanent stoma. The modern management of patients with constipation in a specialist surgical unit involves a multidisciplinary team of professionals, reflecting the multifaceted approach to the different aspects of patient assessment, education, support, and treatment.

Preoperative Assessment

The success of the procedure ultimately lies in patient selection. Thus the importance of a thorough and comprehensive assessment cannot be stressed strongly enough when considering surgery.

As the pathophysiologic mechanisms underlying chronic intractable constipation may be multifactorial, we would recommend full anorectal physiologic investigation in all patients, including colonic transit studies,[55,56] evacuation proctography,[57,58] and rectal sensory testing[59,60] to accurately define abnormalities of function. Delayed colonic transit,[56,61] disordered rectal evacuation, secondary to a mechanical or "functional" obstruction[62–64] and rectal insensitivity (hyposensation),[64–66] all contribute to disturbed function, and occur either in isolation, or (frequently) in combination. Identification of whether the bowel is of normal caliber or dilated may also be of importance. It is essential to recognize that different pathophysiologic processes may result in similar, common presenting symptoms.[61,67] The relationship between specific pathophysiologic abnormalities and clinical outcome following CCC surgery has yet to be identified.

Preoperative Preparation

In addition to clinical assessment, due consideration should also be given to the evaluation of the cognitive and psychological status of potential candidates for surgery. Identical to the importance of thorough psychological assessment prior to colectomy for constipation, careful patient preparation is vital to a successful outcome, as a high level of input from patients is required. They must understand that the enema regimen requires individualization and may take several weeks and modifications to become successful, and thus preoperative counseling is imperative. Patients must also understand that there is a failure rate, and they may subsequently require a permanent standard stoma.

Patients are admitted before surgery for full bowel preparation. It is essential to empty the bowel preoperatively to facilitate easy postoperative irrigation[68] and to attempt to reduce morbidity related to infection.[43] The clinical nurse specialist should mark the position of the conduit aperture, usually in the right hypochondrium. Prophylactic antibiotics are administered perioperatively.

Operative Technique (Fig. 23.1)[69]

The patient is placed in the supine position, and a urinary catheter and nasogastric tube are inserted. Through a midline incision, the large

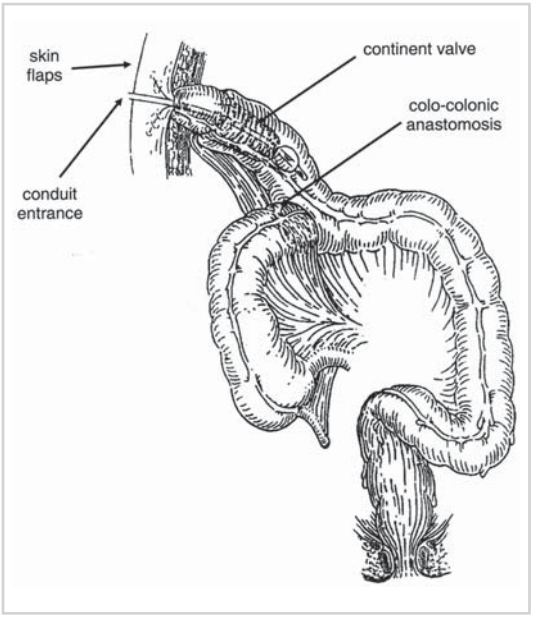


Figure 23.1. The continent colonic conduit. Reprinted from Keighley MRB, Williams NS (eds.). Constipation. In: Surgery of the Anus, Rectum and Colon, second edition. London: WB Saunders, 1999, pp 737–55, copyright 1999, with permission from Elsevier.

bowel is mobilized from the cecum to the proximal transverse colon. The conduit is usually performed at the hepatic flexure, and is marked using a Babcock forceps, and distally from here a 15-cm length of bowel is measured (Fig. 23.2A). The greater omentum is removed from this segment of colon, and where necessary, excess fat is removed from the mesocolon, taking care not to damage the mesenteric vessels. This defatting allows the colon to be intussuscepted during the formation of the valve. The ascending colon is transected approximately 15 cm from the ileocecal junction as previously marked, and 15 cm distally a 2-cm colotomy is made. A Babcock forceps is then passed retrograde through the colotomy and the full thickness of the colon is grasped 5 cm from the site of transection. The bowel is intussuscepted through the transverse colon and stabilized using longitudinal rows of nonabsorbable sutures and staples. The valve is a minimum of 5 cm long to prevent reflux of irrigant and colonic contents through the abdominal aperture.

A Silastic Foley catheter (14 F) is inserted from the open proximal end of the colon through the valve, and secured using two nonabsorbable purse-string sutures at the apex of the valve, leaving a 1-cm gap to allow intubation of the conduit. The catheter balloon is inflated and together with the valve is positioned back in the transverse colon through the colotomy, which is then closed using a continuous Maxon suture. The base of the valve is secured with circumferentially placed interrupted sutures from its external aspect to the afferent limb of the conduit to further protect against deintussusception of the valve. The afferent limb is narrowed using a linear stapler (Fig. 23.2B), the excess bowel is trimmed off and the staple line oversewn, to form the irrigation conduit.

An end-to-side anastomosis between the ascending and distal transverse colon is performed to restore intestinal continuity. At the aperture site, skin flaps forming an inverted wine-glass shape are fashioned (Fig. 23.3A), preserving subcutaneous tissue and thus an adequate vascular supply to prevent stenosis. The catheter and conduit are then passed through the abdominal wall without tension. A small V is then excised from the conduit wall, and its entrance sutured to the lateral skin flap (base of the wine glass; Fig. 23.3B). The arms of the skin flap are then sutured to the conduit entrance,

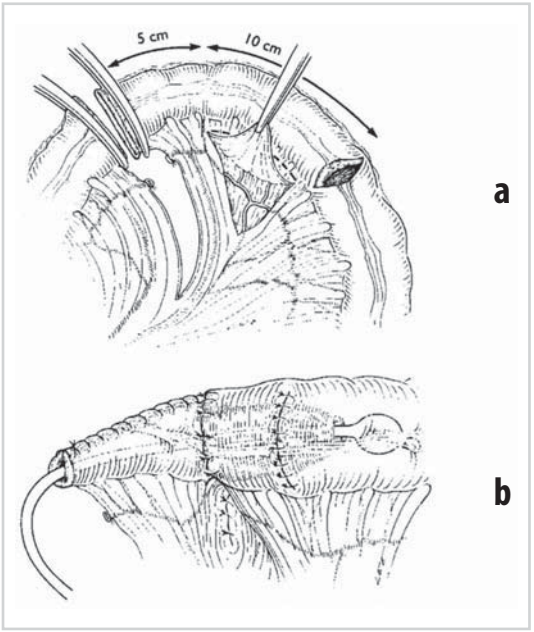


Figure 23.2. Creation of the conduit. a: Identification and preparation of conduit site at the hepatic flexure, with formation of transverse colotomy 15 cm distal to transection of the ascending colon. b: Appearance of the afferent limb of the conduit after narrowing by stapling, with intussuscepted conduit valve reinserted through the colotomy and stabilized with sutures. Reprinted from Keighley MRB, Williams NS (eds.). Constipation. In: Surgery of the Anus, Rectum and Colon, second edition. London: WB Saunders, 1999, pp 737–55, copyright 1999, with permission from Elsevier.

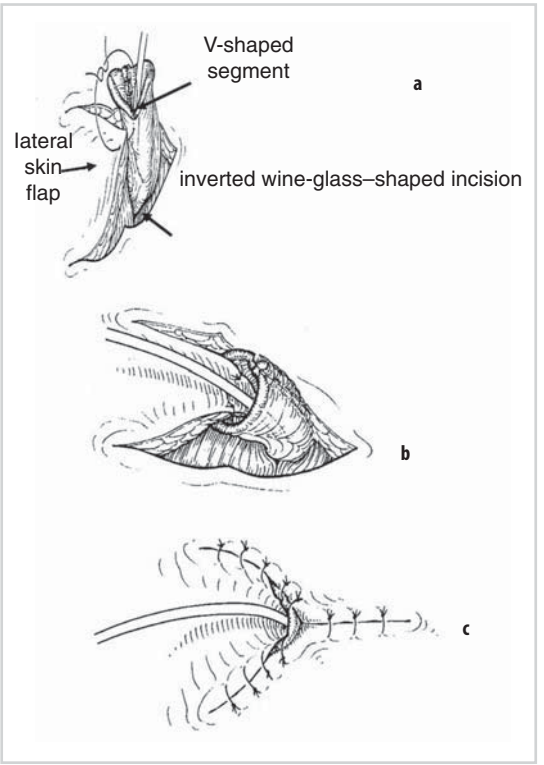


Figure 23.3. a–c: Formation of the conduit entrance, showing inverted wine-glass–shaped incision of the abdominal wall, through which the conduit is delivered, and sutured to the lateral skin flap following excision of a V-shaped segment from the afferent limb. Reprinted from Keighley MRB, Williams NS (eds.). Constipation. In: Surgery of the Anus, Rectum and Colon, second edition. London: WB Saunders, 1999, pp 737–55, copyright 1999, with permission from Elsevier.

forming a slightly recessed aperture that has an acceptable cosmetic appearance, minimizes leakage, and allows easy catheterization of the conduit (Fig. 23.3C). The abdomen is then closed and the catheter sutured to the abdominal wall to prevent dislodgement. Any coexistent anatomic abnormality of the rectum considered to significantly obstruct rectal emptying during preoperative proctographic assessment (functional rectocoele) can be repaired at the same time as conduit construction.[45]

Postoperative Care and Advice

A water-soluble contrast study, to confirm the integrity of the valve and colonic anastomosis, is performed between 7 and 10 days postoperatively via the catheter. Irrigation is then performed daily, via the catheter, using 1 to 1.5 L of tap water warmed to body temperature using a colostomy irrigation set. A teaching program is continued on a daily basis until patients feel sufficiently confident to undertake irrigation at home; they are then discharged. Four weeks following surgery, the indwelling catheter is removed, and the patient is taught to catheterize using a 24-F Rausch rectal catheter.[68] Continued patient education and support is provided by highly skilled nurses, who are essential to recovery and rehabilitation, and successful outcome.

Postoperative Evaluation

To date, we have reported the results of colonic conduit formation in 21 patients with constipation resistant to maximal medical therapy,[3,45] six patients who developed a severe rectal evacuatory disorder following electrically stimulated gracilis neosphincter (ESGN) surgery,[70,71] nine patients with fecal incontinence associated with difficulty in rectal evacuation,[44] and 14 patients with combined ESGN and CCC as part of total anorectal reconstruction for congenital abnormalities.[53] Initially, the sigmoid colon was the preferred site of conduit formation, but this was later abandoned in favor of the proximal transverse colon. Although regular rectal emptying was achieved with a sigmoid conduit,[3] longer term follow-up revealed poorer resolution of abdominal pain and bloating in comparison to patients with a transverse site of conduit placement[45]; indeed, most patients who underwent sigmoid CCC have now had their conduits excised, the majority of whom underwent end-ileostomy formation.[45] By comparison, the majority of patients with a transverse colonic conduit have achieved symptomatic relief with regard to abdominal pain and bloating, and reported rectal emptying to be equally impressive as those with a sigmoid conduit.[45]

Complications

Postoperative complications and morbidity appear equivalent to those encountered with the ACE procedure (see above). We have reported both minor (including superficial wound infection, slight stomal reflux) and major complications (including stomal stenosis or prolapse, and persistent reflux of gas or liquid contents through the conduit), the latter occurring in 14% to 28% of constipated patients,[45,70] sometimes

requiring either refashioning or excision of the conduit. Compatible with the ACE procedure, some patients also complain of abdominal cramping pains and dizziness during irrigation[70]; use of antispasmodics prior to administration of the irrigant has been advocated.[21] To date, excision of transverse conduits has occurred in one quarter of those patients with either chronic constipation or rectal evacuatory dysfunction secondary to ESGN surgery.[45,70] In those patients with a CCC as part of total anorectal reconstruction, 42% have eventually been excised because of refractory incontinence. Notably, however, failure in this group was significantly associated with severe perineal sepsis, resulting in anal stenosis and scarring, and reduced neo-anal compliance, and thus was not as a consequence of poor CCC function per se.[53]

Clinical Outcome

In patients with chronic intractable constipation, effective evacuation is achieved with a transverse CCC, with complete symptom resolution of abdominal pain and bloating in 71% and 78%, respectively.[45] In the majority (70%) of patients who developed a severe rectal evacuatory disorder following ESGN surgery, no further aids were required to effect complete evacuation. In addition, continence was significantly improved following CCC construction, with 86% of patients being continent to solid and liquid stool.[44,70] A similar, impressive result was obtained in those patients who underwent CCC in combination with ESGN, in whom perineal sepsis did not complicate outcome (see above), with seven of nine patients (78%) being continent to solid or liquid stool.[53] Despite this apparent symptomatic relief, however, we have yet to demonstrate an overall improvement in quality of life, or anxiety and depression scores.[45] This finding emphasizes the complexity of the condition, and highlights the influence of psychological factors, present in certain patients, on clinical outcome.

Functional Outcome

In patients with chronic constipation, stool frequency was increased from a median of 1.5/week (range 0.25–7) preoperatively, to 7/week (range 3–7) after surgery ($p < .05$).[3] Similar results were obtained in patients with a refractory rectal evacuatory disorder following ESGN surgery, or those with combined CCC and ESGN, who used one irrigation per day (range 0.5–2), to achieve satisfactory emptying of the colon.[53,70]

Irrigation

Irrespective of the reason for CCC formation, median irrigation volumes were similar (1–1.5 L),[3,44,45,53,70] although there was a tendency for those with rectal evacuatory dysfunction following ESGN surgery to use higher volumes (maximum 4 L).[70] Median time for irrigation was 30 to 40 minutes (range 10–70),[3,44,45,53,70] which represents a significant reduction in comparison to reported time spent evacuating prior to surgery (up to several hours).[3,45]

In contrast to the ACE procedure, where numerous enema regimens have been described,[54] the most common being either tap water[28] or a phosphate enema solution, followed by saline lavage,[21] the majority of patients with the CCC use only warm tap water as the irrigant. Although concerns have been raised regarding the potential for dangerous metabolic complications, secondary to electrolyte imbalance in children using saline or tap water as the irrigant fluid for ACE,[72,73] such electrolyte abnormalities appear to be extremely rare.[72] In a small number of patients with CCC, intermittent phosphate enemas per conduit are required to facilitate complete emptying.[45,70] Fletchers' arachis oil enema may provide an alternative option.[21]

Quantitative scintigraphic assessment of colonic emptying in severely constipated patients with an ACE has shown complete evacuation of the rectosigmoid, descending colon and transverse colon, with 50% emptying of the cecum and ascending colon. Some reflux of radiolabeled irrigant was observed in a minority of patients.[74] Whether such impressive emptying occurs in patients with a transverse CCC remains to be determined, although functional results appear to be comparable.

Conclusion

Thus far, CCC surgery has been performed in heterogeneous groups of patients with chronic intractable constipation in whom

pathophysiology and etiology often differed. For example, patients with both slow-transit constipation and disordered rectal evacuation, secondary to either a mechanical (large rectocoele) or functional obstruction (pelvic floor dyssynergia) have been included, as have patients with lifelong idiopathic symptoms, as well as patients who have acquired their symptoms following pelvic surgery (hysterectomy; secondary to continence-restoring operations). In addition, we have combined CCC formation with an ESGN procedure, as part of total anorectal reconstruction for patients born with anorectal atresia, who have had a poor functional result (persistent soiling, constipation) following initial surgery. Although early results with the CCC are promising, and equivalent to those of the more established ACE, with successful evacuation, improved continence, and resolution of abdominal symptoms appearing possible in all patient groups studied, the numbers are small and controlled trials (perhaps in comparison to other methods of antegrade irrigation), involving more homogeneous patient groups, may help to identify specific determinants of success for this procedure. Certainly, patient education and multidisciplinary support are integral to obtaining a successful outcome, and patients must be highly motivated and be capable of self-administering the enema.

In our experience, the CCC has particularly revolutionized bowel care in a small highly selected subset of patients with chronic constipation or soiling/constipation secondary to anorectal atresia, who wish to avoid a permanent end-stoma. Notably, failure of this procedure does not preclude further surgical intervention. Despite these very exciting preliminary results, its place as a therapy for idiopathic constipation remains to be determined.

References

1. Hasegawa H, Radley S, Fatah C, Keighley MRB. Long-term results of colorectal resection for slow transit constipation. Colorectal Dis 1999;1:141–145.
2. Knowles CH, Scott M, Lunniss PJ. Outcome of colectomy for slow transit constipation. Ann Surg 1999;230: 627–638.
3. Williams NS, Hughes SF, Stuchfield B. Continent colonic conduit for rectal evacuation in severe constipation. Lancet 1994;343:1321–1324.
4. Wald A. Outlet dysfunction constipation. Curr Treat Options Gastroenterol 2001;4:293–297.
5. Sotos JF, Cutler EA, Finkel MA, Doody D. Hypocalcemic coma following two pediatric phosphate enemas. Pediatrics 1977;60:305–307.
6. Sweeney JL, Hewett P, Riddell P, Hoffmann DC. Rectal gangrene: a complication of phosphate enema. Med J Aust 1986;144:374–375.
7. Smith I, Carr N, Corrado OJ, Young A. Rectal necrosis after a phosphate enema. Age Ageing 1987;16:328–330.
8. Bell AM. Colonic perforation with a phosphate enema. J R Soc Med 1990;83:54–55.
9. Hewitt J, Reeve J, Rigby J, Cox AG. Whole-gut irrigation in preparation for large-bowel surgery. Lancet 1973; 2:337–340.
10. Crapp AR, Tillotson P, Powis SJ, Cooke WT, Alexander-Williams J. Preparation of the bowel by whole-gut irrigation. Lancet 1975;2:1239–1240.
11. Smith RG, Currie JE, Walls AD. Whole gut irrigation: a new treatment for constipation. Br Med J 1978;2: 396–397.
12. Dueholm S, Rubinstein E, Reipurth G. Preparation for elective colorectal surgery. A randomized, blinded comparison between oral colonic lavage and whole-gut irrigation. Dis Colon Rectum 1987;30:360–364.
13. Dudley HA, Racliffe AG, McGeehan D. Intraoperative irrigation of the colon to permit primary anastomosis. Br J Surg 1980;67:80–81.
14. Radcliffe AG, Dudley HA. Intraoperative antegrade irrigation of the large intestine. Surg Gynecol Obstet 1983;156:721–723.
15. Muir EG. Safety in colonic resection. Proc R Soc Med 1968;61:401–406.
16. Malone PS, Ransley PG, Kiely EM. Preliminary report: the antegrade continence enema. Lancet 1990;336: 1217–1218.
17. Squire R, Kiely EM, Carr B, Ransley PG, Duffy PG. The clinical application of the Malone antegrade colonic enema. J Pediatr Surg 1993;28:1012–1015.
18. Mitrofanoff P. Cystostomie continente transappendiculare dans le traitement des vessies neurologiques. Chir Pediatr 1980;21:297–305.
19. Webb HW, Barraza MA, Crump JM. Laparoscopic appendicostomy for management of fecal incontinence. J Pediatr Surg 1997;32:457–458.
20. Koyle MA, Kaji DM, Duque M, Wild J, Galansky SH. The Malone antegrade continence enema for neurogenic and structural fecal incontinence and constipation. J Urol 1995;154:759–761.
21. Malone PS, Curry JI, Osborne A. The antegrade continence enema procedure why, when and how? World J Urol 1998;16:274–278.
22. Curry JI, Osborne A, Malone PS. How to achieve a successful Malone antegrade continence enema. J Pediatr Surg 1998;33:138–141.
23. Curry JI, Osborne A, Malone PS. The MACE procedure: experience in the United Kingdom. J Pediatr Surg 1999;34:338–340.
24. Yerkes EB, Cain MP, King S, et al. The Malone antegrade continence enema procedure: quality of life and family perspective. J Urol 2003;169:320–323.
25. Hill J, Stott S, MacLennan I. Antegrade enemas for the treatment of severe idiopathic constipation. Br J Surg 1994;81:1490–1491.
26. Vos A, Cuesta M, Meuwissen S. Antegrade colonic enema (ACE): a new therapeutic approach to chronic constipation. Acta Gastroenterol Latinoam 1996;26: 225–226.

27. Gerharz EW, Vik V, Webb G, Leaver R, Shah PJ, Woodhouse CR. The value of the MACE (Malone antegrade colonic enema) procedure in adult patients. J Am Coll Surg 1997;185:544–547.
28. Krogh K, Laurberg S. Malone antegrade continence enema for faecal incontinence and constipation in adults. Br J Surg 1998;85:974–977.
29. Rongen MJ, van der Hoop AG, Baeten CG. Cecal access for antegrade colon enemas in medically refractory slow-transit constipation: a prospective study. Dis Colon Rectum 2001;44:1644–1649.
30. Christensen P, Kvitzau B, Krogh K, Buntzen S, Laurberg S. Neurogenic colorectal dysfunction—use of new antegrade and retrograde colonic wash-out methods. Spinal Cord 2000;38:255–261.
31. Monti PR, Lara RC, Dutra MA, de Carvalho JR. New techniques for construction of efferent conduits based on the Mitrofanoff principle. Urology 1997;49: 112–115.
32. Marsh PJ, Kiff ES. Ileocaecostomy: an alternative surgical procedure for antegrade colonic enema. Br J Surg 1996;83:507–508.
33. Christensen P, Buntzen S, Krogh K, Laurberg S. Ileal neoappendicostomy for antegrade colonic irrigation. Br J Surg 2001;88:1637–1638.
34. Tackett LD, Minevich E, Benedict JF, Wacksman J, Sheldon CA. Appendiceal versus ileal segment for antegrade continence enema. J Urol 2002;167:683–686.
35. Shandling B, Chait PG, Richards HF. Percutaneous cecostomy: a new technique in the management of fecal incontinence. J Pediatr Surg 1996;31:534–537.
36. Fonkalsrud EW, Dunn JC, Kawaguchi AI. Simplified technique for antegrade continence enemas for fecal retention and incontinence. J Am Coll Surg 1998;187: 457–460.
37. Fukunaga K, Kimura K, Lawrence JP, Soper RT, Phearman LA. Button device for antegrade enema in the treatment of incontinence and constipation. J Pediatr Surg 1996;31:1038–1039.
38. Duel BP, Gonzalez R. The button cecostomy for management of fecal incontinence. Pediatr Surg Int 1999;15: 559–561.
39. Gauderer MW, Decou JM, Boyle JT. Sigmoid irrigation tube for the management of chronic evacuation disorders. J Pediatr Surg 2002;37:348–351.
40. Heriot AG, Tilney HS, Simson JN. The application of percutaneous endoscopic colostomy to the management of obstructed defecation. Dis Colon Rectum 2002;45:700–702.
41. McAndrew HF, Malone PS. Continent catheterizable conduits: which stoma, which conduit and which reservoir? BJU Int 2002;89:86–89.
42. Preston DM, Lennard-Jones JE. Severe chronic constipation of young women: "idiopathic slow transit constipation." Gut 1986;27:41–48.
43. Hughes SF, Williams NS. Antegrade enemas for the treatment of severe idiopathic constipation. Br J Surg 1995;82:567.
44. Hughes SF, Williams NS. Continent colonic conduit for the treatment of faecal incontinence associated with disordered evacuation. Br J Surg 1995;82:1318–1320.
45. Eccersley AJ, Maw A, Williams NS. Comparative study of two sites of colonic conduit placement in the treatment of constipation due to rectal evacuatory disorders. Br J Surg 1999;86:647–650.
46. Maw A, Eccersley AJ, Wiliams NS. Ileocaecostomy: an alternative surgical procedure for antegrade colonic enema. Br J Surg 1996;83:1304–1305.
47. Proano M, Camilleri M, Phillips SF, Brown ML, Thomforde GM. Transit of solids through the human colon: regional quantification in the unprepared bowel. Am J Physiol 1990;258 (Gastrointest Liver Physiol 21): G856–862.
48. Kamm MA, Van Der Sijp JR, Lennard-Jones JE. Observations on the characteristics of stimulated defaecation in severe idiopathic constipation. Int J Colorectal Dis 1992;7:197–201.
49. Lubowski DZ, Meagher AP, Smart RC, Butler SP. Scintigraphic assessment of colonic function during defaecation. Int J Colorect Dis 1995;10:91–93.
50. Halls J. Bowel content shift during normal defaecation. Proc R Soc Med 1965;58:859–860.
51. Bassotti G, Gaburri M, Imbimbo BP, et al. Colonic mass movements in idiopathic chronic constipation. Gut 1988;29:1173–1179.
52. Dinning PG, Bampton PA, Andre J, et al. Abnormal predefecatory colonic motor patterns define constipation in obstructed defecation. Gastroenterology 2004;127: 49–56.
53. Saunders JR, Williams NS, Eccersley AJ. The combination of electrically stimulated gracilis neoanal sphincter and continent colonic conduit: a step forward for total anorectal reconstruction? Dis Colon Rectum 2004;47:354–363.
54. Graf JL, Strear C, Bratton B, et al. The antegrade continence enema procedure: a review of the literature. J Pediatr Surg 1998;33:1294–1296.
55. Hinton JM, Lennard-Jones JE, Young AC. A new method for studying gut transit times using radioopaque markers. Gut 1969;10:842–847.
56. Scott SM, Knowles CH, Lunniss PJ, Newell M, Garvie N, Williams NS. Scintigraphic assessment of colonic transit in patients with slow transit constipation arising de novo (chronic idiopathic) and following pelvic surgery or childbirth. Br J Surg 2001;88:405–411.
57. Mellgren A, Bremmer S, Johansson C, et al. Defecography. Results of investigations in 2,816 patients. Dis Colon Rectum 1994;37:1133–1141.
58. Agachan F, Pfeifer J, Wexner SD. Defecography and proctography. Results of 744 patients. Dis Colon Rectum 1996;39:899–905.
59. Farthing MJ, Lennard-Jones JE. Sensibility of the rectum to distension and the anorectal distension reflex in ulcerative colitis. Gut 1978;19:64–69.
60. Penning C, Steens J, van der Schaar PJ, et al. Motor and sensory function of the rectum in different subtypes of constipation. Scand J Gastroenterol 2001;36: 32–38.
61. Knowles CH, Eccersley AJ, Scott SM, Walker SM, Reeves B, Lunniss PJ. Linear discriminant analysis of symptoms in patients with chronic constipation: validation of a new scoring system (KESS). Dis Colon Rectum 2000;43:1419–1426.
62. Locke GR III, Pemberton JH, Phillips SF. American Gastroenterological Association Medical Position Statement: guidelines on constipation. Gastroenterology 2000;119:1761–1778.
63. Chan CL, Scott SM, Knowles CH, Lunniss PJ. Exaggerated rectal adaptation—another cause of outlet obstruction. Colorectal Dis 2001;3:141–142.

64. D'Hoore A, Penninckx F. Obstructed defecation. Colorectal Dis 2003;5:280–287.
65. Gladman MA, Scott SM, Chan CL, Williams NS, Lunniss PJ. Rectal hyposensitivity: prevalence and clinical impact in patients with intractable constipation and fecal incontinence. Dis Colon Rectum 2003;46:238–246.
66. Gladman MA, Scott SM, Williams NS, Lunniss PJ. Clinical and physiological findings, and possible aetiological factors of rectal hyposensitivity. Br J Surg 2003;90: 860–866.
67. Kamm MA. Constipation and its management. BMJ 2003;327:459–460.
68. Stuchfield B. The continent colonic conduit in the management of severe constipation. Br J Nurs 1995;4: 1012–1016.
69. Keighley MRB, Williams NS, eds. Constipation. In: Surgery of the Anus, Rectum and Colon, 2nd ed. London: WB Saunders, 1999:737–755.
70. Saunders JR, Eccersley AJ, Williams NS. Use of a continent colonic conduit for treatment of refractory evacuatory disorder following construction of an electrically stimulated gracilis neoanal sphincter. Br J Surg 2003; 90:1416–1421.
71. Williams NS, Patel J, George BD, Hallan RI, Watkins ES. Development of an electrically stimulated neoanal sphincter. Lancet 1991;338:1166–1169.
72. Yerkes EB, Rink RC, King S, Cain MP, Kaefer M, Casale AJ. Tap water and the Malone antegrade continence enema: a safe combination? J Urol 2001;166:1476–1478.
73. Schreiber CK, Stone AR. Fatal hypernatremia associated with the antegrade continence enema procedure. J Urol 1999;162:1433.
74. Christensen P, Olsen N, Krogh K, Laurberg S. Scintigraphic assessment of antegrade colonic irrigation through an appendicostomy or a neoappendicostomy. Br J Surg 2002;89:1275–1280.

24

Surgical Treatment of Hirschsprung's Disease

Alberto Peña and Marc A. Levitt

History

Hirschsprung's disease represents the most common cause of intestinal obstruction in the newborn. The term *Hirschsprung's disease* is used to describe a condition that is a functional colonic obstruction. These patients do not suffer from a real mechanical obstruction but rather from a serious disturbance in the normal colonic peristalsis, due to a lack of ganglion cells. Dr. Harald Hirschsprung[1] presented what is considered a classic description of this condition in the Pediatric Congress in Berlin in 1886. The description, however, referred only to a congenital dilation of the colon, without a real understanding of the histology and pathogenesis.

It was Tittel[2] in 1901 who mentioned the absence of ganglion cells in the distal colon in a child suffering from this condition. In 1948 Whitehouse and Kernohan[3] and Zuelzer and Wilson[4] documented the absence of ganglion cells in the distal part of the colon. The recognition of aganglionosis in the distal part of the colon as the main cause of the symptoms in these patients led to the rational surgical treatment used presently. Swenson and Bill[5] described the first rational surgical approach, consisting of the resection of the aganglionic segment and a pull-through of a normoganglionic piece of colon to be connected to the anal canal. Subsequently, different variants to this basic principle were introduced into the literature including the Duhamel approach,[6–8] the Rehbein approach in 1959,[9] the Soave operation,[10] and the Boley modification.[11] All of them are actually modifications from the previous approach. More recently, a transanal resection of the aganglionic bowel as well as a complete transanal pull-through was described by De La Torre and Ortega.[12] During the last few years, laparoscopically assisted techniques have been added to the treatment of this condition.[13–16]

Etiology, Pathophysiology, and Incidence

The absence of ganglion cells in the submucosa (Meissner plexus) and intermuscularly (Auerbach plexus) in the distal intestine, as well as a marked increase in nerve fibers that extend into the submucosa, seemed to be the hallmark of this condition. There is also an increase in the activity of acetylcholinesterase.[17–22] The lack of ganglion cells affects the most distal part of the rectosigmoid in about 80% of the cases, which represent the so-called typical cases of Hirschsprung's disease.[23,24] The extension of the aganglionosis varies. It may reach the descending colon as well as the splenic flexure and part of the transverse colon, which is called "long segment Hirschsprung's disease."[25] It may affect the entire colon, which is called "total colonic aganglionosis,"[26,27] and there are reports in the literature of patients with a universal aganglionosis (total intestinal aganglionosis), a condition that so far has been incompatible with life.[28]

There is also a rather controversial condition called "ultrashort" Hirschsprung's disease.[29] In this condition, the aganglionic segment supposedly measures only a few centimeters and is located immediately above the anal canal. Not everyone agrees with the existence of this condition because normal individuals have an

area of aganglionosis in the distal few centimeters of the rectum.

The aganglionic segment of the colon is never distended; however, proximal to this affected bowel, there is enlargement of the colon (megacolon). In between the aganglionic, nondistended, and normoganglionic megacolon, there is a transition zone in which there is a decreased number of ganglion cells (hypoganglionosis). The aganglionic portion of the colon most probably represents an area with lack of continuity of the peristalsis, which translates into a functional obstruction. There is accumulation of fecal matter proximal to the aganglionosis. This has also been referred to as "lack of relaxation" of the distal aganglionic segment. In the area of absent ganglion cells, there is a marked increase in the innervation provided by the extrinsic nervous system. The aganglionic colon is conceived as a permanently contracted piece of bowel interfering with a normal peristalsis.

There is a conspicuous absence of nitric oxide synthase in the myenteric plexus of the aganglionic tissue.[30–32] Although the pathophysiology of Hirschsprung's disease is still a matter of mystery, it is much more than just a functional colonic obstruction. The fecal stasis that occurs in the proximal normoganglionic bowel does not produce just a fecal impaction, as in cases of idiopathic constipation. These patients suffer from other not well-understood aggravating functional abnormalities that may explain other more serious symptoms. The fecal stasis leads to bacterial overgrowth, which produces an explosive type of diarrhea, abdominal distention, fever, and a very serious toxic condition. An inflammatory infiltrate of the intestinal mucosa occurs and eventually, the mucosa becomes ulcerated. The bacteria can then traverse the intestinal epithelium, and abnormal bacteria proliferate, particularly *Clostridium difficile*. This condition is called "enterocolitis" and may occur from the very few hours after the baby is born before surgery or even after a successful operation. There are many unknown factors contributing to this serious and mysterious condition in which the babies become extremely sick. They suffer from a state of endotoxemia and die if not aggressively and effectively treated.[33–38] It seems likely that the local immune system is also abnormal in these children, as well as the characteristics of the mucus of the bowel.[39,40]

The incidence of Hirschsprung's disease has been reported to be 1 in 4000 to 1 in 7000.[41,42] There is a definite male preponderance except for the long segment type of Hirschsprung's, in which the ratio seems to be 1:1 male to female.[43] Male patients with long-segment Hirschsprung's disease and sons of affected females have a 24% chance of being affected.[44]

Clinical Manifestations

Traditionally, Hirschsprung's disease was suspected in children who suffered from constipation. However, progressively, over the last several decades, the index of suspicions for this condition increased, which has allowed the recognition of this disease earlier in life.

In the United States today, it is rather unusual to find an undiagnosed patient with this condition at school age. The most common manifestation of Hirschsprung's disease during the newborn period is the lack of passage of meconium during the first 24 hours. When a baby does not pass meconium during that period, it should be considered highly suspicious for Hirschsprung's disease. Subsequently, the abdomen becomes distended and the baby vomits. The symptoms progress as in any other case of colonic obstruction because the baby looks toxic, lethargic, dehydrated, and septic. Rectal stimulation either with a thermometer or with a finger provokes characteristic explosive bowel movements, followed by the passing of large amount of fetid gas, all of which gives the baby temporary relief, but a few hours later the symptoms recur. A small percentage of patients may survive without medical help; over time, they develop clinical signs of severe constipation, abdominal distention, and failure to thrive.

Hirschsprung's disease during the newborn period should be differentiated from other causes of colonic obstruction such as imperforate anus. Imperforate anus is easily diagnosed by a simple inspection of the perineum. A very unusual condition is atresia of the colon; this very rare defect produces enormous dilatation of the proximal colon. Since the distal colon is not developed, and a severe microcolon is demonstrated with contrast study through the rectum. Meconium ileus may also simulate the clinical picture of Hirschsprung's disease, but this condition has characteristic features; all these babies suffer from cystic fibrosis that can be easily diagnosed at this stage by a sweat test, and radiologically, the inspissated meconium shows a

characteristic pattern described as "ground-glass image" located in the lower abdomen.

Untreated patients with Hirschsprung's disease who survive and reach school age suffer from severe megacolon. These patients must be differentiated from patients with idiopathic constipation. Patients with Hirschsprung's disease have a large amount of stool located in the very dilated proximal colon. However, the distal, aganglionic segment is usually empty of stool. Patients with severe idiopathic constipation have a megarectum and fecal impaction located all the way down in the area of the anal canal. The finger of an examiner will perceive the presence of a huge fecal impaction located very low in the pelvis, while patients with Hirschsprung's disease are described as having an empty rectum. Patients with Hirschsprung's disease characteristically do not soil their underwear. Again, it is very unusual to see patients with Hirschsprung's disease at this age. Survivors in fact represent a very small percentage of all Hirschsprung's patients. A majority of undiagnosed patients die in the early stages of the condition when they go untreated.

Diagnosis

A high index of suspicion is the most important element for the early diagnosis and treatment of this condition. An abdominal plain film shows very dilated loops of bowel. Unfortunately, during the newborn period, it is extremely difficult, on a plain abdominal film, to differentiate small bowel from large bowel. These babies have a dilated colon, proximal to the aganglionic portion.

When babies are born with Hirschsprung's disease, they still do not develop a severe degree of megacolon. As time goes by, the colon, proximal to the aganglionic segment, becomes more and more dilated, showing dramatic contrast with the undilated distal bowel and the transition zone. The clinician should not expect to find a conspicuous megacolon with a distal narrow segment in the newborn.

A contrast enema is extremely important for the diagnosis of this condition. This study does not demonstrate a transition zone in 100% of cases, but its value varies from institution to institution and depends very much on the experience of the observer.[45–47] A positive contrast study shows a nondilated distal portion followed by a dilated proximal aganglionic segment. Sometimes the diagnosis is very obvious and sometimes, for unknown reasons, the transition between dilated and nondilated colon is not so well demarcated. In patients with total colonic aganglionosis, the entire colon is nondilated and the main dilatation of the bowel affects the small bowel.

The contrast study in these babies must be performed by an experienced pediatric radiologist. A catheter is introduced through the rectum not more than 4 cm. Passing the catheter more than necessary will result in the injection of the contrast material directly into the dilated portion of the colon, bypassing the nondilated portion as well as the transition zone, and therefore precluding making the diagnosis. Failing to pass the contrast material in the 24 hours following the study is considered highly suggestive of the diagnosis of Hirschsprung's disease.

Occasionally, an unattended baby may suffer from a bowel perforation; the perforation is usually located in the cecum. These patients require emergent surgery. The presence of a perforation in the cecum raises the likelihood of Hirschsprung's disease.

Anorectal Manometry

The inflation of a balloon in the rectum in a normal individual produces decreased anal canal pressure called the "anorectal reflex" and is present in all normal individuals. Anorectal manometry in children with symptoms suggestive of Hirschsprung's disease is performed with the goal of eliciting such a reflex. A lack of relaxation of the anal canal is considered diagnostic of Hirschsprung's disease.[48–53] However, there is a significant degree of controversy about the value of this diagnostic test, and most pediatric centers and surgeons do not use this diagnostic modality.

Rectal Biopsy

A rectal biopsy represents the definitive diagnostic test in children with Hirschsprung's disease. It requires, however, interpretation by an experienced pediatric pathologist. Most surgeons and pediatric centers use a suction rectal biopsy for the diagnosis of this condition.[54–57] This biopsy can be performed at the bedside and

is considered highly diagnostic, again provided that the pediatric pathologist is experienced with the interpretation of this kind of biopsy. One of the limitations of this type of procedure is that often the specimen does not include the submucosa and therefore is not adequate for an accurate diagnosis. Another limitation is performing the biopsy too distal in the rectum where supposedly there is a normal area absent of ganglion cells.[58] A suction rectal biopsy, however, only makes the diagnosis of aganglionosis but does not determine the length of the abnormality.

Although a full-thickness rectal biopsy provides a much better specimen, it must be done under anesthesia.[59] This biopsy is still done in institutions where the pathologist is not familiar with the diagnosis of Hirschsprung's with a suction biopsy or in institutions where the surgeons do not have the suction biopsy device to perform such a procedure. An increase in the activity of acetylcholinesterase is also considered diagnostic,[55,56] but not all pathologists rely on this analysis.

Treatment

The newborn baby suffering from abdominal distention, vomiting, dehydration, or explosive fetid bowel movements, or who looks toxic and lethargic, needs emergency management. Intravenous fluids, antibiotics, and most importantly, rectal irrigations must be promptly started.

Little is known about the pathophysiology of this potentially lethal enterocolitis. However, stasis seems to be the most important predisposing factor and therefore these babies will dramatically improve by decompressing the colon, which can be done on a temporary basis by passing a rectal tube. Sometimes the characteristics of the meconium and the fecal matter may interfere with the drainage of gas and liquid from the colon through the tube. Therefore, the lumen of the tube should be cleared by the infusion of small amounts of saline solution, and the tube must be moved back and forth. This maneuver produces a spectacular decompression of the colon with dramatic improvement of the patient's symptoms. However, this temporary measure cannot be considered adequate long-term treatment because a few hours after the decompression the baby will start to become distended again and the symptoms will recur. Regardless of their transient benefit, rectal irrigations are still considered extremely valuable; they maintain the baby in good condition until a more permanent type of treatment is indicated. Sometimes the babies are so sick that one cannot consider performing a contrast enema because of the risk of perforation. The rectal irrigations, antibiotics, and intravenous fluids may return the baby to a better clinical condition in order to perform other diagnostic and therapeutic procedures. When the baby recovers from the acute state of enterocolitis, the rectal biopsy is performed, establishing the definitive diagnosis.

Traditionally, patients with Hirschsprung's disease were treated in three stages. The first stage consisted of opening a diverting colostomy, which decompressed the colon; it allowed the baby to recover and be discharged. Most surgeons open a colostomy in the right transverse colon or establish an ileostomy in babies with total colonic aganglionosis. The second stage consists of resection of the aganglionic segment and pull-through of the normoganglionic bowel to be anastomosed to the anal canal with the technique of preference for the specific surgeon. The third stage consists of closure of the colostomy after the baby recovers completely from the main pull-through procedure. This three-stage approach is now considered rather historical.

Subsequently, surgeons trying to avoid surgical trauma to the babies devised a two-stage type of repair. In the first operation, a colostomy was created immediately proximal to the transition zone, which is called a "leveled colostomy." In the second and definitive stage, the surgeons performed the pull-through, pulling down what used to be the colostomy into the anal canal and leaving the patient without a protective colostomy.

Finally, the most recent approach involves performing the main pull-through during the first few days, weeks, or months of life, as a primary procedure without a protective colostomy.[60–63] This approach avoids two operations for the baby (colostomy opening and colostomy closure) and has been demonstrated to be feasible without adding extra morbidity to the patient. However, a colostomy is still an extremely valuable operation for babies with Hirschsprung's disease under special

circumstances. For instance, a very sick baby suffering from other aggravating factors or enterocolitis could still be a candidate for this kind of preliminary procedure. In general, most surgeons take these babies to the operating room for a pull-through with a plan for a colostomy if necessary. When the technical circumstances of a pull-through are not satisfactory and the surgeons have doubts about the viability of the pull-through bowel in terms of blood supply or any other kind of technical difficulties, they can always protect the pull-through with a proximal colostomy. Also, in hospitals, cities, or countries were the surrounding circumstances for the baby, as well as the infrastructure, are not adequate, a surgeon can save the baby's life with a colostomy.

To perform the primary neonatal pull-through, one should expect to have a newborn baby in excellent clinical condition with a completely decompressed colon, typically over several days. The patients receive parenteral nutrition and undergo colonic irrigations.

Main Repair

Swenson Procedure

This procedure has the merit of being the first rationally designed surgery to treat this condition.[5] It was used for many years by Dr. Swenson himself.[23] A few surgeons in the world still perform the original Swenson operation.[64,65] For this kind of pull-through operation, the patient must be prepared so that the surgeon can approach the abdomen as well as the perineum. Basically, the entire body, below the rib cage is prepared in the usual manner so that the surgeon can approach the abdomen or the perineum several times either by turning the patient from supine into prone position or simply by lifting up the legs to approach the perineum and then down to approach the abdomen. Transabdominally, the aganglionic portion of the colon is resected including the most dilated portion of the bowel (Fig. 24.1A). In a case of typical Hirschsprung's disease, only the splenic flexure

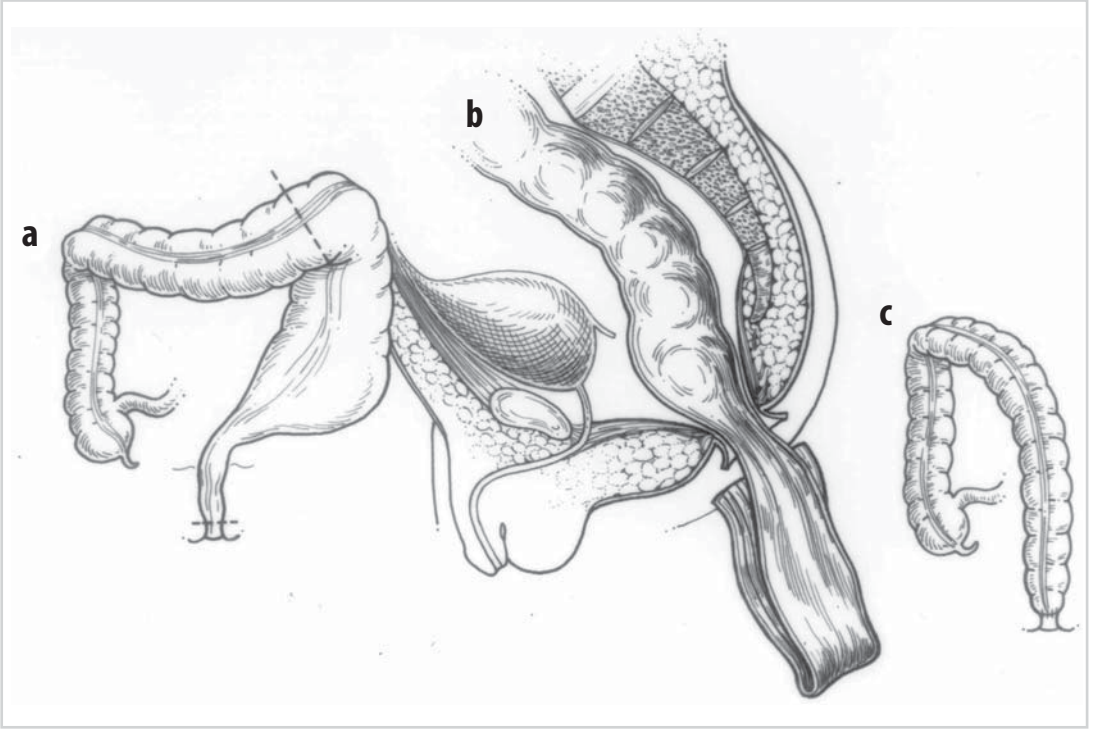


Figure 24.1. The Swenson surgical technique. a: Resection of the aganglionic and dilated bowel. b: Pull-through of normal ganglionic bowel. c: Operation finished. From Peña A. Surgical treatment of Hirschsprung's disease. In: Wexner SD, Bartolo DCC, eds. Constipation: Etiology, Evaluation and Management. New York: Butterworth-Heinemann, 1995:168–175, reproduced by permission of Edward Arnold.

must be mobilized. Conversely, dealing with a long segment type of disease, it may be necessary to mobilize the right colon to obtain adequate length for the pull-through. The aganglionic portion of the colon below the peritoneal floor is dissected in a very precise manner, staying as close as possible to the rectal wall down to the level of the levator ani muscle. Dissection of the rectum includes the ligation of the middle hemorrhoidal vessels and the use of cautery to the perirectal vasculature (Fig. 24.1). Special care is taken to preserve the anal canal, above the pectinate line. The aganglionic segment of the colon is resected and the new, normoganglionic colon is pulled through (Fig. 24.1B,C) the same space in the pelvis and anastomosed by a conventional, transanal, hand-sewn technique. The basic principles of this procedure are still observed in most modern operations. Swenson developed extraordinary experience with this operation and he and his followers claimed good results.[64,65] Despite these reports, some patients operated on by other surgeons were reported to suffer signs and symptoms related to damage of important nerve structures in the pelvis. Because of nerve injury, other procedures were designed, with the specific purpose of avoiding nerve damage in the pelvis. Such procedures were created by Duhamel and Soave.

Duhamel Procedure

Duhamel[6–8] designed his procedure with the specific purpose of avoiding extensive pelvic dissection. This avoidance is reportedly accomplished by preserving the pelvic portion of the aganglionic rectum, dividing the bowel at the peritoneal reflection as distally as possible (Fig. 24.2A). The aganglionic rectal stump is then closed. The normoganglionic bowel is pulled down directly in front of the sacrum in a safe space behind the rectum that is created by blunt dissection (Fig. 24.2B). Lateral dissection is therefore avoided, which prevents nerve damage. The posterior rectal wall is incised above the dentate line, entering the previously dissected retrorectal space. The normoganglionic bowel is pulled through the rectal incision in the posterior wall of the rectum and a GIA stapler or (in the past) two large crushing clamps are used to create an anastomosis between the aganglionic rectum and the normoganglionic pulled-down bowel (Fig. 24.2C–F). The anastomosis between the pulled-through colon and the aganglionic rectum is created as wide as possible, and the rectal stump must be as small as possible in order to avoid fecal accumulation (Fig. 24.2G).

This procedure still has many followers all over the world;[24] it is a very appealing operation because it is easy and technically reproducible. The problem with this operation is that the portion of rectum that is aganglionic still suffers from the same dysmotility disorder of the primary Hirschsprung's condition. As a consequence, these patients tend to accumulate stool into that rectal stump and return for follow-up with a hypertrophic aganglionic rectum with fecal impaction. Many require reoperation to remove the aganglionic portion and create an end-to-end anastomosis as in Swenson's operation.

Soave Procedure

Franco Soave,[10] an Italian surgeon, created this ingenious and appealing operation, with the specific theoretical purpose of avoiding the consequences of nerve damage provoked by an imprecise Swenson dissection. The aganglionic rectosigmoid is resected by an endorectal dissection, theoretically minimizing the risk of pelvic injury (Fig. 24.3A,B).

The normoganglionic colon is passed through the rectal muscular cuff left after the endorectal dissection (Fig. 24.3C,D). There is no aganglionic segment of rectum left, such as that left with the Duhamel procedure. This operation is less reproducible than the Duhamel procedure and requires meticulous technique in the dissection of the mucosa from the muscular cuff. The endorectal dissection is performed immediately around the mucosal layer and inside the smooth muscle layer of the bowel (Fig. 24.3C). This dissection is usually initiated 1 or 2 cm above the peritoneal reflection. It is carried down to a point about 1 cm above the pectinate line in order to preserve the anal canal with its sphincteric mechanism and sensation. The normoganglionic colon is anastomosed to the anal canal about 1 cm above the pectinate line (Fig. 24.3D). Soave originally performed this operation without a colostomy, leaving a portion of the pulled-through colon protruding well beyond the anal skin margin. About a week later, this portion of the bowel was resected and an anastomosis was created between the normoaganglionic bowel

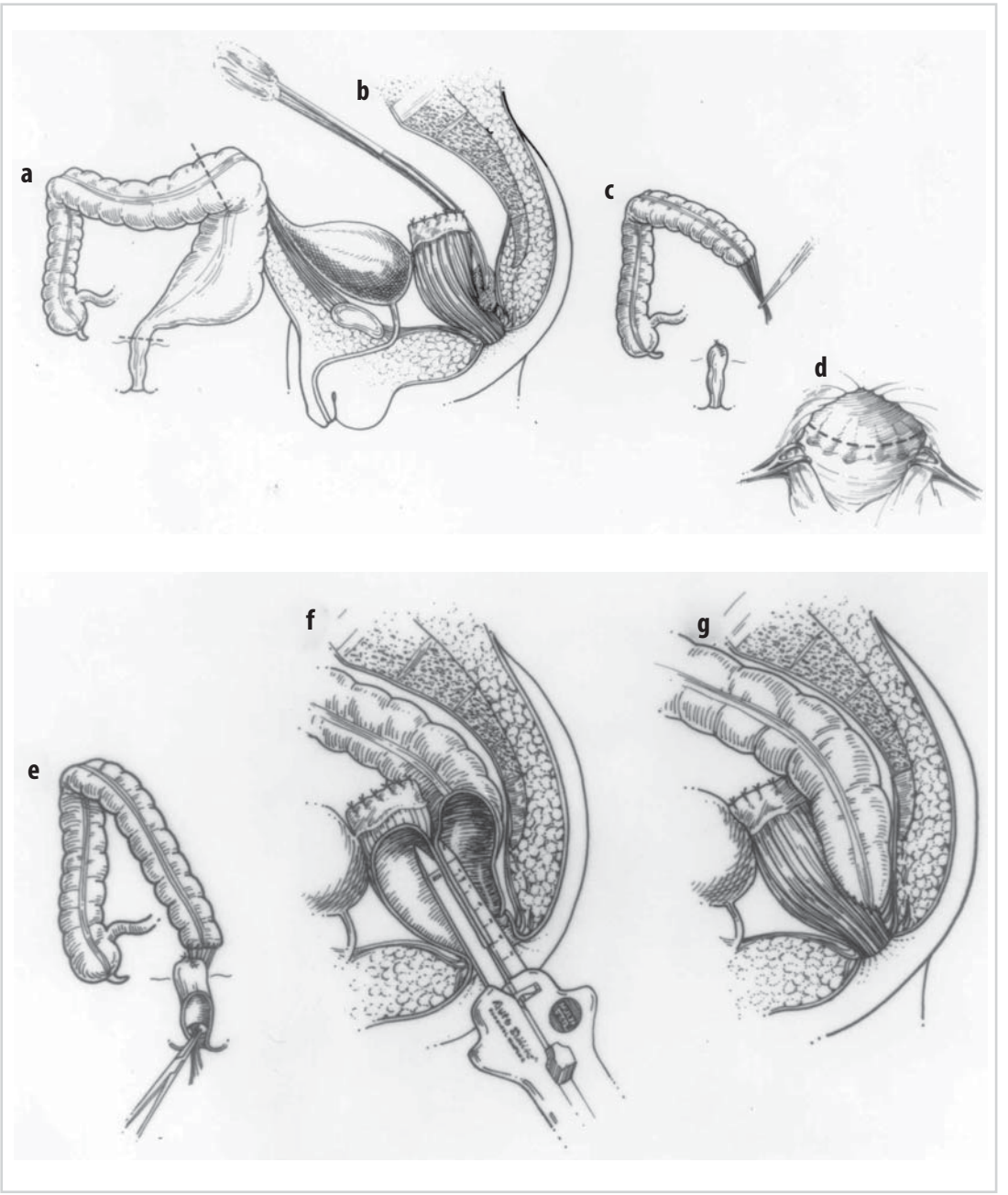


Figure 24.2. Duhamel technique. a: Resection of the dilated portion and part of the aganglionic segment. b: Presacral, retrorectal dissection. c: Pull-through of normal ganglionic bowel. d: Incision of the posterior rectal wall, above the pectinate line. e: Pull through of normal aganglionic colon through the window in the posterior rectal wall. f: Creating a wide anastomosis between normal ganglionic and aganglionic segment. g: Finished operation. From Peña A. Surgical treatment of Hirschsprung's disease. In: Wexner SD, Bartolo DCC, eds. Constipation: Etiology, Evaluation and Management. New York: Butterworth-Heinemann, 1995:168–175, reproduced by permission of Edward Arnold.

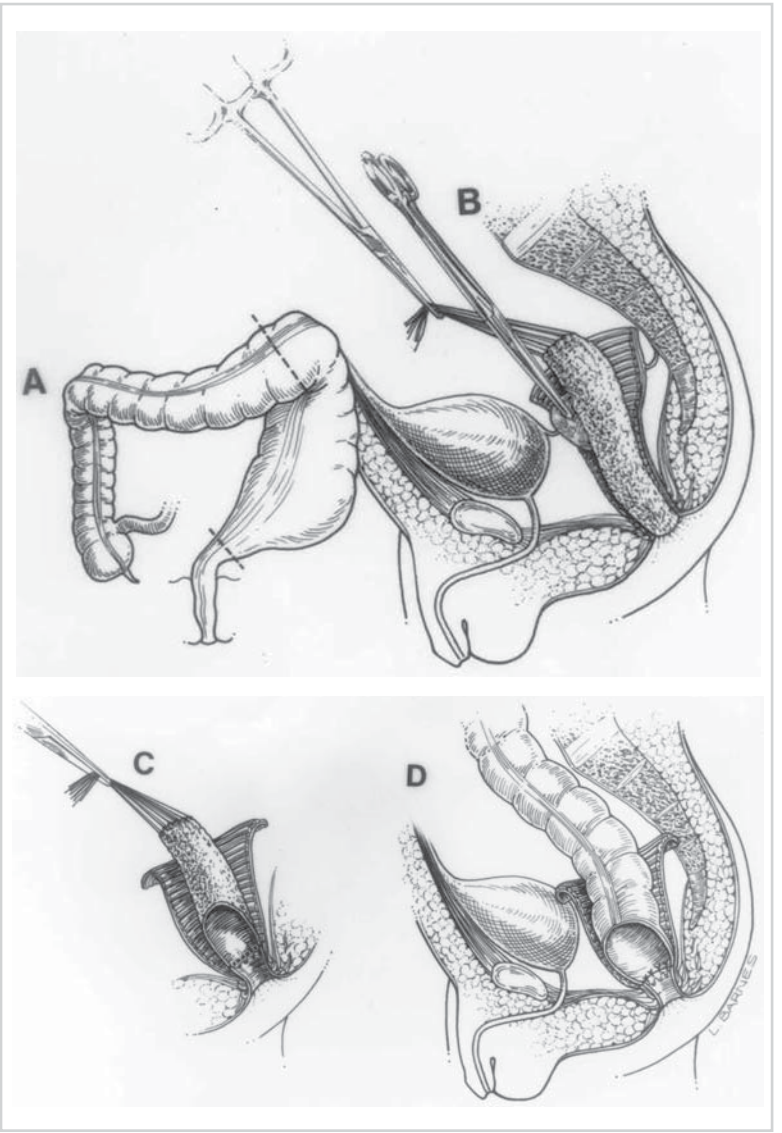


Figure 24.3. Soave technique. A: Resection of dilated colon plus intraperitoneal aganglionic segment. B: Endorectal intrapelvic dissection. C: Resection of the mucosal aganglionic segment down to the pectinate line. D: Pull-through of normal ganglionic bowel through the muscle cuff and anastomosis 1 cm above the pectinate line. From Peña A. Surgical treatment of Hirschsprung's disease. In: Wexner SD, Bartolo DCC, eds. Constipation: Etiology, Evaluation and Management. New York: Butterworth-Heinemann, 1995:168–175, reproduced by permission of Edward Arnold.

and the anal canal. This operation was modified by Boley,[11] who proposed a primary anastomosis, avoiding the second procedure.

Laparoscopic-Assisted Procedures

Laparoscopic-assisted techniques have been used in the management of Hirschsprung's disease.[13–16] The purpose of this technology is to be less invasive in children and substitute a formal laparotomy with a minimally invasive technique that helps the patient to suffer less postoperative pain and leads to a smoother recovery and earlier discharge. Laparoscopy has been useful in the management of these patients. The surgeons still can use the technique of their preference (Swenson, Duhamel, or Soave) but can make the procedure less invasive by adding a laparoscopic portion rather than a laparotomy. Long-term results of adding a laparoscopic approach to these techniques are still pending. We believe, however, that laparoscopy will not have any negative impact on the results. Therefore, we favor the use of this technology when available.

Transanal Approach

More recently, De La Torre and Ortega[12] created a simple but ingenious and original way to treat this condition. They demonstrated first in animals and then in humans that the rectosigmoid can be resected in a purely transanal fashion. The resection is performed and the aganglionic segment is simultaneously pulled down through the anus. Interestingly, in the most common type of Hirschsprung's disease (the so-called classic type), the entire aganglionic segment can be transanally resected and the normoganglionic colon can be anastomosed to the anal canal transanally, avoiding any kind of laparotomy or laparoscopy. Fortunately, the so-called classic form of Hirschsprung's represents approximately 80% of the cases, which gives extra value to this ingenious technique. The transanal approach has been rapidly adopted, and larger series of cases have been reported.[66,67]

The patient is placed in lithotomy position or alternatively can be placed in a prone position with the pelvis elevated. A special retractor (Lone Star, Houston, Texas) is used to expose the anal canal (Fig. 24.4A). The great advantage of this

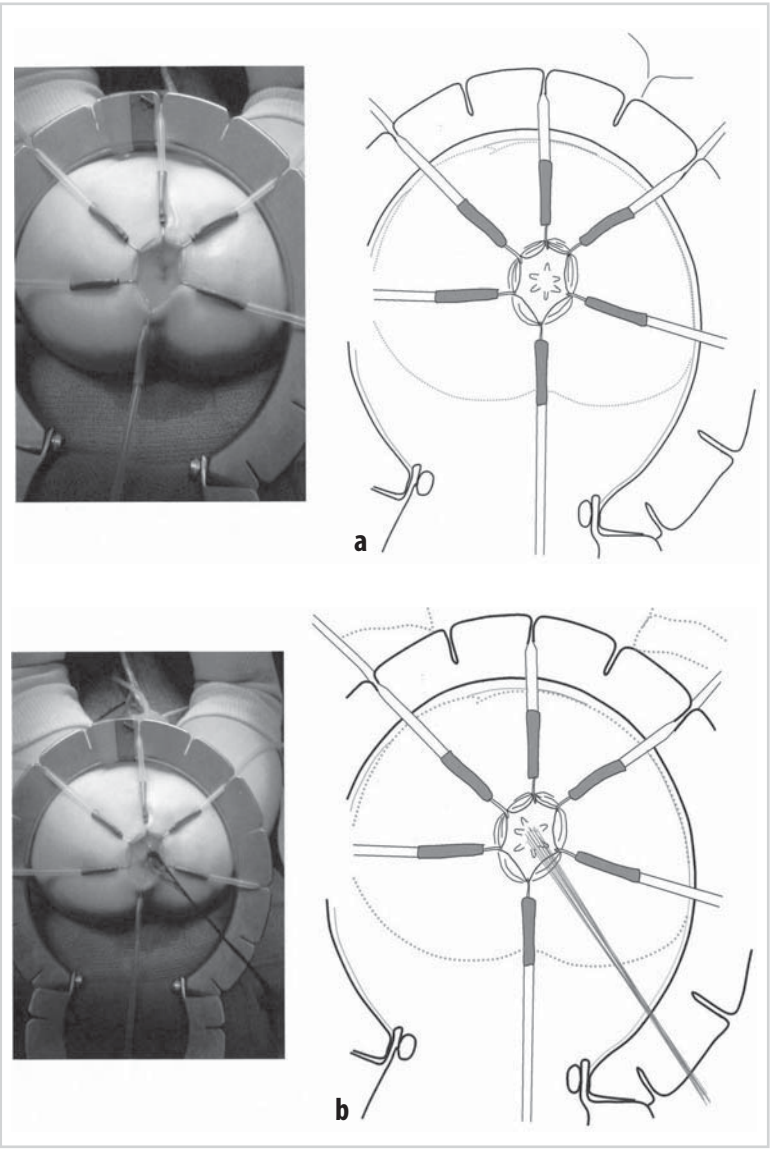


Figure 24.4. Transanal technique (De La Torre). a: "Lone star" retractor exposing the rectal mucosa and pectinate line. b: Multiple silk sutures lifting the rectal mucosa above the pectinate line. c: Full-thickness dissection of the rectum after the peritoneal reflection and beyond. d: Anastomosis of normal ganglionic bowel to the rectum 1 cm above the pectinate line.

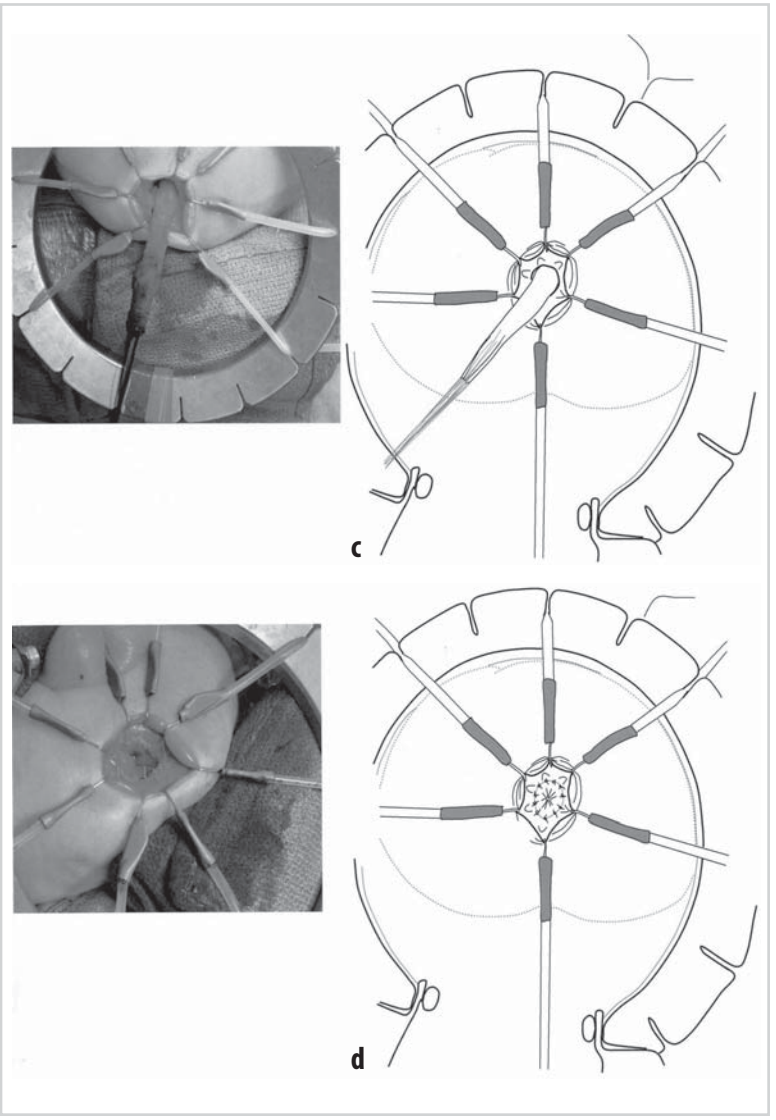


Figure 24.4. *Continued*

retractor is that it can dilate the anus in a symmetric circumferential fashion to very clearly expose the anal canal. Multiple 6-0 silk sutures are placed, incorporating the rectal mucosa above the anal canal in order to exert the uniform traction that is very important to perform an efficient and neat dissection of the rectum above the pectinate line (Fig. 24.4B). The original De La Torre technique is an endorectal technique performed from below. At our institution, we have been using a transanal full-thickness dissection, or a transanal Swenson procedure. Both ways are equally successful and can be done depending on the experience of the operator. While applying uniform traction to the multiple 6-0 sutures, a circumferential dissection is performed either submucosally or full-thickness, dividing and cauterizing the extrinsic blood supply of the rectum. By performing this procedure, length is gained in the dissection and, surprisingly, the peritoneal reflection can be reached very rapidly (Fig. 24.4C). As the dissection progresses, one can take full-thickness biopsies.

We advise taking full-thickness biopsies every 4 cm during this dissection. The dissection must continue until the normoganglionic bowel is reached. If, at that point, the surgeon perceives that the colon is already normoganglionic but

very dilated, it is mandatory to continue the dissection until normoganglionic and nondilated colon is reached. One can usually dissect and resect comfortably and safely the rectosigmoid up to the junction of the sigmoid with the descending colon. Endeavoring to go higher than that, even when feasible, makes the procedure rather risky and uncomfortable. At that point, one can continue laparoscopically or by laparotomy.

We routinely perform an end-to-end anastomosis with two layers of interrupted 6-0 long-term absorbable sutures between the normoganglionic, nondistended portion of the colon and the anal canal (Fig. 24.4D). The patient receives parenteral nutrition, and oral feeding is initiated 2 to 4 days after the operation.

Complications

Operative complications in Hirschsprung's disease can be divided into two categories: preventable and unpreventable. Preventable complications include fecal incontinence, dehiscence, retraction, fistula formation, and constipation. These complications can be avoided by observing a meticulous technique.

Fecal Incontinence

Fecal incontinence is still a relatively frequent problem observed in patients operated on for Hirschsprung's disease. We believe that incontinence occurs mainly when the surgeon violates the basic principles applicable to the repair of this problem regardless of the type of technique used. Basically, it consists of damaging the anal canal. The crucial area extending from 1 cm above the pectinate line down to the skin must be preserved, regardless of the surgical technique used in the treatment of Hirschsprung's disease. It contains the most sensitive area of the gastrointestinal tract and the sphincter mechanism. We have seen patients suffering from fecal incontinence operated on at other institutions in whom careful examination of the anus and rectum demonstrates often that this area has been damaged.

Dehiscence and Retraction

Dehiscence and retraction usually occur as a consequence of a deficient technique in the management of the blood supply of the normoganglionic bowel. It is very important to carefully observe the blood supply of the colon before making a decision to ligate a branch of the inferior mesenteric, middle colic, or ileocolic vessels, to be sure that the segment to be pulled down still receives adequate blood supply through the arcades of the colonic vessels. The pulled-through colon must lie in its position in a tension-free manner.

Constipation

Constipation occurs mainly in patients in whom normoganglionic but dilated colon has been pulled down. We have learned through the years that a very dilated piece of colon is almost as bad as an aganglionic segment. There is evidence that abnormally dilated portions of any hollow viscus loses its peristalsis. Therefore, regardless of the technique that the surgeon uses, it is imperative to pull down a normoganglionic nondilated part of the colon. However, there must be as yet undefined and unknown factors responsible for the hypomotility observed in normoganglionic colon, since many patients still suffer from postoperative constipation, in spite of the surgeon's pulling down a nondilated portion of the colon.

Unpreventable Complications

Enterocolitis is the most feared, mysterious, unpreventable, and unpredictable complication seen in Hirschsprung's disease. Some surgeons claim that they do not see enterocolitis in their patients. One can only suspect that this is perhaps because they do not look for it. Perhaps they only think of enterocolitis when they see an extremely sick child. We always try to detect these cases very early by taking x-ray films very early postoperatively. One can see varying degrees of dilatation of the colon as well as irregularities in the bowel mucosa indicating that the patient is at risk for developing enterocolitis. We treat these patients with rectal irrigations and metronidazole by mouth and sometimes by rectum. A combination of these measures helps avoid the full picture of enterocolitis. We are unaware of any specific ways to prevent enterocolitis. Besides the medical treatment, consisting of the use of irrigations and metronidazole, some surgeons use myectomies or anal

dilatations and claim that these yield good results in the management of enterocolitis.[68] Other surgeons have reported the use of botulinum toxin injected into the internal sphincter. Results have been good but only for short periods of time.[69]

Results

Mortality, in general, has been reported to be between 0% and 3.3%.[70,71] Swenson claims that 13% of their patients suffer from temporary soiling and 16% to 27% from postoperative enterocolitis. in 16–27%.[64,65] Duhamel's advocates reported a 10% complication rate.[6–8,72] Soave[10] reported a 12% incidence of strictures.

We believe that enterocolitis has been underestimated and underreported. The incidence of this complication in different analyses varies from 10% to 30%.[33–38]

Results of the transanal approach for Hirschsprung's disease are still considered preliminary due to the lack of long-term follow-up. Early follow-up, however, indicates that the results do not seem to be better or worse than those obtained with previous techniques. The transanal approach, however, has obvious advantages over the other operations because it is the least invasive, including laparoscopy. The main concern with the transanal approach is the possibility of interfering with bowel control due to the stretching of the sphincter mechanism that is required to expose the anal area needed to perform this operation.

Total Colonic Aganglionosis

This particular variant of Hirschsprung's still represents a serious technical challenge. Different treatments have been designed to deal with this condition, but all of them are considered less than ideal in terms of results in quality of life. In 1968, Lester Martin[73] described his technique for the treatment of total colonic aganglionosis. Patients with total colonic aganglionosis, in order to fulfill the basic principles of treatment of this condition, would require resection of the entire colon and pull-through of the normoganglionic small bowel anastomosed to the anal canal. As expected, these patients suffer from multiple bowel movements during the day and night, severe diaper rash, and a tendency to suffer dehydration. To avoid these problems, Martin thought that it could be useful to preserve a significant portion of the aganglionic colon to take advantage of its water absorption capacity and also to create a kind of reservoir that would allow the patient to hold the stool and to decrease the number of daily bowel movements. Martin[74] proposed preserving the rectosigmoid and sometimes even longer portions of the colon. The normal ganglionic terminal ileum is then pulled down through the presacral space (like the Duhamel technique), and anastomosed to the rectum. A long laterolateral anastomosis is created between the terminal ileum and the rectosigmoid; those patients frequently suffer from abdominal distention and bouts of enterocolitis. In retrospect, we know that the small bowel functions well with rapid transit. Stasis in the small bowel produces an inflammatory process that results not only in lack of absorption of water but also a secretory type of diarrhea and enterocolitis. Many of these patients have to be reoperated on to resect the pouch or patch of aganglionic bowel. After Martin, others attempted modifications to his original procedure. Kimura et al,[75,76] for instance, created a right colon patch basically following the same principles as Martin. Generally the Martin and Kimura procedures, most of the time, are performed with a protecting ileostomy.

References

1. Hirschsprung H. Stuhltragheit neugeborner in folge von dilatation and hypertrophie des colons. Jaharb Kinderch 1987;27:1.
2. Tittel K. Uber eine angeborene missbildung des dickdrmes. Wien Klin Wochenschr 1901;14:903.
3. Whitehouse ER, Kernohan JW. Myenteric plexus in congenital megacolon. Arch Intern Med 1948;82:75.
4. Zuelzer WW, Wilson JL. Functional intestinal obstruction on a congenital neurogenic basis in infancy. Am J Dis Child 1948;75:40.
5. Swenson O, Bill AH. Resection of rectum and rectosigmoid with preservation of the sphincter for benign spastic lesions producing megacolon. Surgery 1948;24:212.
6. Duhamel B. A new operation for the treatment of Hirschsprung's disease. Arch Dis Child 1960;35:38.
7. Duhamel B. Retrorectal and transanal pull-through procedure for the treatment of Hirschsprung's disease. Dis Colon Rectum 1964;7:455.
8. Duhamel B. Une nouvelle operation pour le megacolon congenital: l'abaissement retrorectal et trans-anal du

colon, et son application possible au traitement de quelques autres malformations. Presse Med 1956;64: 2249.
9. Rehbein F, von Zimmermann VH. Ergebnisse der intraabdominellen Resektion bei der Hirschsprung'schen. Krankheit Zbl Chir 1959;84:1744.
10. Soave F. Hirschsprung's disease: a new surgical technique. Arch Dis Child 1964;39:116.
11. Boley S. An endorectal pull-through operation with primary anastomosis for Hirschsprung's disease. Surg Gynecol Obstet 1968;127:353.
12. De La Torre L, Ortega J. Transanal endorectal pullthrough for Hirschsrpung's disease. J Pediatr Surg 1998;33:1283.
13. Curran TJ, Raffensperger JG. The feasibility of laparoscopic Swenson pull-through. J Pediatr Surg 1994;29: 1273.
14. Smith BM, Steiner RB, Lobe TE. Laparoscopic Duhamel pullthrough procedure for Hirschsprung's disease in childhood. J Laparoendosc Surg 1994;4:273.
15. Georgeson KE, Fuenfer MM, Hardin WD. Primary laparoscopic pullthrough for Hirschsprung's disease in infants and children. J Pediatr Surg 1995;30:1017.
16. Georgeson KE, Cohen RD, Hebra A, et al. Primary laparoscopic assisted endorectal colon pullthrough for Hirschsprung's disease: a new gold standard. Ann Surg 1999;229:678.
17. Ikawa H, et al. Acetylcholinesterase and manometry in the diagnosis of the constipated child. Arch Surg 1986;121:435.
18. Bodian M. Pathologic aids in the diagnosis and management of Hirschsprung's disease. In: Dyke SD, ed. Recent Advances in Clinical Pathology. London: Churchill Livingstone, 1960.
19. Ikawa H, et al. A quantitative study of the acetylcholine in Hirschsprung's disease. J Pediatr Surg 1980;15:48.
20. Lake BD, Malone MT, Risdon RA. The use of acetylcholinesterase (AchE) in the diagnosis of Hirschsprung's disease and intestinal neuronal dysplasia. Pediatr Pathol 1989;9:351.
21. Lake BD, Puri P, Nixon HH, et al. Hirschsprung's disease: an appraisal of histochemically demonstrated acetylcholinesterase activity in suction rectal biopsy specimens as an aid to diagnosis. Arch Pathol Lab Med 1978;102:244.
22. Schofield DE, Devine W, Unis EJ. Acetylcholinesterase-stained suction rectal biopsies in the diagnosis of Hirschsprung's disease, J Pediatr Gastroenterol Nutr 1990;11:221.
23. Swenson O, Sherman JO, Fisher JH. Diagnosis of congenital megacolon: an analysis of 501 patients. J Pediatr Surg;1973;8:587.
24. Vane D, Grosfeld J. Hirschsprung's disease, experience with the Duhamel operation in 195 cases. Pediatr Surg Int 1986;1:95.
25. Ikeda K, et al. Long segment aganglionosis (Hirschsprung disease) in brothers. Shujutsu 1968;22:806.
26. Ikeda K, Goto S. Total colonic aganglionosis with or without small bowel involvement: an analysis of 137 patients. J Pediatr Surg 1986;21:319.
27. Prevot J, et al. Hirschsprung's disease with total colonic involvement. Therapeutic problems. Prog Pediatr Surg 1972;4:63.
28. Ziegler MM, Ross AJ, Bishop HC. Total intestinal aganglionosis: a new technique for prolonged survival. J Pediatr Surg 1987;22:82.
29. Neilson IR, Yazbeck S. Ultrashort Hirschsprung's disease: myth or reality. J Pediatr Surg 1990;25:1135.
30. Bealer JF, et al. Effect of nitric oxide on the colonic smooth muscle of patients with Hirschsprung's disease. J Pediatr Surg 1994;29:1025.
31. Kobayashi H, O'Brian DS, Puri P. Lack of expression of NADPH—diaphorase and neutral cell adhesion molecule (NCAM) in colonic muscle of patients with Hirschsprung's disease. J Pediatr Surg 1994;29:301.
32. O'Kelly TJ, et al. Abnormalities of nitric-oxide producing neurons in Hirschsprung's disease: morphology and implications. J Pediatr Surg 1994;29:294.
33. Bill JAH, Chapman ND. The enterocolitis of Hirschsprung's disease: its natural history and treatment. Am J Surg 1962;103:70.
34. Caneiro P. Enterocolitis in Hirschsprung's disease. Pediatr Surg Int 1992;7:356.
35. Elhalaby EA. Enterocolitis associated with Hirschsprung's disease: a clinical-radiological characterization based on 168 patients. J Pediatr Surg 1995;30:76.
36. Elhalaby EA, et al. Enterocolitis associated with Hirschsprung's disease: a clinical histopathological correlative study. J Pediatr Surg 1995;30:1023.
37. Fujimoto J, Puri P. Persistence of enterocolitis following diversion of fecal stream in Hirschsprung's disease. A study of mucosal defense mechanisms, Pediatr Surg Int 1988;3:141.
38. Lifschitz CH, Bloss R. Persistence of colitis in Hirschsprung's disease. J Pediatr Gastroenterol Nutr 1985;4: 291.
39. Wilson-Storey D, Scobie WG. Impaired gastrointestinal mucosal defense in Hirschsprung's disease: a clue to the pathogenesis of enterocolitis? J Pediatr Surg 1989;24: 462.
40. Wilson-Storey D, Scobie WG, Raeburn JA. Defective white blood cell function in Hirschsprung's disease: a possible predisposing factor to enterocolitis. J R Coll Surg Edinb 1988;33:185.
41. Russell MB, Russell CA, Niebuhr E. An epidemiological study of Hirschsprung's disease and additional anomalies. Acta Paediatr 1994;83:68.
42. Spouge D, Baird PA. Hirschsprung's disease in a large birth cohort. Teratology 1985;32:171.
43. Orr JD, Scobie WJ. Presentation and incidence of Hirschsprung's disease. Br Med J 1983;287:1671.
44. Bielschowsky M, Scholfield G. Studies on the inheritance and neurohistology of megacolon in mice. Proc Univ Otago Med School 1960;38:14.
45. Rosenfield NS, et al. Hirschsprung's disease: accuracy of the barium enema examination. Radiology 1984;150: 393.
46. Smith GH, Cass D. Infantile Hirschsprung's disease is a barium enema useful? Pediatr Surg Int 1991;6: 318.
47. Taxman TL, Yulish BS, Rothstein FC. How useful is the barium enema in the diagnosis of infantile Hirschsprung's disease? Am J Dis Child 1986;140:881.
48. Davies M, Cywes S, Rode H. The manometric evaluation of the rectospincteric reflex in total colonic aganglionosis. J Pediatr Surg 1981;16:300.
49. Loening-Baucke V, Pringle KC, Ekwo EE. Anorectal manometry for the exclusion of Hirschsprung's disease in neonates. J Pediatr Gastroenterol Nutr 1985;4: 596.
50. Loening-Baucke VA. Anorectal manometry: experiences with strain gauge pressure transducers for the

diagnosis of Hirschsprung's disease. J Pediatr Surg 1983;18:595.
51. Meunier P, Marechal JM, Mollard P. Accuracy of the manometric diagnosis of Hirschsprung's disease. J Pediatr Surg 1978;13:411.
52. Tamate S, et al. Manometric diagnosis of Hirschsprung's disease in the neonatal period. J Pediatr Surg 1984;19:285.
53. Yokoyama J, et al. studies on the rectoanal reflex in children and in experimental animals: an evaluation of neuronal control of the rectoanal reflex. Prog Pediatr Surg 1989;25:5.
54. Andrass RJ, Isaacs H, Weitzman JJ. Rectal suction biopsy for the diagnosis of Hirschsprung's disease. Ann Surg 1981;193:419.
55. Athow AC, Filipe MI, Drake DP. Problems and advantages of acetylcholinesterase histochemistry of rectal suction biopsies in the diagnosis of Hirschsprung's disease. J Pediatr Surg 1990;25:520.
56. Challa VR, et al. Histologic diagnosis of Hirschsprung's disease: the value of concurrent hematoxylin and eosin and cholinesterase staining of rectal biopsies. Am J Clin Pathol 1987;88:324.
57. Dobbins WO, Bill AH. Diagnosis of Hirschsprung's disease excluded by rectal suction biopsy. N Engl J Med 1965;272:990.
58. Aldridge RT, Campbell PE. Ganglion cell distribution in the normal rectum and anal canal. A basis for the diagnosis of Hirschsprung's disease by anorectal biopsy. J Pediatr Surg 1968;3:475.
59. Swenson O, Fisher JH, Gherardi GJ. Rectal biopsy in the diagnosis of Hirschsprung's disease. Surgery 1959;45:690.
60. So HB, Schwartz DL, Becher JM, et al. Endorectal pullthrough without preliminary colostomy in patients with Hirschsprung's disease. J Pediatr Surg 1980;15:470.
61. Carcassone M, Morisson LG, Letourneau JN. Primary corrective operation without decompression in infants less than three months of age with Hirschsprung's disease. J Pediatr Surg 1982;17:241.
62. Cass DT. Neonatal one stage repair of Hirschsprung's disease. Pediatr Surg Int 1990;5:341.
63. Cilley RE, et al. Definitive treatment of Hirschsprung's disease in the newborn with a one-stage procedure. Surgery 1994;115:551.
64. Weitzman J. Management of Hirschsprung's disease with the Swenson procedure with emphasis on long-term follow-up. Pediatr Surg Int 1986;1:100.
65. Weitzman JJ, Hanson BA, Brennan LP. Management of Hirschsprung's disease with the Swenson procedure. J Pediatr Surg 1972;7:157.
66. Langer JC, Minkes RK, Mazziott MV, et al. Transanal one stage Soave procedure for infants with Hirschsprung's disease. J Pediatr Surg 1999;34:148.
67. Langer JC, Durrant AC, de la Torre L, et al. One-stage transanal Soave pullthrough for Hirschsprung's disease. A multi-center experience with 141 children. Ann Surg 2003;238:569.
68. Lynn HB, van Heerden JA. Rectal myectomy in Hirschsprung's disease: a decade of experience. Arch Surg 1975;110:991.
69. Ron Y, Avni Y, Lukovetski A, et al. Botulinum toxin type-A in therapy of patients with anismus. Dis Colon Rectum 2001;44:1821.
70. Kleinhaus S, et al. Hirschsprung's disease—a survey of the members of the surgical section of the American Academy of Pediatrics. J Pediatr Surg 1979;14:588.
71. Rescorla FJ, et al. Hirschsprung's disease. Evaluation of mortality and long-term function in 260 cases. Arch Surg 1992;127:934.
72. Talbert JL, Seashore JH, Ravitch MM. Evaluation of a modified Duhamel operation for correction of Hirschsprung's disease. Ann Surg 1974;179:671.
73. Martin LW. Surgical management of Hirschsprung's disease involving the small intestine. Arch Surg 1968;97:183.
74. Martin L. Surgical management of total aganglionosis. Ann Surg 1972;176:343.
75. Kimura K, Mishijima E, Muraji T. A new surgical approach to extensive aganglionosis. J Pediatr Surg 1981;16:840.
76. Kimura K, et al. Extensive aganglionosis: further experience with the colonic patch graft procedure and long-term results. J Pediatr Surg 1988;232:52.

25

Chagasic Megacolon

Hélio Moreira, Joffre M. de Rezende, Hélio Moreira Jr., and José Paulo T. Moreira

The term *megacolon* has been the source of some confusion in the international literature. Searching for "dilatation of muscular hollow organs," more than 20 different terms can be found. There are also many diverging theories regarding the possible pathogenesis. Frequently, it has been termed "idiopathic dilatation." Etymologically, megacolon means "large colon" and thus the term has been used to describe any dilatation of the colon regardless of its etiology. Koeberle[1] believed that the term *megacolon* should be used exclusively to define cases in which altered motility as a consequence of a damaged myenteric nerve plexus is the cause of bowel dilatation. This etiology includes Chagas' disease and parasympathetic pharmacologic blockage. The latter condition is observed in patients with Parkinson's disease who have been chronically treated with atropine-like drugs.

Shepherd and Wright[2] as well as Böhm and Smith[3] described a disorder affecting the population of Uganda, which they called "African megacolon." This disorder can be considered a true megacolon according to Koeberle's definition. Its cause is unknown, and the main damage seems to be located at the sacral parasympathetic innervation. Koeberle and other investigators have definitely linked endemic megacolon to Chagas' disease, which is a major health hazard in South America. There are some regions in Brazil where this infectious disease is highly prevalent. This subgroup of megacolon (Chagasic megacolon) is the subject of this chapter.

Historical Perspective

In 1909, a great scientific event occurred in Brazil: the discovery by a Brazilian scientist named Carlos Chagas (Fig. 25.1) of the American trypanosomiasis (Chagas' disease).[4] This is a protozoan infection caused by the flagellate *Trypanozoma (Schizotrypanum) cruzi*, widespread in the American continent, mainly among small wild mammals (enzootic sylvatic cycle). Bioecologic and socioeconomic factors leave rural poor populations of South and Central America in contact with the sylvatic cycle, where the parasite is transmitted by natural vectors of the infection, determining human Chagas. In 1916, after observing the onset of dysphagia in acute cases, Chagas attempted to correlate this symptom to the disease he had discovered.

In 1912, Arthur Neiva and Belizario Penna[5] took a scientific trip through the Brazilian hinterland. They traveled through the interior of Bahia, Pernambuco, Piaui, and Goias. Many cases of dysphagia were found in these states locally named *mal de engasgo*. In addition to dysphagia, they noted alterations in the heart rhythm, popularly called "vexame," and constipation, "caseira." Megaesophagus and megacolon were extensively studied during the 1930s and 1940s in Brazilian universities. The starting point at São Paolo School of Medicine was in 1932 when Amorim and Netto[6] published their report describing lesions of the myenteric plexus not only in the esophagus and colon but also throughout the entire digestive tract.

Subsequently Etzel[7] demonstrated the pathogenic identity of megaesophagus and megacolon and its systemic character. Several other authors established a link between the megas and Chagas' disease based on clinical and epidemiological evidence.

The theory of Chagasic etiology was reinforced by two important studies performed in 1946. De Freitas[8] submitted 80 patients with megaesophagus and megacolon to the complement fixation test for Chagas' disease and

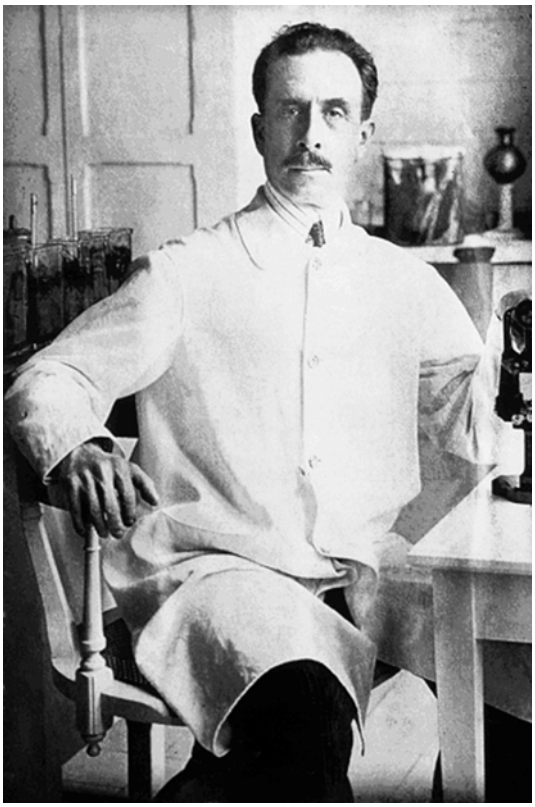


Figure 25.1. Professor Carlos Chagas, who discovered Chagas' disease.

observed a 91.2% positive result. Laranja et al[9] conducted an identical study on 81 patients with megaesophagus and found 97% positive reactions. This high serologic positivity could never have been a random occurrence and clearly indicated the etiologic relationship between Chagas' disease and the "megas."

Koeberle[10–12] provided the definitive anatomopathologic confirmation of this relationship. His famous studies were performed at the School of Medicine of Ribeirao Preto, University of São Paulo, beginning in l955. These studies demonstrated that Chagas' disease causes lesions of the nervous intramural plexuses described earlier. By counting the cells of the esophagus and colon during autopsy on patients with Chagas' disease, Koeberle detected the ubiquitous presence of a variable degree of denervation in the intramural plexuses.

Koeberle's studies on the esophagus and colon were extended to other segments of the digestive tract, as well as to the other organs, demonstrating the presence of universal autonomic denervation in Chagas' disease.[13,14] Other authors later confirmed this denervation.[15,16] The great contribution made by Koeberle was to regard Chagas' disease as a disorder of the autonomic nervous system.

One of the difficulties in accepting megaesophagus and megacolon as manifestations of Chagas' disease was the fact that these phenomena can be very rare or even absent in some regions where Chagas' disease is endemic. This regional difference in Chagas' disease occurs due to the existence of different strains of *Trypanosoma cruzi*. Differences among strains can be demonstrated by biologic and biochemical studies of the parasite.[17–19] In 1959 Rezende[20] pointed out the clinical manifestations of the digestive tract of Chagas' disease.

Incidence

Megacolon, one of the clinical manifestations of Chagas' disease or American trypanozomiasis, is described in all endemic areas. The change of the natural triatominae's habitat into human domicile exposed more than 90 million individuals to infection risk, including populations from the south of the United States to Argentina.[21,22] However, better living standards in North American dramatically diminished the potential of vector transmission of Chagas' disease. In fact, there are even marked regional differences in the incidence of megacolon among Latin American populations suffering from Chagas' disease. These differences are probably due to different protozoa strain prevalences over these areas. Brazilian investigators have reported the largest number of cases with particularly high incidences in the states of São Paulo, Minas Gerais, Goias, and Bahia.

Outside Brazil, megacolon is found in Chile, where, according to Atias[23] megacolon is more frequent than is megaesophagus. Chagasic megacolon is also found in Argentina, more commonly in the northern provinces.[24] Autochthonous cases have also been reported in Peru and Bolivia[25], while in other endemic areas of Chagas' disease, including Venezuela, Colombia, and Panama, chagasic megacolon is not found. These reports reinforce the theory of different protozoa strains. In the central region of Brazil, megacolon is the most common of all colon diseases (Fig. 25.2).

Figure 25.2. Map of geographic distribution of Chagas' disease in Latin America.

Patients and Their Social Conditions

Most patients with Chagas' disease come from endemic regions, living in rural areas in huts with walls of mud-covered wattle, which are infested by Triatominae. Approximately 90% of all megacolon patients are field laborers or their relatives. The remaining 10% reported that they have lived for some time on farms or small villages where they were in contact with the insects. Table 25.1 shows the age distribution of 622 patients. A high prevalence is noted between the fourth and sixth decades of life; there is no gender preference for chagasic megacolon.

Table 25.1. Age distribution of 622 patients with chagasic megacolon

Age group (years)	No. of cases	%
0–9	2	0.32
10–19	22	3.54
20–29	84	13.50
30–39	136	21.86
40–49	170	27.33
50–59	141	22.67
60–69	51	8.20
70+	16	2.57
Total	622	100.0

Table 25.2. Lapsed time between the onset of symptoms and initial presentation in 867 patients

Interval (years)	No. of cases	%
0–4	370	42.68
5–9	168	19.38
10–14	148	17.07
15–19	87	10.03
20–24	65	7.50
25–29	9	1.04
30+	20	2.31
Total	867	100.0

Clinical Course

The fate of Chagasic patients overcoming the acute phase of the disease and progressing to the chronic phase is unpredictable, as the majority remain apparently asymptomatic for long periods or even permanently. According to surveys made in endemic areas of Brazil, only 8% to 10% of infected people present with the digestive form of the disease, characterized by the presence of megaesophagus, megacolon, or both. This rarity of clinical evolution in Chagas' disease is not well understood. It has been ascribed to infection with different strains of *T. cruzi* and to host-related immunologic factors. Within the limitations of clinical history, it was possible to determine in 867 patients the time that had elapsed between the onset of symptoms and the first medical visit (Table 25.2). The largest number of patients presented within 4 years of symptom onset and most cases are seen within 14 years. However, some patients present after more than 30 years of symptoms.

Etiology and Pathogenesis

It has been demonstrated that Chagas' disease causes a marked reduction in the number of neurons in the enteric nervous system, especially in the myenteric plexus of the intestinal wall. This intrinsic denervation causes motor disorders with stagnation of the feces, dilatation,

hypertrophy, and lengthening of the sigmoid. The mechanism by which the nerve cell destruction occurs has been investigated by many authors and is still a subject of controversy.[26–28]

Pathologic Anatomy

The dilatation and lengthening of the colon are confined, in most cases, to the sigmoid and rectum; however, the entire colon including the cecum can be involved. Initially, the colon (usually the sigmoid) exhibits a hypertrophied muscle wall and a thickened mesocolon. The mucosa appears normal in color, has a redundant aspect, and, in some cases, has one or more ulcers. These lesions presumably result from the trauma of fecaloma. These ulcers are called stercoraceous, contact, or decubitus ulcers, which may eventually cause colonic perforation.

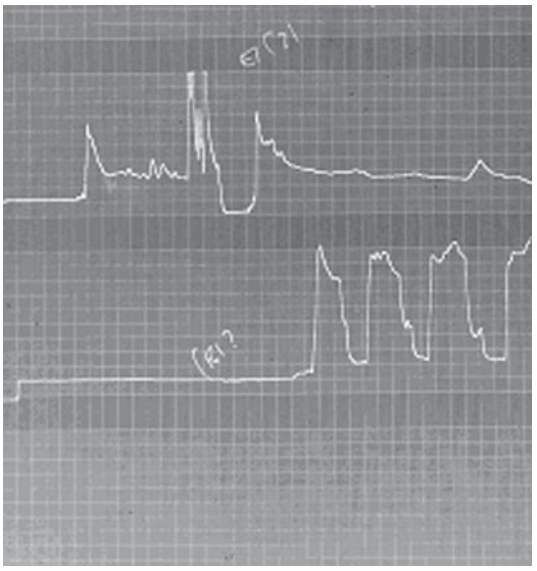


Figure 25.3. Achalasia of the internal anal sphincter in a patient with Chagasic megacolon. Rectal distention (R) fails to relax the internal anal sphincter (E).

Physiopathology

It is known that destruction of the intramural plexuses alters colonic motility. In Chagasic colopathy, there is hyperreactivity to cholinergic stimulation, as confirmed by manometric test. Using of 0.05 mg/kg of methacholine, uncoordinated contraction of the rectum and sigmoid colon are recorded. The result is the opposite to that observed in patients with Hirschsprung's disease. A similar result is obtained with the use of neostigmine.[29,30]

It has been reported that motor incoordination is also present during spontaneous activity of the rectum and sigmoid colon, with simultaneous contraction of both segments. Normal patients do not exhibit this uncoordinated activity. After resection of a segment of dilated colon and coloanal anastomosis, patients with Chagas' disease continue to display the same pattern of colonic motor activity.[31] These data indicate that the entire colon and not only the dilated segment is affected with Chagas' disease. However, after the Duhamel operation the pulled-through colon and the rectal stump synchronism disappears.[30] This motor synchronism may disappear after surgery due to the anatomic continuity between the two segments (lateral-lateral anastomosis). Contradictory data have been obtained after manometric study of basal motor activity. In chagasic megacolon, the gastrocolic reflex is absent. This absence is probably due to hyporeactivity of the denervated colon to the action of pentagastrin, cholecystokinin, and other peptides released into the duodenun.[32,33] Another very important alteration encountered in Chagasic colopathy is the lack of relaxation of the internal anal sphincter when the rectal wall is distended. This loss of the rectoanal inhibitory reflex is known as sphincter achalasia.[34] This phenomenon emphasizes the importance of anorectal manometry in the evaluation of constipation. Figure 25.3 shows achalasia of the internal sphincter; rectal distention fails to relax the internal anal sphincter (the rectoanal inhibitory reflex is absent).

Clinical Signs and Symptoms

Megacolon as an isolated manifestation of Chagas' disease is infrequent, being associated with simultaneous involvement of the esophagus in the majority of cases. The main suspicious signs and symptoms of megacolon are difficulty in intestinal evacuation with consequent retention of feces and gas.

Constipation is usually of insidious onset and is resistant to standard clinical treatment; 70% of 268 patients moved their bowel with 10-day intervals, 11% every 30 to 60 days, and one

Table 25.3. Obstipation observed in 268 patients with Chagasic megacolon

Obstipation (days)	No. of cases	%
1–10	78	29.1
11–20	92	34.3
21–30	61	22.8
31–60	30	11.2
61–90	5	1.9
90+	2	0.7
Total	268	100.0

patient had not evacuated for over 6 months (Table 25.3).

Among socioeconomically poor individuals in rural areas, the severity of constipation becomes increasingly worse, favoring the formation of fecalomas. It is understandable how, under these circumstances, megacolon will rapidly evolve. Another frequent symptom is meteorism. The presence of the gas produces abdominal distention, fullness, localized tympany, and frequent abdominal cramps. The patient also reports a sensation of narrowing of the anal canal, which might be a consequence of achalasia of the internal anal sphincter. Physical examination reveals asymmetrical abdominal swelling: the asymmetry may result from the sigmoid colon being medially displaced. Palpation may reveal the presence of fecalomas, which can be recognized by the clay-like consistency. Percussion shows marked tympanism depending on the degree of colonic ectasia. In the presence of a fecaloma, tympanism is replaced by a low-pitched sound.[35]

Disease Associations

Megacolon and Megaesophagus

There is a frequent association of megacolon and megaesophagus. Rezende and Moreira[36] radiologically examined the esophaguses of 101 patients with megacolon. They observed that 92 patients had altered esophageal motility and 71 had megaesophagus.

Megacolon and Chagasic Heart Disease

It is relatively common to find Chagasic heart disease among patients with megacolon. Analysis of 365 patients revealed an abnormal electrocardiogram in 288 (78.9%). The most common changes found were right bundle branch block and ventricular extrasystoles. We often see patients with cardiomegaly when cardiac failure is present (Figure 25.4).

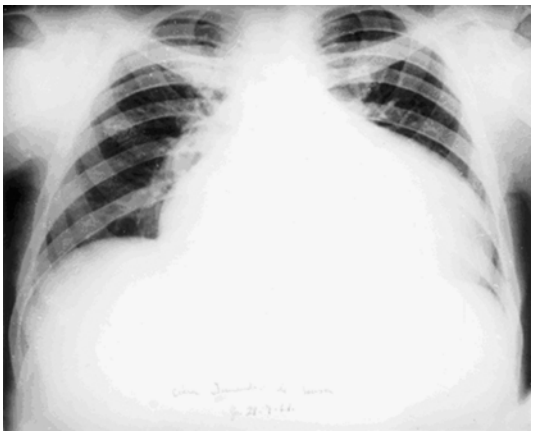


Figure 25.4. Plain radiograph of the chest indicating Chagasic cardiomegaly.

Megacolon and Colon Cancer

Chagasic megaesophagus increases the incidence of esophageal cancer, with a prevalence ranging from 3.9% to 9%. However, there is no known relationship between Chagasic megacolon and colon adenocarcinoma. Despite any formal precursor relationship, there are a few reports in the literature of adenocarcinoma of the colon in patients with chagasic megacolon, one of them found by autopsy.

A serologic screening for Chagas' disease in a hospital-based population located in an endemic area of central Brazil, where a seropositivity prevalence of 7% is expected, showed a similar prevalence of this infection between patients with benign and malignant colorectal disease.[37–39]

More than 95% of the patients with Chagasic megacolon complain of constipation, and the majority have a bowel movement less frequently than every 10 days (Table 25.3). Thus, constipation, as described by many authors, might be considered an important factor in the genesis of colorectal cancer, as it prolongs the contact of potential carcinogens in the stool with the colonic mucosa.[40–42] Therefore, it would be expected that a higher incidence of colorectal cancer would occur in individuals with Chagasic megacolon. However, no such association exists.

Colorectal cancer could be underestimated or misdiagnosed among patients with Chagasic megacolon. However, considering that Chagasic megacolon is mainly surgically treated, the possibility of a misdiagnosis of coloretal cancer in such patients is highly unlikely.

Diagnosis

Chagasic colopathy should be considered in any patient with either megaesophagus (Figure 25.5) or Chagasic heart disease who resides in a zone where Chagas' disease is endemic and who has a history of constipation.

After physical examination involving abdominal and proctologic examination, the patient should undergo a plain radiograph and a barium enema (Figs. 25.6). In cases of incipient megacolon without radiologic enlargement of the sigmoid, manometric studies of the colon and pharmacologic tests for denervation are indicated. A water-soluble contrast enema (rather than barium) may also be of some value (Fig. 25.7).

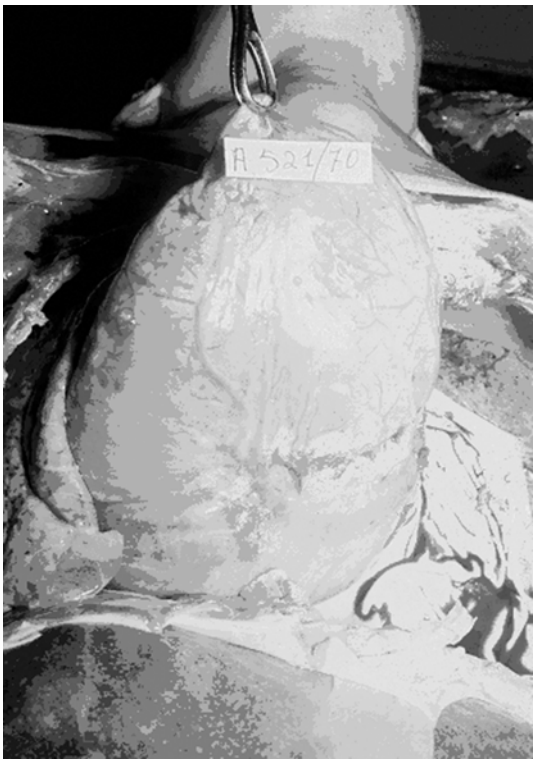


Figure 25.5. Enormous megaesophagus at necropsy.

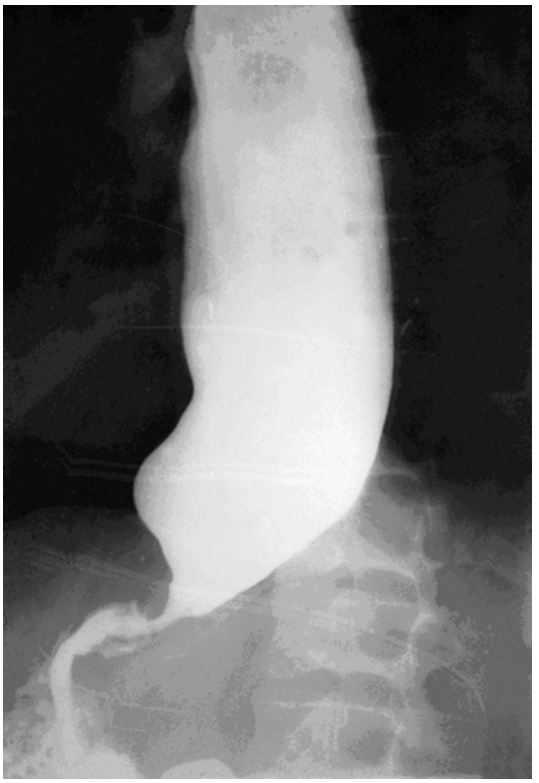


Figure 25.6. Contrast barium view of advanced chagasic megaesophagus.

Serologic Test for Chagas' Disease

The serologic tests for Chagas' disease, including complement fixation tests, hemagglutination, and immunoenzymatic tests, give positive rates in 97% to 100% of cases of Chagasic megacolon. This high serologic positivity detected in acquired megacolon could never be a random occurrence and clearly indicates the etiologic relationship between Chagas' disease and megacolon.

Differential Diagnosis

The differential diagnosis for colonic dilatation includes mechanical obstruction such as carcinoma. All other causes of anorectal stenosis must be excluded. In endemic regions it is sometimes difficult to differentiate between Hirschsprung's disease and Chagasic megacolon; therefore, in young patients, both conditions should be considered. The concomitant

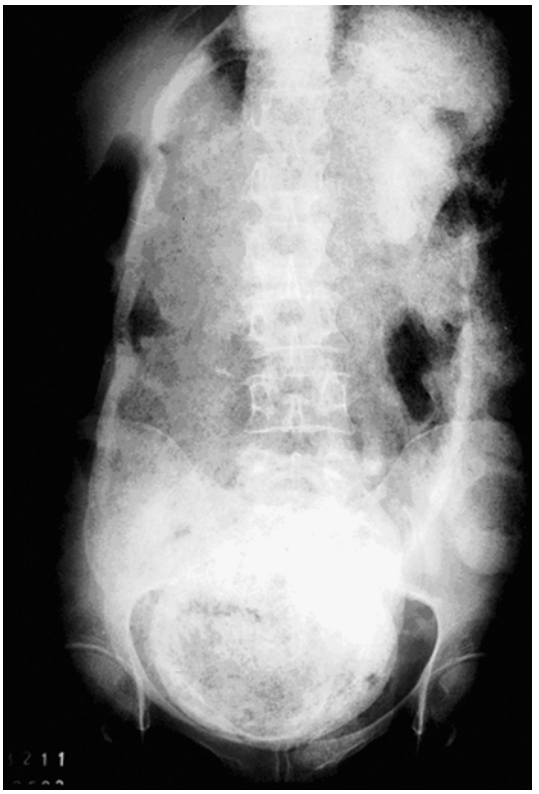


Figure 25.7. Barium enema showing a chronic intrarectal fecaloma.

presence of megaesophagus or heart disease can help in clinical evaluation. Ultimately, rectal biopsy and physiologic studies of the anus, rectum, and sigmoid are needed.

Complications

The most important complications of Chagasic megacolon are fecal impactation, fecaloma, ischemic colitis, and sigmoid volvulus.

Fecaloma

Initially, patients with Chagas' disease attempt to achieve normal evacuation using laxatives and enemas. Ultimately, these patients cease to worry about infrequent evacuation. This lack of bowel activity occurs despite increased refractoriness of the colon to cathartic compounds. The result is an accumulation of feces in the intestine, mostly in the sigmoid colon and even more so in the rectum; with time, the accumulated feces progressively dehydrate, becoming a hard fecal stone, the so-called fecaloma (Fig. 25.8). The authors have observed patients who have retained such fecalomas for up to 3 months.

The diagnosis is made by physical examination; a mass may be palpable either in the abdomen or in the rectum. A plain abdominal radiograph may reveal the fecaloma with its characteristic "breadcrumb" or "ground-glass" appearance. The treatment of the fecaloma depends on its location and duration.

Fecalomas that are not too hard can sometimes be resolved with intestinal lavage with saline irrigation. This procedure should only be performed in a hospital setting due to the risk of perforation. Scybalous stools require manual evacuation, preferably spinal anesthesia as a disimpaction method. The feces need to be broken up and removed step by step initially with a finger, until the first and most hardened portions that acted as the plug have been removed. Following this procedure, intestinal lavage is undertaken with judicious use of lukewarm water, until the terminal portion of the intestine has been fully cleansed.

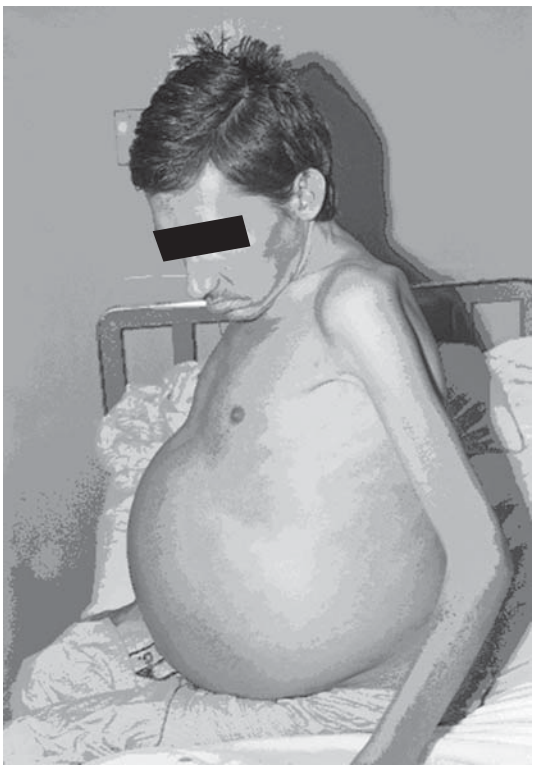


Figure 25.8. Patient with Chagasic megacolon and fecaloma.

Figure 25.9. Fecaloma inside of a resected sigmoid colon.

In rare cases the fecaloma may be located in the upper rectum or sigmoid colon. In such cases the above maneuver will be unsuccessful and laparotomy is indicated. The preferred operation is a Hartmann's procedure, with resection of the segment, which includes the fecaloma with subsequent and later surgical treatment of the primary disease (megacolon).

A rare event is a patient with total fecaloma (a fecaloma which extends in continuity from the rectum to the cecum). Another rare event is a long chronic fecaloma (Fig. 25.9). Both of these lesions can cause pressure necrosis/ischemia followed by a stercoral ulcer. Stercoral perforation causes severe peritonitis. In 533 cases of patients with Chagasic megacolon at our institution, we reported an incidence of fecaloma of 43%.

Fecal Impaction and Ischemic Colitis

Fecal impaction is the obliteration of the intestinal lumen caused by a large static fecaloma, causing an intestinal occlusion. These patients complain of abdominal distention and abdominal pain; fortunately, the incidence of this complication is very low.

Ischemic colitis in Chagasic megacolon is an inflammatory process of the colonic mucosa due to an ischemic process, the etiology of which remains unknown. It may be due to microthrombosis in the vascular territory of the colon, as associated cardiac arrhythmia in patients with Chagas' disease is quite commonly observed. The endoscopic aspect may be similar to ulcerative colitis. Santos et al[43] reported 38 patients with ischemic colitis, 24 of whom had Chagasic megacolon.

Sigmoid Volvulus

Chagas' disease is associated with a high incidence of sigmoid volvulus. In most cases of volvulus the authors have observed the presence of localized mesenteritis at the sigmoid colon, which may be a contributing factor. Patients with Chagasic colopathy have hypermotility of the colon and sometimes mesenteritis. In the author's experience, the sigmoid twist is usually incomplete. Moreover, volvulus does not occur in patients with fecalomas since the weight of the fecal mass may prevent major movements of the colon loop. Rarely, a volvulus appears in patients with Chagasic megacolon with normal intestinal rhythm. In these rare cases the first manifestation of Chagasic colopathy is actually the sigmoid volvulus.

The clinical scenario of volvulus includes a distal intestinal obstruction. The patient often presents with an acute onset of lower abdominal pain and concurrent obstipation. The most important sign is the gradual and progressive increase in abdominal distention. Vomiting is not seen during the first hours and the general condition of the patient is deceptively good; the majority of patients are fully ambulatory. However, in the next few hours, clinical deterioration is expected as vascular compromise ensues.

Radiologic examination is of fundamental importance to confirm the diagnosis. A simple abdominal radiograph shows a considerably enlarged sigmoid colon, forming a loop, with an empty, gas-free rectum. At at more advanced stage, a fluid level may be seen; if necrosis has progressed to colonic perforation, pneumoperitoneum may be found. Barium enema is obviously contraindicated because of the risk of perforation.

The management of sigmoid volvulus depends both on the surgeon's experience and on the presence or absence of necrosis and gangrene of the twisted loop. The most commonly used procedures are intubation, laparotomy with detorsion of the loop (Fig. 25.10) and construction of a colostomy, Hartmann procedure, and sometimes resection and immediate anastomosis. The surgical choice is contingent upon both intraoperative findings and the patient's general condition, including comorbidities and any sepsis.

The authors' preference is Moreira's[44] procedure, as it greatly facilitates subsequent surgery. The technique consists of laparotomy with volvulus detorsion and anterior sigmoidostomy as close as possible to the rectosigmoid junction.

The fundamental characteristic of this sigmoidostomy is that the surgeon exteriorizes only the anterior wall of the sigmoid colon that acts as a mucous fistula. The distal colon progressively decreases its diameter until it reaches near-normal caliber.

Subsequently, based on the studies by Moreira, when the Duhamel surgical procedure is undertaken, there will be no need for resection of a large segment of colon as the length of the rectal stump is adequate. The authors' experience demonstrates that none of their patients required mobilization of the splenic flexure of the colon during the subsequent Duhamel operation. As expected, this technique facilitates and expedites the surgical procedure.

According to our experience, the incidence of sigmoid volvulus in Chagasic megacolon is approximately 30%; 174 of over 538 patients with Chagasic megacolon had volvulus.[44]

Treatment

The treatment of megacolon is mainly surgical. Laxatives or intestinal lavage are entirely palliative and are consequently indicated for patients in whom surgical intervention is either temporarily or permanently contraindicated. Dietary management is not generally worthwhile to improve symptoms. Excellent results are obtained with surgery as described by Duhamel[45] in 1956 for the treatment of congenital megacolon.

The technique consists of an abdominal and perianal approach. After laparotomy, a sigmoid loop resection is performed, suturing the rectal stump as a Hartmann's operation. The retrorectal space is then dissected up to the tip of the coccyx. The perianal stage follows, with dissection of the submucosal space of the posterior hemicircumference of the anal verge extending 3 to 4 cm from the dentate line. At this level, the posterior rectal wall is incised, opening a communication from the submucosal space to the already dissected retrorectal space. The mobilized left colon is exteriorized through this dissected tunnel to the anal verge. The colon is fixed to the posterior mucocutaneous margin of the anal canal. The anterior pulled through colonic wall and the posterior rectal mucosa, which was previously dissected, are double clamped in a V-shaped fashion. The clamps are

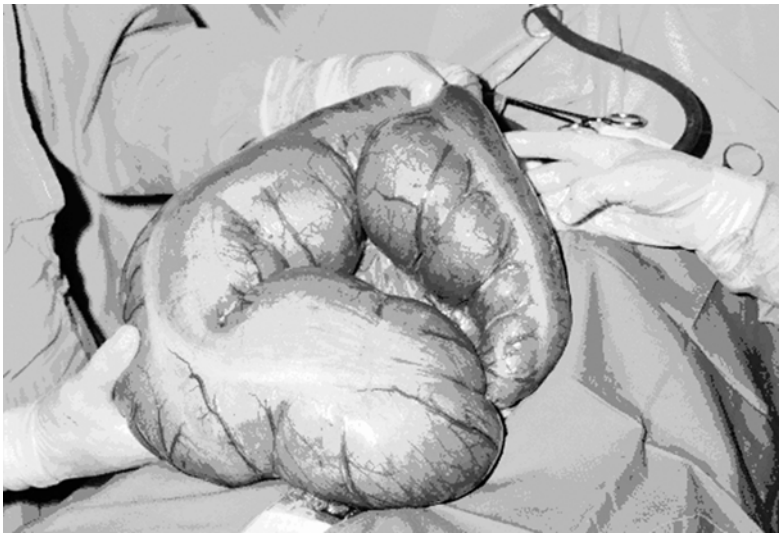


Figure 25.10. Detorsed sigmoid volvulus.

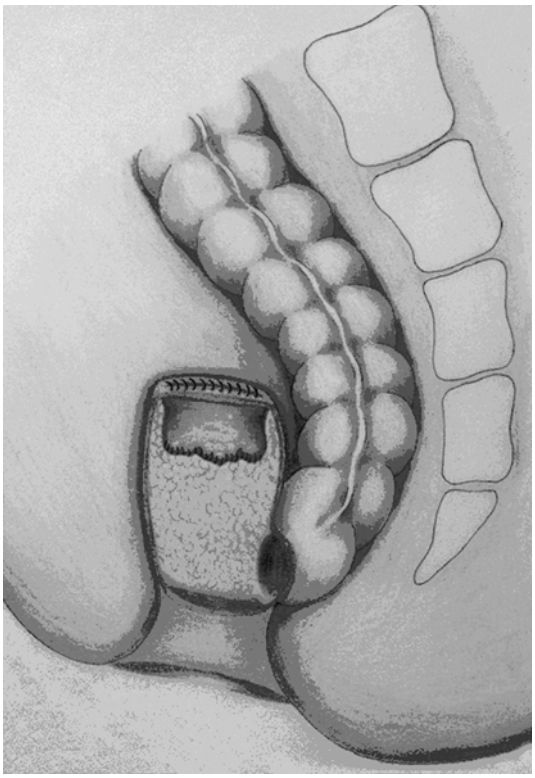


Figure 25.11. Duhamel operation.

left in place until they spontaneously fall apart, usually around the fifth postoperative day. This technique is illustrated in Figure 25.11, and the postoperative radiograph (enema) is shown in Figure 25.12.

In 1968, Haddad[46] proposed a modification of the Duhamel's technique. This variation consisted mainly of replacement of the clamps by a perineal colostomy, which was resected together with the rectocolic septum in a second operative stage. The latter procedure is performed 7 to 10 days later. This operation has gained popularity throughout Brazil and most other South American countries.

In 1974, Moreira[47] performed the Duhamel procedure in three patients with Chagasic megacolon with a large megacolon, and instead of sigmoid resection, this enlarged bowel segment was pulled through the retrorectal space, with delayed lateral-lateral sigmoid-rectal anastomosis. Long-term follow-up demonstrated that regardless of megasigmoid resection, this surgical technique successfully corrected the constipation. Moreover, a progressive reduction of sigmoid diameter was demonstrated on subsequent contrast barium enema. Based on this result, the authors are encouraged that the Duhamel operation does help ameliorate the physiopathologic mechanisms of Chagasic megacolon.

Despite good results in the Duhamel operation for Chagasic megacolon, no consensus was found in the literature for the universal best surgical technique. At present, however, the authors prefer the Duhamel operation. From 1966, surgeons at the School of Medicine at the University of Goias, Brazil, exclusively performed the Duhamel procedure with several technical modifications[48–51] on a total of 1145 patients

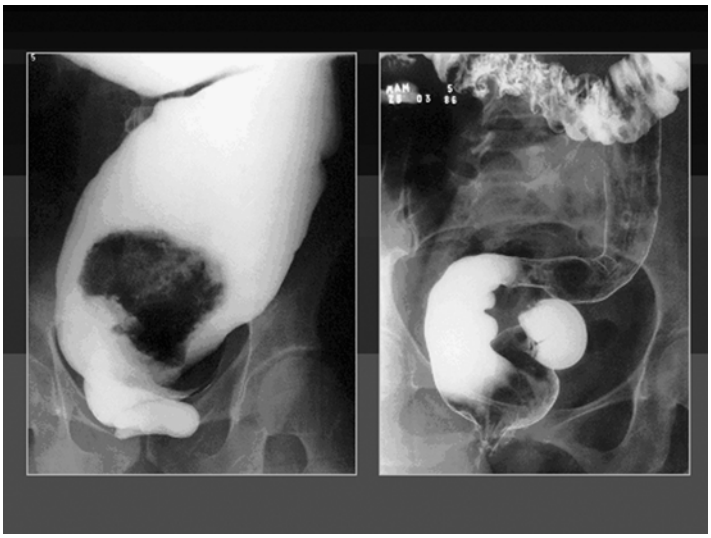


Figure 25.12. Pre- and post-Duhamel operation for a large megacolon with a rectal fecaloma. Postoperatively, the rectal stump and the pulled-through colon are seen in the retrorectal space.

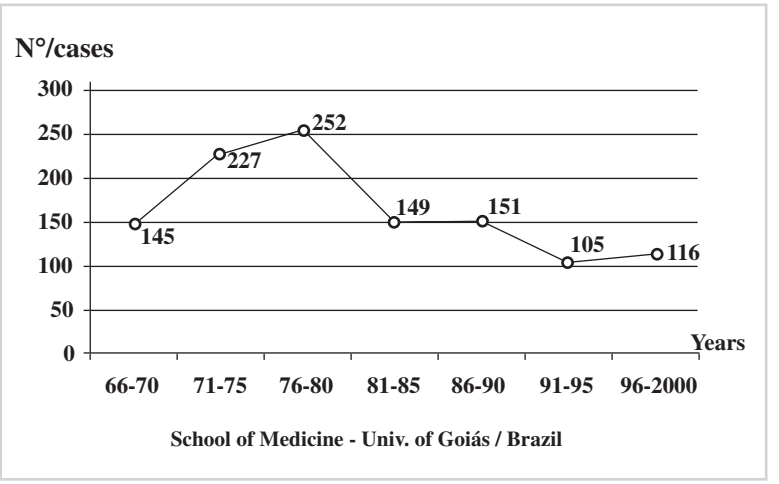


Figure 25.13. Patients operated for Chagasic megacolon through Duhamel's technique (1.145 cases) (Feb/1966 to Feb/2000).

operated between February 1966 and February 2000 (Fig. 25.13). Duhamel surgery, with an experienced surgical team, is associated with low recurrence rates (3%). Moreover, recurrent symptoms are rarely associated with dilatation of the pulled-through colon and are less severe than the preoperative condition. This may be caused by inappropriate surgical technique, including a long rectal stump or a low colorectal septum. The morbidity and mortality rates are unexpectedly low (15% and 1%, respectively), as these patients are usually severely ill with associated Chagasic cardiopathy and megaesophagus, which ultimately results in severe malnourishment. Moreira[52] performed anorectal manometry in patients with Chagasic megacolon before and after the Duhamel surgery was undertaken. There was a statistically significant symmetric decrease in the postoperative anal resting and squeeze pressures compared to the preoperative values. As well, an improvement was also seen in the rectal sensory threshold (p = .030), rectal capacity was significantly decreased postoperatively (p = .029), and rectal compliance was improved (p = .027). Moreira concluded that Duhamel's surgery decreases sphincter pressures at rest and during voluntary contraction of the anal canal. It also improves the rectal sensory threshold, decreases both rectal capacity and compliance, and, ultimately, normalizes intestinal function.

References

1. Koeberle F. Megacolon. J Trop Med Hyg 1958;61:21–24.
2. Shepherd JJ, Wright PG. Observations on megacolon. East Afr Med J 1965;42:401–406.
3. Böhm GM, Smith AB. Pathology of an East African megacolon. The Journal of The British Society of Gastroenterology—GUT 1966;7:662–665.
4. Chagas C. Nova tripanozomiase humana. Estudos sobre a morfologia e o evolutivo do Schizotrypanum cruzi n.gen.n.sp. agente etiológico de nova entidade mórbida do homen. Memórias do Instituto Oswaldo Cruz 1909;1(Fasc. II):1–62.
5. Neiva A, Penna B. Viagem cientifica pelo norte da Bahia. Sudeste do Piaui e do norte a sul de Goias. Mem Inst Oswaldo Cruz 1916;8:74.
6. Amorim M, Netto C. Histopatologia e pathogenese do megaesophago e megarrecto Consideracoes em torno de um caso de "Mal de Engasgo." Ann Fac Med Univ Sao Paulo 1932;8:101.
7. Etzel E. Neuropatologia do megaesofago e megacolo Estudo de 5 casos. Ann Fac Med Univ Sao Paulo 1934;10:383.
8. De Freitas JLP. Contribuiçao para o estudo do diagnostico da molestia de Chagas por processos de laboratorio. Sao Paulo Thesis. Faculty of Medicine. University of Sao Paulo, Sao Paolo, Brazil, 1947.
9. Laranja FS, Dias E, Nobrega G. Estudo electrocardiografico de 81 casos de megaesofago. Mem Inst Oswaldo Cruz 1948;46:473.
10. Koeberle F. Chagas Krankheit: eine Erkrankung de neurovegetativen peripherie. Wien Klin Wochenschr 1956;68:333.
11. Koeberle F. Molestia de Chagas—enfermidade do sistema nervoso. In: Congresso Internacional sobre Doenca de Chagas. Rio de Janeiro, 1959, vol. 2. Rio de Janeiro: Anais, 1961:691–716.
12. Koeberle F. Patologia y anatomia patologica de la enfermedad de Chagas Bol Sanit. Panam 1961;51:404.
13. Koeberle F. Cardiopatia Chagasica Hospital (Rio de Janeiro) 1958;53:311.
14. Koeberle F. Bronquiectasia Chagasica. In: Congresso Internacional sobre Doenca de Chagas, Rio de Janeiro, 1959, vol. 2. Rio de Janeiro: Anais, 1961:683–690.
15. de Costa R, de Alcantara FG. Gastropatia Chagasica cronica. Rev Bras Med 1965;22:667.
16. de Costa RB, de Alcantara FG. Duodenopatia chagásica crônica. Rev Brás Med 1966;23:158.
17. Andrade SG. Caracterização de cepas do Trypanosoma cruzi isoladas no reconcavo baiano. Contribuição ao

estudo da patologia geral da doença de Chagas no nosso meio. Rev Patol Trop 1974:3–65.
18. Miles MA. Transmission cycles and the heterogeneity of Trypanosoma cruzi. In: Lumsden W, Evans DA, eds. Kinetoplasiidae. New York: Academic Press, 1979:117–196.
19. Morel C, Chiari E, Camargo EP, et al. Strains and clones of Trypanosoma cruzi can be characterized by pattern of restriction endonuclease products of kinctoplast DNA minicircle. Proc Natl Acad Sci 1980;77:68–70.
20. Rezende JM. Forma digestiva da doença de Chagas. Rev Goiana Med 1959;5:193–227.
21. Marsden PD. The transmission of trypanosoma cruzi infection to man and its control. In: Croll NA, Cross JH, eds. Human Ecology and Infectious Diseases. London: Academic Press, 1983.
22. WHO. Control of Chagas disease. Report of a WHO Expert Committee, Geneva WHO Technical Report Series. 1991;811:95.
23. Atias A. Enfermeded de Chagas digestiva en Chile. Bol Chileno Parasitol 1969;24:70–74.
24. Scaro FJ. Destruccion experimental de los plexus de Meissner e Auerbach mediante hipoxia. Rev Goiana Parasitol 1969;24:70–74.
25. Jauregui L. Enfermedad de Chagas en Bolivia. Com. WHO? PAHO meeting. Caracas, Nov. 1971:26–29.
26. Tafuri WL. Patogenese das lesões do sistema nervoso autonomo do intestino na doença de Chagas experimental. Estudo ao microscopio eletronico. Rev Goiana Med 1968;14:11–19.
27. Muniz J, Azevedo AP. Novo conceito da patogenia da doença de Chagas. Hospital 1947;32:165–183.
28. Koeberle F. Patologia do megacolo adquirido. Am I Congr Latino, Am 2 Intern, 10. Bras Proct 1960;1:299–377.
29. Vieira CB, Godoy R, Carril CF. Hipersensibilidade do instestino grosso de pacientes com doenças de Chagas e Megacolon ao sagentes colinergicos. Ver Bras Gastroenterol 1964;16:41.
30. Moreira H. Estudo eletromagnético da atividade motora do coto retal e do colo descendente em pacientes Chagasicos submetidos as operaçoes de Hatman e de Duhamel. Rev Goiana Med 1974;20:125.
31. Habr-Gama A. Motilidade do colon sigmoide e do reto (contribuicão a fisiopatologia do megacolo chagasico). Thesis, Faculty of Medicine, University of Sao Paulo, Sao Paolo, Brazil, 1966.
32. Meneghelli UG, Godoy RA, Oliveira RB, et al. Effect of pentagastrin on the motor activity of the dilated and non-dilated sigmoid and rectum in Chagas disease. Digestion 1983;27:152.
33. Meneghelli UG. Chagas disease: a model of denervation in the study of digestive tract motility. Bras J Med Res 1985;18:255.
34. Habr-Gama A, Costa Curta L, Raia A. Anatomia e fisiologia do esfincter interno do ânus. Rev Soc Bras Coloproctologia 1970;3:21.
35. Moreira H, Rezende JM, de Sebba F, Azevedo IF, Leite ACA, Soares FP. Chagasic megacolon. Coloproctology 1985;7:260–267.
36. Rezende JM de, Moreira H. Chagasic megaesophagus and megacolon. Historical review and present concepts. Arq Gastroenterolog São Paulo 1988;25(special issue)(32):43.
37. Rocha A, Almeida HO, Esper DM, Santos EP, Teixeira VPA. Associação entre megaesofago e carcinoma de esofago. Rev Soc Bras Med Tropical 1983;16:94–97.
38. Zucoloto S, Rezende JM. Mucosal alterations in human chagasic esophagopathy. Digestion 1990;47:138–142.
39. Menezes AC, Lopes MA, Rocha A, et al. Megas e cancer. Cancer de intestino grosso em chagasico com megacolon. ARQ Gastroenterology 1989;26:13–16.
40. Fagundes JJ, Góes JRN, Coy CSR, et al. Associação entre megacolon chagásico e cancer do intestino grosso: apresentação de casos e revisão da literatura. Rev Bras Coloproctologia 2002;22:252–256.
41. Kune GA, Kune S, Field B, Watson LF. Role of chronic constipation, diarrhea, and laxative use in the etiology of large-bowel cancer. Dis Colon Rectum 1988;31:507–512.
42. Greenwald P. Colon cancer overview. Cancer 1992;70(5 suppl.):1206–1215.
43. Santos JCM Jr, Guimarães AS, Aprili F, Gomes DR, Rocha JJR. Colite isquêmica como complicação do megacolo XXXVI Congresso Brasileiro de Coloproctologia, Foz do Iguaçu. Resumos 1987:84–85.
44. Moreira H. Tratamento cirurgico do volvulo de sigmoide no megacolo chagasico. Rev Goiana Med 1979;78:73–76.
45. Duhamel B. Une nouvelle opération pour le megacolon congenital: rabaissement retro-rectal et transanal du colon et son application possible au traitement de quelques autres malformations. Presse Med 1956;64:2249–2250.
46. Haddad J. Tratamento do megacolo adquirido pelo abaixamento retro-retal do colo com colostomia perineal (operacao de Duhamel modificada). Rev Hosp Clin Fac Med Sao Paulo 1968;23:235–253.
47. Moreira H. Contribuicão ao estudo da fisiopatologia do tratamento cirurgico do megacolo chagasico. In: Manzione A, ed. Patologia Colorectal. Sao Paulo: Kronos, 1974:243.
48. Lins Neto MAF. Operação de Duhamel modificada com anastomose colorretal imediata para o tratamento do megacolo chagásico. Tese Fac. Med. University of Sao Paolo, 1997.
49. Moreira H. Megacolo chagásico. In: A Gastroenterologia no Brasil. Rio de Janeiro: Revinter, 2001:377–407.
50. Reis Neto JÁ, Quilici FA, Cordeiro F, Pinto QL, Reis JÁ Jr. Cirurgia video laparoscopica colorretal. Rev Bras Coloproctologia 1995;15:58–64.
51. Habr Gama A, Nahas SC, Bocchini S, et al. Resultado do tratamento cirurgico do megacolo chagásico pela retossigmoidectomia com anastomose colorretal mecanica termino-lateral (Técnica de Habr-Gama). Rev Bras Coloproctologia 1999;19(suppl 1):71.
52. Moreira JPT. Avaliação eletromanométrica no pré e no pós-operatório de pacientes portadores de megacolon chagásico submetidos à cirurgia de Duhamel. Post graduation thesis at Institute of Tropical Pathology and Public Health of the Federal University of Goiás, Brazil, 2001.

26

Surgical Treatment of Puborectalis Hypertrophy

De-hong Yu and Hei-ying Jin

Defecation is a complicated procedure in which pelvic floor muscles actively participate in the process. Rectal distention evokes the desire to defecate and induces relaxation of the anal sphincter. Under conducive circumstances, the act of defecation is completed by adoption of a suitable posture, contraction of the diaphragm and abdominal muscles to increase the intraabdominal pressure, and relaxation of the two striated muscle of the puborectalis and external anal sphincter. Puborectalis relaxation allows widening and lowering of the anorectal angle. Coordination between abdominal contraction and pelvic floor relaxation is crucial to this process (Fig. 26.1).

The puborectalis muscle is the most important component of the levator mechanism relating to continence and defecation. This muscle originates from the inferior border of the pubis and the superior fascia of the urogenital diaphragm, and slings around both sides of the rectum to exert a pull and create the anorectal angle. If the puborectalis muscle cannot relax or even contracts during defecation, the anorectal angle will not change or may even decrease, defecation will be difficult, and constipation can ensue.[1,2] In 1964, Wasserman[3] termed this syndrome "puborectalis syndrome," which is characterized by difficult and painful defecation and, occasionally, the inability to defecate for several days. On the basis of pathologic findings that have shown marked hypertrophy of the muscle fibers, this type of anorectal stricture was known due to spasmodic hypertrophy of the puborectalis muscle. The main causes of puborectalis syndrome are paradoxical puborectalis contraction (PPC) and puborectalis hypertrophy (PH). When PPC is a functional disorder, it is also known as spastic pelvic floor syndrome or pelvic outlet obstruction. In patients with PPC, the structure of the puborectali muscle is normal but the puborectalis muscle cannot properly relax and contract.[4] Therefore, the ideal treatment should aim at restoring the normal puborectalis function rather than at removing normal tissue.[5]

Jorge et al[6] reported that the mean success rate for biofeedback for constipation was 68.5%, attributable to paradoxical puborectalis syndrome. Other nonsurgical methods, such as botulinum toxin injection and anal dilation, can also offer improvement to some patients with PPC who do not respond to biofeedback.[7,8] Another, often neglected cause of puborectalis syndrome is PH. The etiology of PH is unclear. The most common cause may be due to inflammation around the puborectalis, which causes puborectalis edema and stimulates hypertrophy. Gradually, the puborectalis loses its elasticity and cannot contract and relax functionally.[9,10] The authors reviewed 200 cases of PH and found sepsis around the puborectalis in 15% to 30%.[9] Other factors such as congenital trauma and chronic diarrhea may also play a role in the development of PH. The structure of the puborectalis is abnormal among patients with PH. Successful treatment cannot rely on biofeedback and other conservative methods, but does respond favorably to segmental excision of the puborectalis muscle.

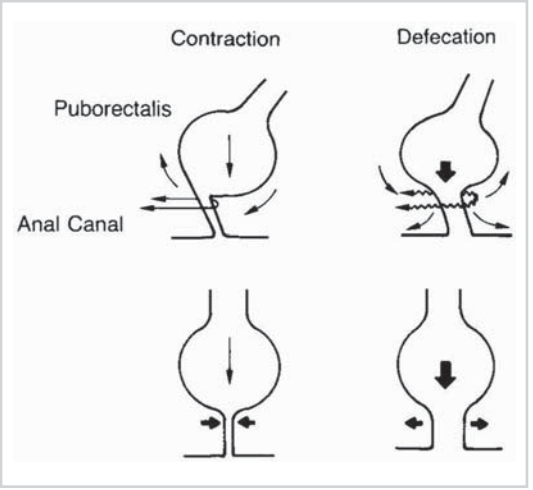


Figure 26.1. Mechanism of the puborectalis muscle. Top: lateral view; bottom: anteroposterior view.

Diagnosis and Differential Diagnosis of Puborectalis Hypertrophy

Clinical Manifestation

The most common complaint of patients with PH is difficult defecation, including frequent attempts, a sense of incomplete evacuation, and prolonged straining. Approximately 50% of these patients require 15 to 30 minutes, and some require 60 minutes or more, to evacuate. Although all patients desire to defecate once or more every day, they are usually unsuccessful. Digital rectal examination shows that there is increased anal sphincter tension in most of these patients and the puborectalis is clearly palpable, thick and stiff with a sharp border. When queried, these patients do try to push; however, the puborectalis has limited movement. The length of the anal canal is generally more than 4 cm and any attempt to force the examining finger through the anal canal causes more spasm and pain. There is a residue of dry and hard stool in the rectum even after defecation. Anorectal manometry generally confirms the functional length of the anal canal of more than 4 cm, although the resting pressures are in the normal range from 5 to 8.6 cm. The maximal squeeze pressures are generally 3 to 8 cm, without a significant amount of puborectalis contraction. Thus, the ability of the puborectalis to contract is decreased in patients with PH. Although balloon expulsion test shows that most patients can expel the balloon, the time of expulsion is longer than that in nonconstipated individuals. Colonic transit time study can show either rectal retention or colonic inertia, or it can be normal. Puborectalis electromyography (EMG) shows many fibrillation potentials at rest without significant increases in action potentials when the patient is asked to squeeze or push (Figs. 26.2 and 26.3). Single-fiber electromyography (SFEMG) shows that the single-fiber conduction time (SFCT) is often longer than 3.4 µsec and the fiber density increases.[11–14] Cui et al[12] studied 64 patients with PH and found that 92.2% showed abnormal EMG and 95.3% showed abnormal SPEMG. The EMG and SPEMG differences between PPC and PH are reported in Table 26.1.

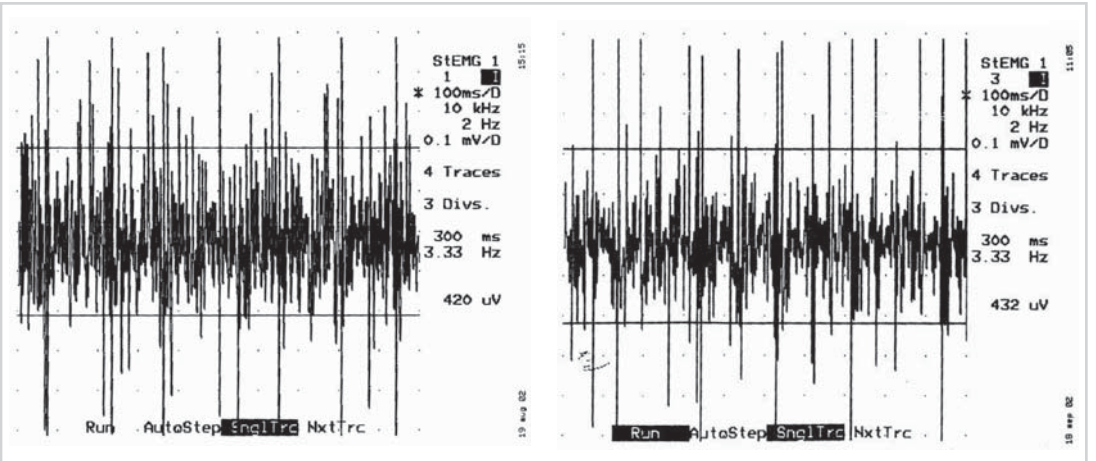


Figure 26.2. Electromyography (EMG) of the puborectalis muscle of patients with puborectalis hypertrophy (PH). A: EMG at rest. B: EMG during straining.

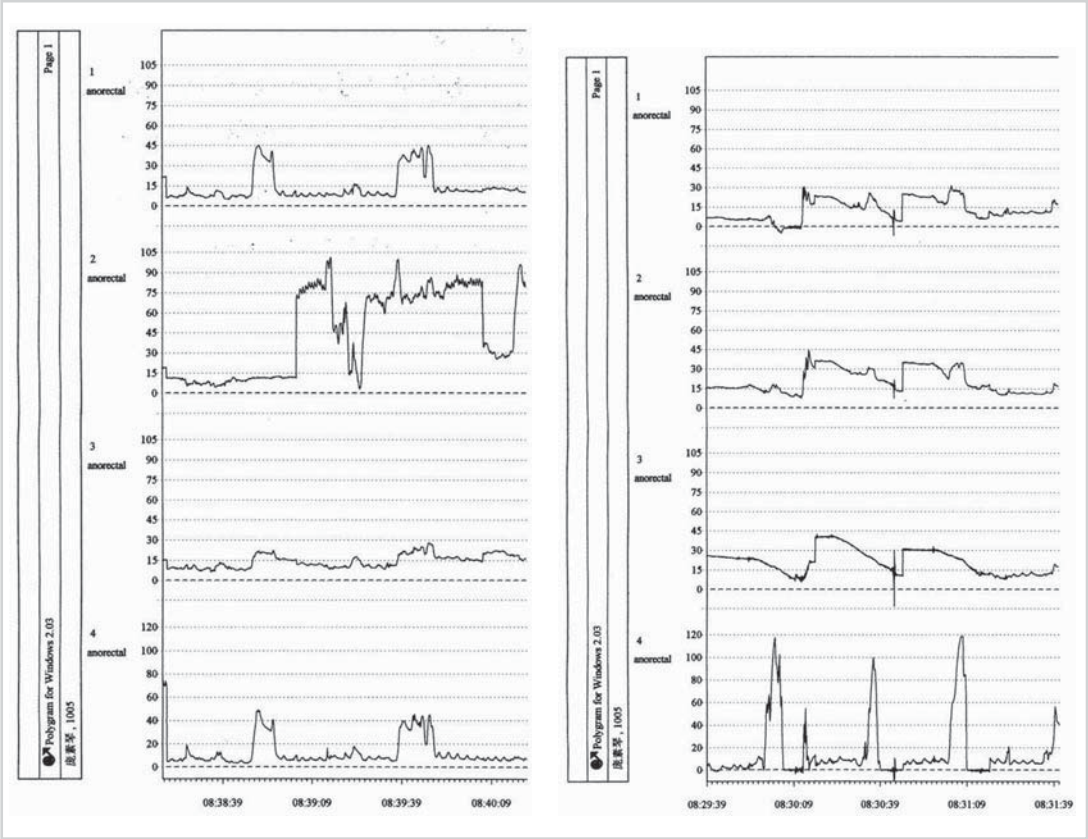


Figure 26.3. Anal manometry of PH; the final functional anal canal length is increased, and the anal canal pressures do not change between the rest and strain phases. The anorectal reflex is inhibited.

Table 26.1. The EMG and the SFEMG difference(s) between PPC and PH

	PPC ($n = 38$)	PH ($n = 64$)
EMG		
Rest	Little fibrillation potential	Great fibrillation potential
Slight contraction	Polyphasic motor unit potential	Dominant in short spike wave
Exertion contraction	High wave amplitude	Low wave amplitude
Push	Paradoxical electrical activity	No or slight electrical activity
SPEMG		
SFCT	2.8 µsec	>3.4 µsec
Fiber density	Normal	Increase(d)

EMG, electromyography
SPEMG, single fiber electromyography
PPC, paradoxical puborectalis contraction
PH, puborectalis hypertrophy
SFCT, single fiber conduction time

The most important examination of PH is defecography. The anorectal angle becomes acute paradoxically in most cases of PH. At rest, the mean anorectal angle is 91 ± 11 degrees, and in most patients it is less than 90 degrees. During defecation, the mean anorectal angle is 93 ± 16 degrees and the angle is in fact less than 90 degrees in more than half of these patients. These angles see little change between rest and defecation,[9] unlike the anorectal angle of normal individuals, which can increase by more than 20 degrees during defecation. Furthermore, the anal length becomes longer rather than shorter during evacuation as shown by defecography. The most significant sign of PH in defecography is the "shelf" sign, which can be noted in the lateral sitting position and is caused by the upper position of the anorectal junction without changing between rest and defecation (Fig. 26.4).[9,10] This telltale sign can be noted in all patients with PH but is not seen in other patients with constipation. During a 10- to 15-minute evacuatory effort, little or none of the barium is

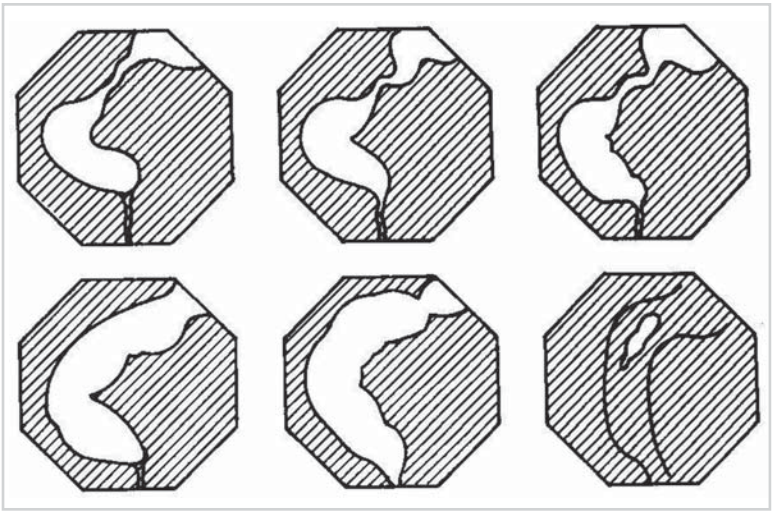


Figure 26.4. The shelf sign. The top row shows the typical shelf sign preoperatively at rest (left), squeeze (center), and defection (right); the barium retained in the rectum cannot be evacuated. Postoperatively (bottom row), the anorectal angle is still 90 degrees at rest (left), while at straining (middle) and defecation (right) the anorectal angle is greater than 90 degrees and the barium can be evacuated.

expelled.[6,11,15] During videodefecography,[16] the anorectal angle does not change or changes less than 3 degrees in patients with PH, while it can change more than 3 degrees between rest and defecation in patients with PPC or other reasons for constipation. Pathologic examination of the puborectalis demonstrates marked hypertrophy of the skeletal muscle in patients with PH.

Differentiation Between Paradoxical Puborectalis Contraction and Puborectalis Hypertrophy

Paradoxical puborectalis contraction is a very common disorder and is thought to be the sole cause of puborectalis syndrome, especially since biofeedback is successful in some patients with PPC.[17] Few series include patients with PH, and many surgeons believe that division of the puborectalis should be abandoned due to the potential for incontinence. However, in these authors' experience, PH is also a very important cause of puborectalis syndrome. Ger et al[14] studied 116 patients with chronic constipation and found that the evacuation pressure by anorectal manometry (ARM) was divided into a normal relaxed pattern, an equivocal or nonrelaxed pattern, and a paradoxical contracted pattern. Some patients with the equivocal or nonrelaxing pattern may have had PH. If PPC is the only cause of puborectalis syndrome, then theoretically biofeedback should cure all patients. However, at most only 70% of patients with PPC respond to biofeedback. In fact, more recent data suggest success rates of approximately 55%.[5] Therefore, PH is an important cause of puborectalis syndrome, although seldom recognized. The differences between PPC and PH are summarized in Table 26.2.

Table 26.2. The differences between PPC and PH

	PH	PPC
Etiology	Puborectalis organic abnormal	Puborectalis functional abnormal
Length of the anal canal	More than 4 cm	Less than 4 cm
Evacuation pressure	Not change or slightly decrease	Increase paradoxical
EMG and SFEMG	See Table 26.1	See Table 26.1
Shelf sign	Yes	No
Change of the anorectal angle in video defecography	Less than 3 degrees	More than 3 degrees
Paradoxical contraction	No	Yes
Biofeedback	No response	Respond mostly
Pathology of puborectalis	Hypertrophy	Normal

PPC, paradoxical puborectalis contraction
PH, puborectalis hypertrophy
EMG, electromyography
SFEMG, single fiber electromyography

Diagnostic Criteria of Puborectalis Hypertrophy

1. Difficult defecation, including frequent attempts at defecation, a sense of incomplete evacuation, and/or prolonged straining with incomplete evacuation.
2. Elongated anal canal confirmed by digital examination, anal manometry, and defecography.
3. Anal canal resting pressure is normal or slightly increased, and there is no significantly change during evacuation.
4. Fibrillation potential is common at rest, while the action potential does not significantly change when the patient squeezes or pushes; SFCT is more than 3.4 μsec.
5. No paradoxical contraction is found by digital anal examination, manometry, or videodefecography.
6. "Shelf sign" can be found in all patients, and the anorectal angle changes less than 3 degrees between rest and push during defecography.
7. Does not respond to biofeedback.
8. PH can be found on pathologic examination.
9. PPC has been excluded.

Treatment

Conservative Treatment

Patients with PH and mild symptoms of constipation should initially be given conservative treatment, which includes (1) a high-fiber diet of at least 15 g per day and adequate water intake of 2000 to 3000 mL per day; (2) physical exercise (habit training is also very important for patients with PH); (3) bulk or lubricated laxatives, which can be given if evacuation is very difficult and painful, but stimulant laxatives should be avoided; and (4) puborectalis exercises in the knee–chest position, with contraction and relaxation of the puborectalis at least 500 times per day to help recover the elasticity of the puborectalis. According to these authors' experience, conservative treatment in approximately 200 patients with PH has resulted in significant symptomatic relief in 50%.

Anal Dilation

Anal dilation is indicated for those patients who are unresponsive to conservative treatment. Maria et al[8] treated 13 patients with puborectalis syndrome with 10-minute daily progressive anal dilations by insertion of three dilators sized 20, 23, and 27 mm in diameter, from the smallest to the largest, for a 3-month period. Six months after completion of treatment, all patients reportedly had good clinical outcome and none reported any incontinence. Spontaneous bowel movement frequency increased from zero to six per week and the need for laxative use decreased from 12 patients with a weekly mean of 4.6 to two patients once per week. During straining, tone measured with anal manometry decreased from 93 to 62 mm Hg 6 months after completion of therapy, and the anorectal angle measured by defecography during strain increased from 95 to 110 degrees. The authors concluded that daily progressive anal dilation should be considered as the first and simplest therapeutic procedure in patients with puborectalis hypertrophy. However, daily progressive anal dilation is time-consuming and is not universally appealing to patients. Alternatively, after local anesthesia, a Pratt speculum can be inserted into the anus and gradually opened to its maximum aperture after which it is held in that position for 5 minutes. These authors have treated 100 patients with PH by this method since 1999 with an 80% improvement rate. There was decreased anal resting pressure and an increased anorectal angle; no incontinence was reported at a follow-up that ranged from 1 to 5 years.

Partial Resection of the Puborectalis Muscle

Indications

1. Meets diagnostic criteria of PH.
2. Defecation cannot be improved by conservative methods and dilation.
3. An abscess around the puborectalis is found by intrarectal ultrasonography, computed tomography (CT) scan, or magnetic resonance imaging (MRI).
4. No colonic inertia or other abnormalities that can cause outlet obstruction-type constipation are present.

Contraindications

1. Findings of PPC.
2. Identification of one or more abnormalities that cause obstruction, constipation, or colonic inertia.

Surgical Procedure

Either sacral or lumbar anesthesia is administered prior to positioning the patient. The surgeon should stand on the patient's left side. The patient is then placed in the prone jack-knife position with the buttocks retracted with adhesive straps, keeping the posterior median raphe in the midline. A low 3- to 5-cm midline incision is made from the posterior anal verge to the tip of the coccyx. A longer incision does not facilitate superior exposure. The incision is subsequently deepened by diathermy until the tip of the coccyx is exposed, as the coccyx is the landmark of the superior border of the puborectalis muscle. The surgeon's left index finger is introduced into the rectum and the puborectalis muscle is elevated into the surgical field. The superior border of the puborectalis muscle lies just beneath the tip of the coccyx, to which it is attached. Curved clamps are used to separate the puborectalis muscle posteriorly and laterally. Simultaneously, the finger in the rectum is used to guard against enterotomy. The puborectalis is clamped laterally and then the intervening muscle is excised for a width of approximately 1.5 cm. The remaining end of the muscle is ligated with 00 silk sutures or absorbable sutures. After resection, a well-defined V-shaped defect should be palpable by the finger in the rectum. Any remaining fibers on the wall of the rectum should be resected and not merely divided. The wound is irrigated and, if necessary, a small drain is inserted. Finally, the subcutaneous tissue and the skin are closed with interrupted sutures. The surgical treatment of PH is illustrated in Figures 26.5 to 26.8.

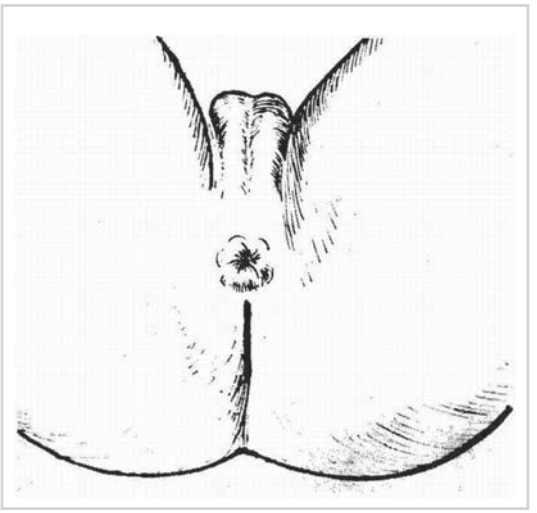


Figure 26.5. Surgical procedure for PH: an incision is made while the patient is in the prone jackknife position (PH, puborectalis hypertrophy).

Results and Follow-Up

Between 1985 and 2003, 69 cases of PH fulfilled the inclusion criteria outlined earlier in this chapter and subsequently underwent partial division of the puborectalis muscle. The day following the procedure, all patients reportedly had frequent discharge of gas, and within 7 days 90% of the patients were passing soft or formed stools at least once daily. Defecography performed 4 weeks after the procedure revealed a flatter anorectal angle during evacuation than that noted prior to surgery. The defecography of two typical patients are shown in Figures 26.9 and 26.10. At a median follow-up of 6 years (range 1–18), 42 (61%) of patients can freely defecate whereas 19 (28%) still experience some difficulty and require laxatives or have subsequent anal dilation. Six patients evacuate with significant difficultly and require the use of enemas for complete evacuation. The two patients who evacuate less than once weekly had endorectal ultrasonographic findings of perineal abscess. In these patients, a second division of the puborectalis was undertaken. Three patients reported slight incontinence to gas and liquid while all patients were fully continent.

Wasserman[3] proposed spasmodic hypertrophy of the puborectalis muscle. He reported on four patients, three of whom underwent partial resection of the puborectalis muscle with excellent results. Partial resection of the puborectalis muscles was advocated by Wallace and Madden,[18] based on their series of 33 adults and 11 children. Kawano et al[19] reported relief of symptoms in three of seven patients who under-

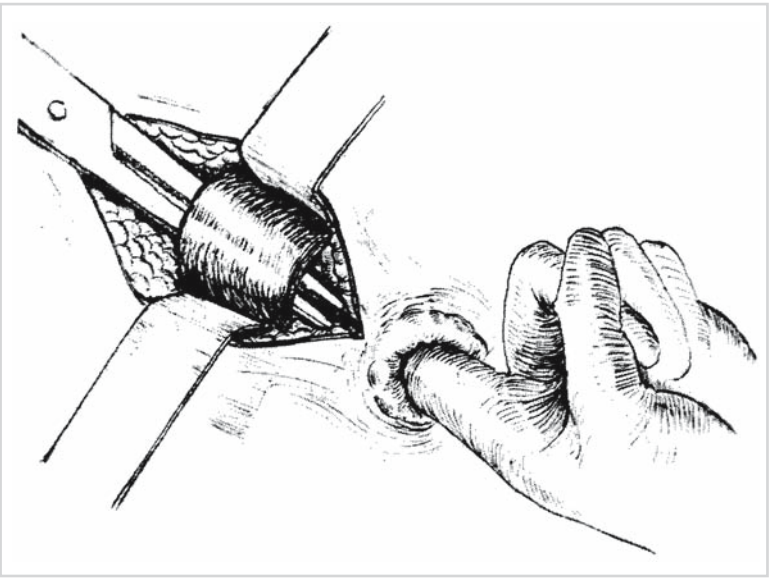


Figure 26.6. Surgical procedure for PH: dissection (PH, puborectalis hypertrophy).

Figure 26.7. Surgical procedure for PH: clamping the puborectalis muscle (PH, puborectalis hypertrophy).

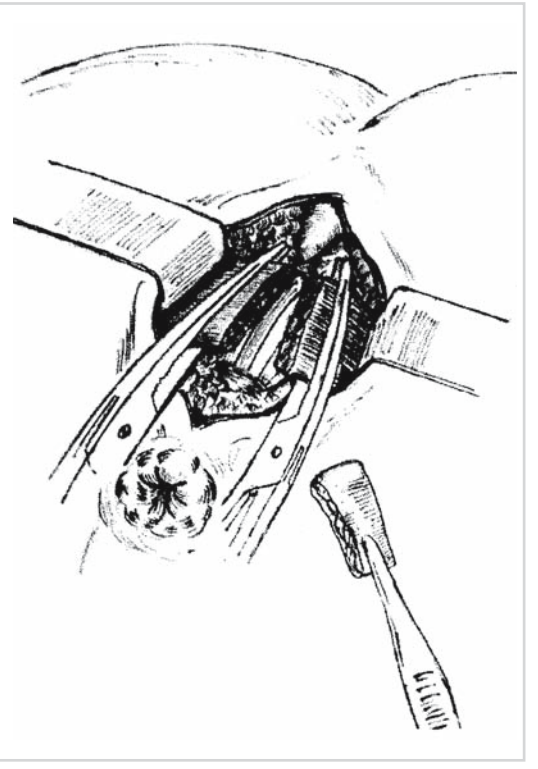


Figure 26.8. Surgical procedure for PH: resection (PH, puborectalis hypertrophy).

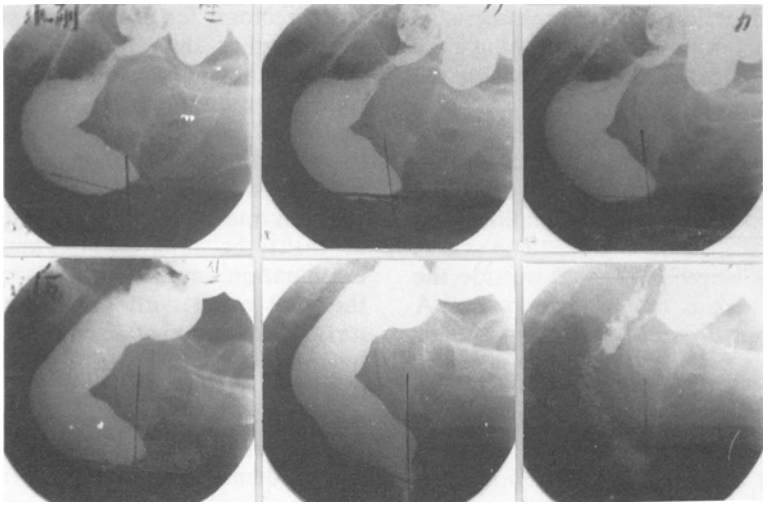


Figure 26.9. Preoperative defecography (top) and postoperative defecography (bottom).

went partial resection of the puborectalis muscle. However, in the series of Barnes et al,[20] only two of nine patients who received complete division of the puborectalis muscle obtained relief, while seven had symptomatic improvement. This report suggests that complete division is not as effective as partial resection, and the rate of fecal incontinence is higher after complete puborectalis division. Liu et al[21] studied 149 patients who underwent partial division of the puborectalis muscle and found complete resolution of symptoms and no incontinence in 134

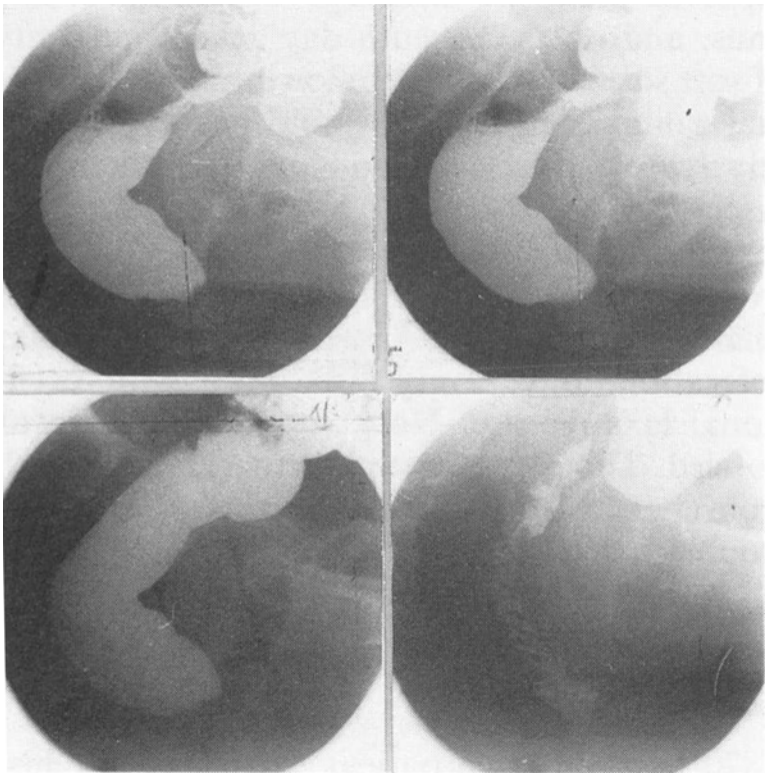


Figure 26.10. Preoperative (top) defecography. Note the shelf sign at rest (left) and during attempted but unsuccessful evacuation (right). Postoperative defecography (bottom) shows normal anatomy at rest (left) and during successful evacuation (right).

Table 26.3. The results of division of the puborectalis muscle

Reference	Diagnosis	Procedure	*n*	Success rate	
				n	%
Wasserman (1964)[3]	Puborectalis syndrome	Posterior partial resection	4	3	75
Wallace (1969)[18]	Puborectalis syndrome	Posterior partial resection	44	33	75
Keighley (1984)[24]	Outlet syndrome	Partial division	7	1	14
Barnes (1985)[20]	Chronic constipation	Partial division	9	2	22
Kamm (1988)[22]	Chronic constipation	Partial division	18	4	22
Kawano (1997)[19]	Puborectalis syndrome	Partial resection	7	3	43
Yu (1990)[23]	Puborectalis syndrome	Partial resection	18	15	83
Liu (2001)[21]	Puborectalis syndrome	Partial resection	149	134	90
Xu (2002)[25]	Puborectalis hypertrophy	Partial resection	29	28	97

(90%) patients. The results of division of the puborectalis muscle are summarized in Table 26.3.

Two factors may explain the significant variability of the operative results. One is the diversity in the operative indications among the various series. For instance, Kamm et al[22] included megarectum as an indication for puborectalis division. Other series include patients who have had one or more concomitant causes of outlet obstruction constipation. Puborectalis division is only valuable in patients with PH without other concomitant causes of constipation. A second factor is the differing surgical techniques among the surgeons. There are three methods for this procedure: posterior partial resection; posterior division; and lateral, unilateral, or bilateral resection. Division of the puborectalis alone may not allow complete muscle end retraction, as adhesions may develop and can cause symptom recurrence. For this reason, the partial resection should extend from the posterior rectal wall to the puborectalis muscle, dissecting both cut ends as widely as possible. At least a 1.5-cm width of muscle should be resected.

Why does partial resection of the puborectalis muscle fail? The reasons for failure may include concomitant unrecognized anatomic outlet obstruction due to either intussusception or rectocele. The authors emphasize the importance of thorough preoperative physiologic evaluation and exclusion or successful treatment of all other causes of constipation. Incompletely resected adhesions or fibrous bands between the puborectalis muscles and rectal wall may result in a persistent stricture and continued symptoms. If an insufficient width of puborectalis muscle (less than 1.5 cm) is resected, the cut ends may readhese and cause stricture recurrence. Postoperative balloon dilation of the rectum may prevent adhesion recurrence. The authors treated two patients whose symptoms recurred owing to adhesions between the resected ends who subsequently underwent a second procedure.

Conclusion

Constipation is a complex disorder, the understanding of which remains superficial. Partial resection of the puborectalis muscle only releases the abnormal mechanism of defecation. This procedure, therefore, should be restricted to those patients who have definite evidence of outlet obstruction caused by hypertrophy of the puborectalis muscle and who fail to respond to conservative therapy. It is also imperative to correct inappropriate bowel habits and diet prior to surgery.

Both PPC and PH are poorly understood conditions which require further investigation. Puborectalis hypertrophy is a condition that causes outlet obstruction constipation. Although it has some similarity with PPC, it is an organic disorder caused by hypertrophy of the puborectalis muscle due to inflammation, congenital structure, trauma, or other etiologies. While PPC is a functional disorder and the structure of the puborectalis is normal, it does respond to biofeedback and botulinum toxin type-A injection, unlike PH. Only those patients who have definite evidence of outlet obstruction caused by hypertrophy of the puborectalis muscle, and who fail to respond to conservative therapy, should undergo division of the puborectalis muscle.

References

1. Bharucha AE. Obstructed defecation: don't strain in vain! Am J Gastroenterol 1998;93:1019–1020.
2. Schouten WR, Briel JW, Auwerda JJ, van Dam JH, Gosselink MJ, Ginai AZ, Hop WC. Anismus: fact or fiction? Dis Colon Rectum 1997;40:1033–1041.
3. Wasserman JF. Puborectalis syndrome, rectalis sternosis due to anorectal spasm. Dis Colon Rectum 1964;7:87–98.
4. Prather CM, Ortiz-Camach CP. Evaluation and treatment of constipation and fecal impaction in adults. Mayo Clin Proc 1998;73:881.
5. Lau CW, Heymen S, Alabaz O, Iroatulam AJ, Wexner SD. Prognostic significance of rectocele, intussusception, and abnormal perineal descent in biofeedback treatment for constipated patients with paradoxical puborectalis contraction. Dis Colon Rectum 2000;43: 478–482.
6. Jorge JM, Habr Gama A, Wexner SD. Clinical applications and techniques of cinedefecography. Am J Surg 2001;182:93–101.
7. Ron Y, Avni Y, Lukovetski A, et al. Botulinum toxin type-A in therapy of patients with anismus. Dis Colon Rectum 2001;44:1821–1826.
8. Maria G, Anastasio G, Brisinda G, Civello IM. Treatment of puborectalis syndrome with progressive anal dilation. Dis Colon Rectum 1997;40:89–92.
9. Yu DH, Meng RG, Li SZ. Puborectalis syndrome: a cause of obstinate constipation. Zhonghua Wai Ke Za Zhi 1989;27:267–268.
10. Lu R, Chen D, Yu DH. Defecographic diagnosis of puborectalis syndrome. Zhonghua Yi Xue Za Zhi 1991;71: 633–634.
11. Fucini C, Ronchi O, Elbetti C. Electromyography of the pelvic floor musculature in the assessment of obstructed defecation symptoms. Dis Colon Rectum 2001;44:1168–1175.
12. Cui Y, Hu HH, Cheng JS, Zheng HM, Liu Y. Significance of electromyography and single fiber electromyography in puborectalis. J Clin Electroencephalogr 1996;5:202–204.
13. Fleshman JW, Dreznik Z, Cohen E, Fry RD, Kodner IJ. Balloon expulsion test facilitates diagnosis of pelvic floor outlet obstruction due to nonrelaxing puborectalis muscle. Dis Colon Rectum 1992;35:1019–1025.
14. Ger GC, Wexner SD, Jorge JM, Salanga VD. Anorectal manometry in the diagnosis of paradoxical puborectalis syndrome. Dis Colon Rectum 1993;36:816–825.
15. Jorge JM, Wexner SD, Ger GC, Salanga VD, Nogueras JJ, Jagelman DG. Cinedefecography and electromyography in the diagnosis of nonrelaxing puborectalis syndrome. Dis Colon Rectum 1993;36:668–676.
16. Pfeifer J, Oliveira L, Park UC, Gonzalez A, Agachan F, Wexner SD. Are interpretations of video defecographies reliable and reproducible? Int J Colorectal Dis 1997;12:67–72.
17. Glia A, Gylin M, Gullberg K, Lindberg G. Biofeedback retraining in patients with functional constipation and paradoxical puborectalis contraction: comparison of anal manometry and sphincter electromyography for feedback. Dis Colon Rectum 1997;40:889–895.
18. Wallace WC, Madden WM. Experience with partial resection of the puborectalis muscle. Dis Colon Rectum 1969;12:196–200.
19. Kawano M, Fujiyoshi T, Takasi K, et al. Puborectalis syndrome. J Jpn Soc Coloproctol 1997;40:612.
20. Barnes PRH, Hawley PR, Preston DM, et al. Experiences of posterior division of the puborectalis muscle in the management of colonic constipation. Br J Surg 1985;72:475–477.
21. Liu YG, Zang JX, Li YW, Gao CF, Xu Z. Treatment of musculi puborectalis syndrome with partial resection of musculi puborectalis: analysis in 149 cases. J LuoYang Med Coll 2001;19:17–18.
22. Kamm MA, Hawley PR, Lennard Jones JE. Lateral division of the puborectalis muscle in the management of severe constipation. Br J Surg 1988;75:661–663.
23. Yu DH, Cui FD. Surgical treatment of puborectalis syndrome. J Pract Surg 1990;10:1599–1600.
24. Keighley MR, Shouler P. Outlet syndrome: is there a surgical option: J R Soc Med 1984;77(7):559–563.
25. Xu DK, Chen LL. Clinical observation of the therapeutic effect of 2 different surgical procedure for pubotrectalis hypertrophy. Chin J Coloproctol 2002;22:31–32.

Subject Index

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