Appendicitis

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Berengario DaCarpi, a physician-anatomist, made the first description of the appendix in 1521.[1] Leonardo DaVinci demonstrated the appendix in drawings made in 1492 but not published until the 18th century.[2] The appendix is clearly illustrated in *De Humani Corporis Febrica Liber V* by Andreas Vesalius published in 1543.[3]

Lorenz Heister gave the first unequivocal account of appendicitis in 1711.[4] Heister, a student of Boerhaave, described a perforation of the appendix with a small abscess adjacent to a gangrenous appendix. Heister speculated that the appendix might be the site of acute inflammation. He described the autopsy on the body of a criminal:

"When about to demonstrate the large bowel, I found the vermiform appendix of the caecum preternaturally black. As I was about to separate it, its membranes parted and discharged two to three spoonfuls of matter."

In 1759, Mestivier, a Parisian surgeon, reported autopsy findings of a man who died shortly after drainage of a right lower quadrant abscess.[5] Mestivier identified perforation of the appendix by a pin and presumed that the abscess was due to the perforation. Over the next 100 years, there were many other descriptions of appendicitis including those authored by John Hunter and John Parkinson.[4,6] Interestingly, many of these descriptions emphasized the presence of a foreign body either causing obstruction or perforation of the appendix.

Francois Melier, a Parisian physician, described 6 cases of appendicitis at autopsy and first suggested the possibility of removing the appendix in 1827.[4,7,8] His suggestions were ignored reputedly due to the influence of Barnio Guillame Dupuytren, the leading surgeon of Paris at the time, who did not view the appendix as a cause for right lower quadrant inflammation. Bright and Addison,[9] physicians at London's Guys Hospital, described the symptoms of appendicitis and they believed that the appendix was the cause of many inflammatory processes in the right lower quadrant. Their discussion of appendicitis appeared in the first

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volume of *Elements of Practical Medicine,* published in 1839.[9] Interestingly, surgical treatment was not mentioned.

Thus, the first reports of appendicitis occurred in the early 1700s and Claudius Amyand, Sergeant Surgeon to George II, performed the first known appendectomy in 1735.[10] He operated on an 11-year-old boy with a right scrotal hernia and a fistula. He identified the appendix, perforated by a pin, within the scrotum. He ligated the appendix and removed it. Despite Amyand's achievement, there was scant consideration of the surgical treatment of appendicitis for approximately 150 years. It is likely that despite repeated observations of the appendix as the etiology of right lower quadrant inflammatory disease, the therapeutic implications were not clear. Laparotomy, before the development of general anesthesia and antiseptic techniques, was justifiably considered a dangerous option. Two seminal occurrences in the history of surgery were the introduction of ether, nitrous oxide, and chloroform anesthesia in the mid-1800s and Joseph Lister's first paper on antisepsis published in 1867.[11] Although Lister's precepts were not immediately accepted, abdominal operations were nevertheless "more tolerable, more frequent, and safer" after 1870. Hence, it was not until the late 1800s that the stage was set for consideration of appendectomy in the treatment of appendicitis.

At this juncture, the contribution of Reginald Heber Fitz deserves recognition and emphasis.[12] Fitz was the Shattuck Professor of Pathological Anatomy at Harvard University. He was a member of the ninth generation of Fitzes in America, his ancestors having arrived in Massachusetts in 1639. He was educated at Harvard and spent 2 years in Europe including a period of study of cellular pathology with Rudolf Virchow in Vienna. Fitz returned to Harvard in 1870 as an instructor of pathology. He introduced the microscope to the study of disease at Harvard. He also conducted a private practice and was active in the Boston Dispensary.

On June 18, 1886, he presented a paper to the Association of American Physicians in Washington, DC, entitled "Perforating Inflammation of the Vermiform Appendix: With Special Reference to Its Early Diagnosis and Treatment."[13] Fitz proposed that the appendix is the cause of most inflammatory disease of the right lower quadrant. He went on to describe the clinical features of appendicitis and, importantly, proposed early surgical removal of the appendix:

"In most fatal cases of typhlitis, the caecum is intact while the appendix is ulcerated and perforated. The question should be entertained of immediate opening. If any good result is to arise from such treatment it must be applied early."

Fitz's contribution was critical, not because his observations were original, but because his paper was delivered to an important and influential audience at a time when the potential value of surgical treatment of disease could be appreciated. Although appendectomy had actually been performed earlier, Fitz gave credence to the entity "appendicitis" and, in fact, was the first to coin the term. He promoted the concept of early diagnosis and surgical treatment, thereby paving the way for appendectomy to become a popular and accepted operation.

Indeed, the "coming of age" for the appendix coincides with the late 1800s as noted by more than 2500 books or articles dealing with the appendix having been published by 1889.[14,15] Several surgeons deserve mention for enhancing the popularity of appendectomy.[12] In 1880, Lawson Tait, a leading British abdominal surgeon, removed a gangrenous appendix with recovery of the patient. During the 1880s, Kronlein of Zurich, Groves of Ontario, Hall of New York, and Morton of Philadelphia performed appendectomies that encouraged the surgical community to recognize appendicitis and perform appendectomy. In 1889, McBurney[16] of New York published the first of several important papers regarding the appendix. He suggested early operative intervention and developed the muscle-splitting incision that bears his name and is commonly used today.[17] During the 1890s, surgeons in the United States rapidly accepted appendectomy for appendicitis. Bernays in 1898 reported 71 consecutive appendectomies without mortality.[18] In 1904, Murphy[19] of Chicago reported a personal experience with 2000 appendectomies. By 1950, more than 13,000 books or articles about the appendix had been published.[14,15]

Perhaps the most famous case of appendicitis is that of King Edward VII, the first son of Queen Victoria.[20] After a long, illustrious reign, Queen Victoria died in 1901 at the age of 82. During her reign, Britain rose to the pinnacle of world power and her eldest son, Edward, then 59 years old, had waited a long time for his inheritance. In June of 1902 and less than 2 weeks before the coronation, Edward developed abdominal discomfort. As expected, a staff of physicians attended to Edward and they included 2 prominent British surgeons, Lord Joseph Lister and Sir Frederic Treves. They observed right lower quadrant swelling, tenderness, and fever in the future king. These findings improved initially, but Edward's condition relapsed. The medical staff was unanimous in recommending an operation, but Edward was hesitant on the eve of his coronation, an event he had waited for his entire life. It fell to Lister to persuade Edward that his medical staff agreed that an urgent operation was necessary. Coronations, in addition to burials, of British royalty occur in Westminster Abbey and Edward responded to his medical staff by stating: "I must keep faith with my people and go to the [Westminster]

Abbey for the coronation." Edward was adamant and after hearing him repeat "I must go to the Abbey," Treves replied, "Then, Sir, you will go as a corpse."

Edward consented to surgery and on June 24, 1902, Treves operated on Edward at Buckingham Palace. He opened a large periappendiceal abscess, evacuated pus, and left 2 large drains in place. He did not remove the appendix. The wound was packed open and the entire procedure took approximately 40 minutes. Edward recovered successfully and underwent coronation approximately 7 weeks after surgery. He served as king for the remaining 8 years of his life.

Treves became the most popular surgeon in London and was made a Baronet for his service to the King. Lister was one of the first groups of recipients of the new honor of the Order of Merit created by Edward, undoubtedly for his seminal contributions to surgery in addition to his participation in the king's case. The publicity and successful outcome of Edward's case further advanced appendicitis as a disease entity and appendectomy as its appropriate treatment.

Anatomy[21-23]

Embryologically, the appendix is part of the cecum from which it originates where the 3 tenia coli coalesce at the distal aspect of the cecum. Not surprisingly, the appendix resembles the cecum histologically and includes circular and longitudinal muscle layers. In addition, the appendix contains an abundance of lymph follicles in the submucosa, numbering approximately 200. The highest number of lymph follicles occurs in the 10- to 20-year-old age group, with a decline in number after age 30; lymph follicles are totally absent after age 60.

The appendix arises from the cecum approximately 2.5 cm below the ileocecal valve. It varies in length from complete agenesis to more than 30 cm, but it is usually 5 to 10 cm in length. The mean width is 0.5 to 1.0 cm. The various positions of the appendix are conveniently categorized into the following locations: paracolic (the appendix lies in the right paracolic gutter lateral to the cecum), retrocecal (the appendix lies posterior to the cecum and may be partially or totally extraperitoneal), preileal (the appendix is anterior to the terminal ileum), postileal (the appendix is posterior to the ileum), promontoric (the tip of the appendix lies in the vicinity of the sacral promontory), pelvic (the tip of the appendix lies in or toward the pelvis) and subcecal (the appendix lies inferior to the cecum). Wakeley[24] performed a postmortem analysis of 10,000 cases and described the frequency of the location of the appendix as follows: retrocecal, 65.3%; pelvic, 31%; subcecal, 2.3%; preileal, 1%;

and right paracolic and postileal, 0.4%. Interestingly, Williamson and colleagues[25] observed that of 105 retrocecal appendices removed at operation, 12 (11.4%) extended into the retroperitoneum. In this position, the appendix may extend cephalad up to the kidney and, in fact, 2 of these patients experienced right flank pain on presentation. In essence, the appendix may lie in multiple locations, essentially at virtually any position in a clockwise rotation from the base of the cecum.[26] The clinician must appreciate that the anatomic location of the appendix determines the presentation of symptoms and signs during an episode of appendicitis.

The mesentery of the appendix passes behind the terminal ileum and is contiguous with the lower leaf of the small bowel mesentery. The appendicular artery courses through the mesoappendix and is a branch of the ileocolic artery. An accessory appendiceal branch from the posterior cecal branch of the right colic artery may also be present. The veins from the appendix drain into the ileocolic vein that in turn empties into the superior mesenteric vein. A variable number of lymphatic channels traverse the mesoappendix to empty into the ileocecal nodes. Venous and lymphatic drainage of the appendix mimics drainage of the cecum. Hence, lymphatic drainage of the appendix includes lymph nodes that are found at the arborization and takeoff of the ileocolic and right colic arteries.

The tip of the appendix may lay in the left lower quadrant under 2 circumstances.[21] The patient may have a very long appendix that originates in the normal anatomic position in the right lower quadrant, but the tip may extend across the abdominal cavity into the left lower quadrant. Second, the patient may have situs inversus, in which case there is transposition of abdominal viscera. In either case, inflammation of the appendix will manifest as left lower quadrant abdominal pain and tenderness.

There are several unusual, but interesting congenital anatomic anomalies that are worth mention. Robinson[27] reported a case of congenital absence of the appendix in 1952 and was able to collect only 68 other examples, indicating the rarity of this condition. Likewise, duplication of the appendix is also a rare anomaly, with fewer than 100 reported cases.[28] Wallbridge[29] described duplication of the appendix and proposed a classification scheme. Type A comprises partial duplication of the appendix on a single cecum. Type B includes a single cecum with 2 completely separate appendices. Type B is further subdivided into types B1 and B2. Type B1, also called “birdlike appendix” because of its similarity to the normal arrangement in birds, indicates that there are 2 appendices symmetrically arising from either side of the ileocecal valve. Type B2 comprises 1 appendix arising from the usual site on the cecum, while a second, rudimentary appendix originates from the cecum along the lines of one of the tenia coli. Type C includes 2 ceca, each of which has a normal appendix. Tinckler[30] described a unique case of a triple appendix, associated with a double penis and ectopia vesicae.

Epidemiology

Acute appendicitis is the most common cause of acute abdominal pain that requires surgical treatment. There is an approximately 6% to 7% lifetime risk of appendicitis.[31,32] Appendicitis is primarily a disease of adolescents and young adults with a peak incidence in the second and third decades of life.[32-38] It is very uncommon in children younger than 5 years and by age 50, the risk of appendicitis is 1 in 35 for men and 1 in 50 for women. By age 70, the risk of appendicitis is less than 1 in 100.[22,39,40]

Among teenagers and young adults, males are more commonly affected than females with a male:female ratio of approximately 1.3:1, but the gender distribution becomes equal beyond these age groups.[35-37]

There have been reports of a wide variation in the incidence of appendicitis between countries, between regions of the same country, and between different racial and occupational groups.[32,41,42] However, most attention has been directed to geographic variations in incidence that are probably due to differences in dietary fiber consumption.[43-45] Appendicitis is relatively more common in industrialized nations where a highly refined, low-fiber diet is typically consumed. Appendicitis is rare in developing countries where a less-refined, high-fiber diet that is characteristic of agrarian societies is generally consumed.

It appears that the incidence of appendicitis has decreased in the past several decades. The reasons for the reduced incidence of appendicitis are not clear, but it may be due to the increase in dietary fiber consumption in industrialized nations.

Etiology

An epidemiologist once characterized knowledge of the cause(s) of appendicitis as ". . .a largely disconnected set of observations in search of a theory that ties them together."[46] For a disease that is prevalent and appears relatively simple, there is actually little that is known with regard to its etiologic factors.

Epidemiologists concur that appendicitis is more common in urban, industrialized societies and relatively rare in developing countries where a less-refined, high-fiber diet is typically consumed.[43-45] The etiologic significance of a highly refined, low-fiber diet is not clear, but the striking variation in geographic distribution strongly suggests a dietary role in the etiology of appendicitis. Presumably, the diet in industrialized countries leads to hard stool, higher intracolonic pressure, and formation of fecaliths that can serve as obstructing agents in the appendiceal lumen. Case-controlled studies of fiber intake and its correlation to the development of appendicitis have not been conclusive.

There is conflicting evidence regarding the familial nature of appendicitis. The common prevalence of the disease in the general population makes it difficult to prove a genetic etiology, but a polygenic inheritance pattern with substantial environmental determinants has been suggested.[43,47] Likewise, some have suggested that altered immunity to specific types of infectious agents on a genetic basis is a cause of appendicitis. However, it may also be true that familial association is simply due to a similar environment and dietary habits.

An intriguing, yet unproven theory of appendicitis suggests that improvement in living standards and sanitation correlate with an increasing risk of appendicitis.[48] This hypothesis states that improvements in sanitation have led to less frequent exposure of young children to common enteric or respiratory infectious agents. Accordingly, initial exposure to these agents in late childhood or adolescence evokes a host response with prominent lymphoid hyperplasia at the appendiceal base when the number of lymphoid aggregates is at its maximum, subsequently leading to obstruction and inflammation.

In summary, appendicitis is more prevalent in developed as opposed to developing countries. Dietary, genetic, and infectious or immunologic explanations for the etiology of appendicitis have been advanced, but it has not proven possible to implicate reliably any cause in a given patient.

Pathophysiology

Wangensteen and Dennis[49] demonstrated experimentally that luminal obstruction leads to the development of acute appendicitis. The appendix has a small luminal diameter in relation to its length. Conventional wisdom holds that this configuration predisposes the appendix to closed-loop obstruction and subsequent inflammation. Specifically, proximal obstruction by any number of initiating factors leads to ongoing mucus secretion of the appendiceal mucosa distal to the obstruction into a closed lumen with elevation of intraluminal pressure. Rapid distention of the appendix ensues because of its small luminal capacity and intraluminal pressures can reach 50 to 65 mm Hg. Distension of the appendix stimulates visceral afferent pain fibers, producing a somewhat vague and diffuse periumbilical pain.[50] Distention of the appendix often causes reflex nausea and/or vomiting with a progressive increase in the severity of the visceral pain.

As luminal pressure increases, venous pressure is exceeded and mucosal ischemia develops. Once luminal pressure exceeds 85 mm Hg, thrombosis of the venules that drain the appendix occurs and, in the setting of continued arteriolar inflow, vascular congestion and engorgement of the appendix become manifest.[51] With vascular congestion, the appendiceal mucosa becomes hypoxic and begins to ulcerate, resulting in compromise of the mucosal barrier and leading to invasion of the appendiceal wall by intraluminal bacteria.[52] In the early stages of appendicitis, mucosal disruption with invasive infection and inflammation are characteristic pathologic findings. This inflammatory process progresses to involve the serosa of the appendix that inflames the nearby parietal peritoneum, resulting in the characteristic shift in location of pain to the right lower quadrant along with localized tenderness. If unimpeded, luminal pressure rises to a level that induces venous infarction, full-thickness necrosis, and perforation. Furthermore, stasis of intraluminal contents leads to bacterial overgrowth in the inspissated mucus and if accompanied by appendiceal perforation, results in peritonitis or abscess formation. The length of time required for the disease to progress to gangrene and perforation is highly variable. One study demonstrated a mean duration of abdominal pain of 46.2 hours in patients with gangrene and 70.9 hours for perforation.[53]

Fecal stasis and fecaliths are the most common cause of appendiceal obstruction, followed by lymphoid hyperplasia, vegetable matter and fruit seeds, inspissated barium from previous radiographic studies, intestinal worms (especially ascarids), and tumors such as carcinoid.[54]

Spontaneous resolution of appendiceal inflammation does occur, although its frequency is unknown. Presumably, increasing intraluminal pressure dislodges the obstructing material back into the cecum, thereby relieving the distention and inflammatory process. Evidence of previous inflammation may be recognized subsequently as a fibrotic, kinked, or adhesed appendix when viewed at a future operation. In 1 series of 1000 patients with appendicitis, 9% reported having had a similar clinical illness in the past and 4% reported more than 1 previous attack.[55]

Evidence for obstruction of the appendiceal lumen as the cause of appendicitis comes from pathologic studies that demonstrate luminal obstruction by a fecalith of lymphoid hyperplasia in excised appendices for appendicitis.[22,56] In addition, pathologic studies demonstrate obstruction in virtually all cases of appendicitis with perforation. Although the concept of an obstructing agent leading to a closed-loop obstruction is an attractive explanation for the pathophysiology of acute appendicitis, it is important to note that an inciting factor can be identified in only approximately 50% of patients. It is possible that the offending agent was expelled back into the cecum as intraluminal pressure rises in the appendiceal lumen and at the time of appendectomy, the evidence for a direct cause of appendicitis is absent. However, this is speculative and one must consider that there are other causes of appendicitis than obturation of the appendiceal lumen by an obstructing agent. In fact, one might argue that if obstruction of the lumen is the cause of appendicitis, then the occurrence of appendicitis should be more evenly distributed throughout all age groups as opposed to its relatively prominent incidence in the second and third decades of life. The well-established observation of the significant increase in lymphoid follicles in young adults and their gradual disappearance with age strongly suggests a pathogenetic role for lymph tissue in the development of appendicitis. Some have speculated appendicitis ensues following a lymphoid tissue reaction to enteric pathogens. However, to date, no experimental proof has been offered to substantiate this hypothesis. Accordingly, it is fair to state that luminal obstruction appears to account for many cases of appendicitis, but the cause for a substantial number of cases remains elusive.

Bacteriology

As appendectomy became increasingly popular in the last decades of the nineteenth century and first half of the twentieth century, most clinicians considered appendicitis to be a single-organism entity. Although a wide variety of both aerobic and anaerobic species had been demonstrated in the peritoneal fluid of patients with appendicitis, only single organisms were observed in culture and both aerobic and anaerobic organisms were never recognized together.[57-59] Our understanding of the bacteriology of appendicitis was radically altered with the publication in 1938 of William Altemeier's landmark study documenting the polymicrobial nature of the infected appendix.[60] Altemeier reported, isolating more than 4 different organisms per specimen in patients with perforated appendicitis. The concept of bacterial synergy was developed at roughly the same time that Altemeier published his findings.[61] Together, the observations of the coexistence and synergistic relationship of multiple aerobic and anaerobic organisms significantly advanced the prevailing understanding of mixed intra-abdominal infections in general and appendicitis in particular.

Since Altemeier's seminal publication, there have been substantial improvements in specimen handling and culture techniques as well as the description of many new organisms, especially among the anaerobes. Indeed, microbiologic specimen handling, culture, and transport techniques are a critical factor in the accurate and complete description of the bacteriology of appendicitis. Accordingly, many reports in the 1980s demonstrated an average of 2 to 4 microorganisms cultured from patients with perforated or gangrenous appendicitis.[62-70] However, with advances in specimen handling and culture techniques, more recent reports demonstrate an average of approximately 12 organisms per specimen from patients with gangrenous or perforated appendicitis.[53,71] It appears that the discrepancy from previous reports may be attributed in part to the time-intensive isolation of fastidious anaerobic bacteria that includes the processing and isolation of bacteria in a strict anaerobic environment and the use of culture media that has never been exposed to oxygen. In addition, careful attention to specimen collection and transport so that exposure of atmospheric oxygen to cultured material is absolutely minimized, is crucial to accurate and complete identification of all organisms. The aerobic and anaerobic bacteria recovered with meticulous culture techniques from patients with gangrenous or perforated appendicitis are listed in Tables 1 and 2.[53,56,71] *Bacteroides fragilis* is present in more than 70% of cases. *Escherichia coli* is the most common aerobic Gram-negative species and is also present in more than 70% of cases. In general, more than 10 organisms can be cultured from the infected appendix and typically, anaerobic organisms exceed aerobic species in colony counts by a ratio of 3:1.

An important pathologic development in appendicitis is compromise of the mucosal barrier by progressive ischemia.[52] It is at this juncture that bacterial invasion of the appendiceal wall occurs. Baron and colleagues[72] demonstrated a highly significant difference between the number of bacteria cultured from the appendiceal wall in patients with pathologically proven acute appendicitis (2.3 bacteria/specimen; 0.6 aerobes and 1.7 anaerobes) and the number in patients with gangrenous or perforated appendicitis (9.9 bacteria/specimen; 2.6 aerobes and 7.3 anaerobes). In patients with acute appendicitis only, bacteria are infrequently cultured from the peritoneal fluid. However, bacteria are recovered from the peritoneal fluid or wounds of more than 80% of patients with gangrenous or perforated appendicitis. If cultures are positive, they demonstrate the same organisms that are cultured from the appendiceal wall in the same patients.

Interestingly, the proportions and relative frequency of the recovered bacteria in patients with appendicitis are not the same as in the normal

TABLE 1. Percentage of aerobic and facultative bacteria cultured from patients with gangrenous and perforated appendicitis

Bacteria	Gangrenous (%)	Perforated (%)	All (%)
Escherichia coli	70.4	77.3	74.6
Streptococcus viridans	18.5	43.2	33.8
Streptococcus, group D	7.4	27.3	19.7
Pseudomonas aeruginosa	11.1	18.2	15.5
Entercoccus sp.	18.5	9.1	12.7
Staphylococcus sp.	14.8	11.4	12.7
Pseudomonas sp.	7.4	9.1	8.5
Citrobacter freundii	3.7	6.8	5.6
Beta-hemolytic streptococcus, group F	7.4	4.5	5.6
Beta-hemolytic streptococcus, group C	3.7	4.5	4.2
Enterobacter sp.	7.4	2.3	4.2
Klebsiella sp.	3.7	4.5	4.2
Beta-hemolytic streptococcus, group G	0	4.5	2.8
Moraxella sp.	3.7	2.3	2.8
Corynebacterium sp.	0	2.3	1.4
Serratia marcescens	3.7	0	1.4
Eikenella corrodens	0	2.3	1.4
Hafnia alvei	3.7	0	1.4
Hemophilus influenzae	0	2.3	1.4

From Bennion RS, Thompson JE. Appendicitis. In: Donald E. Fry, editor. Surgical Infections. Boston: Little, Brown; 1995, pp. 241–250. Reproduced by permission.

colon.[73] Specifically, *Clostridium* species, *Enterococcus* species, *Enterobacter cloacae, Lactobacillus* species, *Eubacterium* species, *Bacteroides vulgatus*, and *Bacteroides distasonis* are less frequently encountered than one would predict.[71] The clinical significance of this observation is unclear.

In brief, there are several principles about the bacteriology of appendicitis that are worth reviewing: 1) infection due to appendicitis is polymicrobial with typically more than 10 organisms per specimen and a predominance of anaerobic organisms followed by Gram-negative organisms; 2) cultures of peritoneal fluid are frequently negative in patients with acute suppurative appendicitis only; and 3) in patients with gangrenous or perforated appendicitis, cultures are often positive and generally, the same organisms may be cultured from the wound, peritoneal fluid, and appendiceal wall.

Clinical Presentation

The diagnosis of acute appendicitis remains 1 of the last bastions of clinical medicine.[21] A carefully detailed history and physical examination will provide the proper diagnosis in the majority of cases and expedite

TABLE 2. Percentage of anaerobic bacteria cultured from patients with gangrenous and perforated appendicitis

Bacteria	Gangrenous (%)	Perforated (%)	All (%)
Bacteroides fragilis	70.1	79.5	76.1
Bacteroides thetaiotaomicron	48.1	61.4	56.3
Bilophila wadsworthia	37.0	54.5	47.9
Peptostreptococcus micros	44.4	45.5	45.1
Eubacterium sp.	40.7	29.5	33.8
Bacteroides intermedius	33.3	27.3	29.6
Bacteroides vulgatus	18.5	34.1	28.2
Bacteroides splanchnicus	25.9	27.3	26.8
Fusobacterium sp.	22.2	27.3	25.4
Bacteroides ovatus	18.5	27.3	23.9
Microaerophilic streptococci	29.6	20.5	23.9
Peptostreptococcus sp.	29.6	18.2	22.5
Lactobacillus sp.	22.2	20.5	21.1
Bacteroides uniformis	22.2	18.2	19.7
Bacteroides distasonis	14.8	20.5	18.3
Clostridium clostridioforme	18.5	18.2	18.3
Bacteroides gracilis	11.1	15.9	14.1
Actinomyces sp.	11.1	11.4	11.3
Other *Bacteroides*	22.2	34.1	29.6
Other *Clostridia*	33.3	20.5	25.4
Other Gram-negative rods	7.4	13.6	11.3

From Bennion RS, Thompson JE. Appendicitis. In: Donald E. Fry, editor. Surgical Infections. Boston: Little, Brown; 1995, pp 241–250. Reproduced by permission.

appropriate treatment. Furthermore, in many other areas of clinical medicine, an initially tentative or even misguided diagnosis is not necessarily harmful as laboratory or imaging investigations are completed to confirm or refute the initial suspicions. However, with acute appendicitis, delays in diagnosis can be harmful and may convert a relatively uncomplicated case into a case with substantial morbidity or even, mortality in patients with significant comorbid illnesses.[21,22,26] The patient with an atypical presentation of appendicitis can be a taxing diagnostic problem, yet delay in diagnosis often results in advanced disease with perforation and a marked increase in the complication rate. Delay or error in diagnosis of acute appendicitis is now 1 of the most frequent allegations of medical malpractice that are leveled against general surgeons, emergency medicine physicians, and primary care physicians. Phillips and colleagues[74] analyzed the Physician Insurers Association of America malpractice claims data from 1985 through 2000. These investigators evaluated 49,345 primary care claims of which approximately one third were classified as "diagnosis error." Within this group of claims, they found a significantly disproportionate risk of certain condition-specific negligent event claims relative to the actual frequency of the condition in the population. Specifically, they found that appendicitis was 25 times more likely to generate a claim of medical malpractice than breast cancer.

As diagnostic studies of all types have progressed in sophistication and accuracy in recent decades, clinicians have often developed the habit of reliance on these studies for confirmation of a diagnosis. Often, that is an appropriate stance. However, the diagnosis of acute appendicitis is often apparent to the astute, bedside clinician and laboratory or imaging studies should be considered as adjunctive, not mandatory, and are primarily useful when the diagnosis is obscure. Indeed, the authors have participated in numerous cases in which obtaining additional investigations added hours of unnecessary delay to the evaluation and treatment of the patient when the history and physical findings were characteristic of appendicitis.

Acute Nonperforated Appendicitis

The characteristic presentation of acute nonperforated or suppurative appendicitis is abdominal pain in a teenager or young adult that progressively worsens over a 12- to 24-hour time period.[35-38,55] Abdominal pain is present in more than 95% of patients with appendicitis. In the early stages of appendicitis, the pain is thought to be mediated by autonomic visceral pain afferent fibers. Accordingly, it begins as a midabdominal or periumbilical ache or discomfort. It is poorly localizing, occasionally crampy, unrelieved by passage of stool or flatus, and unrelated to activity or position. During this stage, more than 90% of patients complain of anorexia and, in fact, a hungry patient should cast doubt on the diagnosis. Sixty percent to 80% of patients are nauseated. Diarrhea is very uncommon, but has been reported in patients with appendicitis. Diarrhea is obviously a common accompaniment of gastroenteritis that is in the differential diagnosis of right lower quadrant pain, but by itself, diarrhea should not rule out the diagnosis of appendicitis.

Six to 12 hours after the onset of the illness, inflammation of the appendix begins to extend to surrounding organs and the parietal peritoneum overlying the appendix. In the process, appendiceal inflammation activates somatic pain fibers that localize pain to the region of the appendix. Subsequently, the poorly localizing midabdominal ache that characterizes the early stages of appendicitis evolves into well-localized, sharp pain that is progressively severe. Conventional wisdom is that the pain of appendicitis localizes at McBurney's point: approximately two thirds of the distance along a line drawn from the umbilicus to the right anterior superior iliac crest. However, the inconstant anatomic location of the appendix manifests itself as appendiceal pain that can localize in a wide variety of positions, although generally in the right lower quadrant of the abdomen. Interestingly, one fourth of all patients with appendicitis present with localizing pain as an initial symptom without prior visceral symptoms. During this period when the pain localizes, any sudden movement, including coughing, elicits intense pain. Indeed, many patients report that the bumps in the road during the automobile ride to the hospital or emergency room were especially excruciating in terms of stimulating their abdominal pain.

John B. Murphy was the first to emphasize the order of occurrence of symptoms[75]: pain, anorexia, tenderness, fever, and leukocytosis. Murphy stated: "The symptoms occur almost without exception in the above order, and when that order varies I always question the diagnosis." There are always exceptions, but an excellent diagnostic tenet is that if nausea or fever precedes the first complaint of pain, then the diagnosis is not appendicitis.

Upon inspection, the patient often assumes the fetal position or lies very still with the right leg flexed at the hip. Temperature elevation of 37.5°C to 38.0°C is common. However, approximately 25% to 50% of all patients with acute appendicitis have a normal temperature (<37.5°C).[36,55] Palpation of the abdomen reveals localized tenderness. Rebound tenderness, voluntary and involuntary guarding, and rigidity may also be present depending on how advanced is the appendiceal inflammation. Cutaneous hyperesthesia may be present in the region of maximal tenderness. It is important to remember that physical signs will vary depending on the position of the appendix. With a retrocecal or pelvic appendix, there may be minimal tenderness to palpation.

Pelvic examination in women and rectal examinations in all patients may be unremarkable with acute appendicitis, but are a mandatory part of the physical examination. If the tip of the appendix is oriented toward the pelvis, then tenderness may be elicited on intra-abdominal palpation by either of these routes, thereby helping to confirm the diagnosis and localize the appendix. Furthermore, the necessity of complete pelvic and rectal examinations to exclude other disease is emphasized by reported series of more than 20% negative appendectomy rates in women explored for suspected appendicitis.

Although unusual, inflammation of the appendix when it abuts the obturator muscles or the psoas muscles will result in increased pain on passive stretching of these muscles.[75] Sensitivity of either muscle group to stretching can help localize the appendix within the abdomen. The "obturator sign" is detected by adductor pain after internal rotation of the flexed thigh. The "psoas sign" is elicited by passive extension of the right thigh with the patient in the left lateral decubitus position. Pain may radiate to the right testicle in men. Rovsing's sign is frequently present and refers to right lower quadrant pain that is stimulated by palpation of the left lower quadrant.

Wagner and colleagues[76] performed a meta-analysis of the clinical presentation of appendicitis and concluded that a diagnosis was most likely in the presence of right lower quadrant pain, tenderness, and migration of the pain from the periumbilical area to the right lower quadrant. However, they stressed that no single finding effectively rules out the diagnosis.

The most signficant abnormal laboratory finding in patients with acute appendicitis is leukocytosis with an average elevation to approximately 15.0×10^9 white blood cells per liter.[35,36,55] Although leukocytosis is helpful in supporting the diagnosis, it may not always be present. Pieper and colleagues[36] reported experience with 493 patients in which only 67% had a leukocyte count greater than 11.0×10^9 white blood cells per liter. Cardall and colleagues[77] performed a prospective study of 293 patients to evaluate the clinical utility of leukocytosis and fever in the diagnosis of appendicitis. The sensitivity of leukocytosis was 76%, the specificity was 52%, the positive predictive value was 42%, and the negative predictive value was 82%. A temperature of more than 99.0°F had a sensitivity of 47%, specificity of 64%, positive predictive value of 37%, and negative predictive value of 72%. In short, their findings suggest that leukocytosis and fever are not reliable diagnostic tests for appendicitis and clinicians should be wary of relying on abnormalities of either in the diagnosis of appendicitis.

The duration of symptoms varies according to the pathologic condition of the appendix; generally, patients with perforated appendicitis report symptoms for longer than the 12- to 24-hour time period that is commonly observed in patients with acute suppurative or nonperforating appendicitis. In addition, abdominal pain is more intense and diffuse when the appendix perforates. Common signs and symptoms of the appendicitis and their frequency are shown in Table 3.[35-38,55]

Appendicitis with Perforation

Perforation occurs overall in approximately 20% to 30% of patients with appendicitis.[35-38,55] In general, patients with perforation have a longer duration of symptoms before surgery that again, emphasizes the principle of expeditious diagnosis and treatment. Some series suggest a

TABLE 3. Frequency of common signs and symptoms in patients with appendicitis

Symptoms	%
Abdominal pain	100
Right lower quadrant	75
Periumbilical	15
Diffuse	10
Anorexia	80
Nausea	80
Vomiting	60
Signs	
Abdominal tenderness	100
Right lower quadrant	95
Other	5
Temperature >37.5°C	70
Rebound tenderness	70
Rectal tenderness	45
Guarding or rigidity	35

Values reported are approximate averages culled from the literature.[35–38,55]
From Bennion RS, Thompson JE. Appendicitis. In: Donald E. Fry, editor. Surgical Infections. Boston: Little, Brown; 1995, pp 241–250. Reproduced by permission.

perforation rate of more than 50% in children younger than 3 years and adults older than 50 years. The high incidence of perforation in these groups is likely related to delays in presentation and diagnosis.

The hallmarks of appendicitis with perforation are increasing intensity of abdominal pain, local or diffuse peritonitis, temperature elevation greater than 38°C, and tachycardia. Nonperforated appendicitis is not commonly associated with temperature elevation over 38°C. Tachycardia is an excellent marker for illness severity and is characteristic of perforated appendicitis with a severe inflammatory response that may signal impending or ongoing systemic sepsis.

Patients who progress to perforation account for most of the morbidity and mortality associated with acute appendicitis. In the 1930s, the mortality rate for perforated appendicitis was 13%.[78] Although most patients with appendicitis can be diagnosed readily, there are many in whom a firm diagnosis cannot be easily reached. Accordingly, it is appropriate to have a liberal approach in making the diagnosis with the understanding that some patients will undergo operation and be found to have a normal appendix. In this manner, some patients with an ambiguous clinical presentation and who actually have appendicitis will undergo surgery before they proceed to perforation and its associated morbidity. In short, the morbidity of a negative appendectomy is preferable to the morbidity of perforated appendicitis. The medical community is generally willing to accept a negative appendectomy rate of 10% to 20%, with higher false negative rates of diagnosis in women than men.[26,32,35,36,38] The recent availability of noninvasive diagnostic tests that may aid in the diagnosis of patients with atypical presentations may minimize negative explorations and facilitate aggressive intervention before perforation. Regardless, the clinician must be prepared to operate in equivocal circumstances, consistent with the principle to remove the appendix before it perforates.

Periappendiceal Abscess

Periappendiceal abscess has been reported to develop in up to 10% of patients with appendicitis.[22] The classic presentation is of a patient who experiences severe right lower quadrant pain for 1 to 2 days associated with fever and then resolves both their pain and fever. After 7 to 10 days, the fever recurs and they notice mild to moderate right lower quadrant discomfort. Physical examination demonstrates a palpable mass in the right lower quadrant. Broadly speaking, any patient with a right lower quadrant mass and fever should be considered to have a periappendiceal abscess until proven otherwise. Imaging with ultrasound or computed tomography (CT) will confirm the diagnosis in most cases.

Management depends on the patient's condition. If the patient is not toxic and signs of sepsis are absent, then it is preferable for the patient to undergo percutaneous drainage of the abscess with systemic antibiotic therapy. If adequate drainage can be achieved, then the abscess cavity will frequently collapse over 5 to 10 days and the inflammatory process will resolve. The patient can be discharged from the hospital once the infection is under control and undergo elective or interval appendectomy 6 to 8 weeks later. This approach avoids the morbidity associated with exploring a patient with a large abscess or phlegmon in whom it is often difficult even to locate the appendix, let alone remove it.

On the other hand, unremitting sepsis or inadequate percutaneous drainage should prompt operative intervention. Drainage should be as complete and dependent as possible. The surgeon should be prepared to encounter substantial inflammation and surgical therapy may be limited to abscess drainage alone. It may not be possible, nor should the surgeon aggressively pursue appendectomy. It is much safer to permit the abscess and surrounding inflammation to resolve before proceeding with a second stage procedure to remove the appendix.

Recurrent and Chronic Appendicitis

Although surgeons debate their existence, both recurrent and chronic appendicitis appear to be real clinical diagnoses.[22] Recurrent appendicitis refers to a pattern of symptoms in which the patient reports mild, self-limited attacks of right lower quadrant pain that typically last for hours before resolving spontaneously. Often, the symptoms are not severe and the patient may not seek medical attention. Eventually, the patient has a severe attack, the diagnosis of acute appendicitis is suspected, and appendectomy is performed. The diagnosis of recurrent appendicitis is a retrospective one in which the patient reports multiple attacks of pain of which all but the most recent one before surgery are mild in severity. Indeed, up to 9% of patients being evaluated for acute appendicitis report a history of similar symptoms.[55] Similarly, if interval appendectomy after medical treatment of appendicitis is avoided, then the likelihood of recurrence is stated to be anywhere from 10% to 80%. Finally, after appendectomy for recurrent appendicitis, pathologic findings frequently include chronic as well as acute inflammation, providing further circumstantial evidence for the entity, "recurrent appendicitis."

Chronic appendicitis is considered to be even rarer and more difficult to diagnose than recurrent appendicitis. It refers to a patient who reports constant well-localized right lower quadrant pain and tenderness with no other identifiable pelvic or abdominal disease. If appendectomy completely relieves the pain and pathologic findings include chronic inflammation of the appendix, then the diagnosis of chronic appendicitis is secured. However, it is important to note that it is very difficult to make this diagnosis preoperatively and this explanation for a patient's abdominal complaints should be used sparingly.

Atypical Presentations[21,22]

It is generally held that approximately one fourth of all patients with appendicitis present with atypical signs and symptoms. In these cases, the presence of common signs and symptoms, and the progression of disease are variable. The danger, of course, is that an atypical presentation obscures the diagnosis until perforation occurs and the necessity for operation is obvious in the face of a toxic patient with an acute abdomen. Nonetheless, there are 3 factors that are associated with most atypical presentations: extremes of age, variable appendiceal position within the abdomen, and associated conditions such as pregnancy, Crohn's disease, prior administration of antibiotics, steroids or other immunosuppressive agents, or patients who are recovering from another operation.

Children with appendicitis tend to be diagnosed at a more advanced stage of inflammation than adults. Historically, perforation rates of 17% to 41% have been reported, with up to 50% of children developing postoperative infectious complications. Improvements in early diagnosis and antibiotic therapy have markedly reduced the complications in recent reports of older children. However, appendicitis in early childhood, although uncommon, remains especially challenging. Children between 1 and 5 years of age have a 70% perforation rate and before 1 year of age, virtually all patients have perforated appendicitis at the time of diagnosis. Explanations have been offered that include a short, incompletely formed omentum and a more aggressive form of disease, but the most likely reason is simply delay in presentation and diagnosis. Jackson[79] made an interesting observation in 313 children with acute appendicitis. The perforation rate in this study was 50% and correlated with the time to presentation. There was a 24% perforation rate in children who presented within 12 hours, a 42% perforation rate in children who presented within 24 hours, a 60% perforation rate in children who presented within 48 hours, and an 83% perforation rate in children who presented after 48 hours. Localizing pain and tenderness are less common in the young child and frequently the only complaint is generalized pain. Progressive illness of greater than 24 hours' duration with diffuse tenderness, high fever, and leukocytosis suggests appendicitis. As in adults, early operative intervention minimizes postoperative morbidity.

The pattern of clinical features in appendicitis in the elderly does not appear to be appreciably different than in younger patients. However, as with children, it is often difficult to diagnose appendicitis in the elderly patient. With increasing age, the differential diagnosis of abdominal pain is more extensive and the occurrence of appendicitis is less common. Although it is difficult to quantify, most surgeons agree that the elderly patient is typically more stoic than the younger patient and this may contribute to a delay in presentation. Up to 40% to 70% of elderly patients have a perforated appendix at the time of surgical exploration. Perforation may be due to delays in presentation or diagnosis, but some have speculated on anatomic differences in the appendix in the elderly that lead to early perforation. These factors include a thinned, atrophic appendix with diminished blood supply and an attenuated inflammatory response to localize or "wall-off" the infected appendix. The morbidity rate of appendicitis in the elderly is reported to be greater than 50% and this probably relates to both the high perforation rate and the frequent presence of comorbid illnesses.

The diagnosis of appendicitis can be very challenging in pregnant women for several reasons and delays in diagnosis that lead to perforation can be catastrophic in terms of fetal demise. The pregnant patient is neither more nor less prone to appendicitis and the incidence is equally distributed among all trimesters. Abdominal pain, nausea, and vomiting are all frequently present during the first trimester of pregnancy and so, there may be initially a low index of suspicion for appendicitis at this stage of pregnancy. In the second and third trimesters, the position of the appendix shifts toward the right upper quadrant and, therefore, the associated pain and tenderness of appendicitis is shifted superiorly as well. Leukocytosis is a normal feature of pregnancy so its presence is difficult to interpret. Complications of pregnancy add to the differential diagnosis so that a firm diagnosis can be difficult to achieve. However, if perforation and subsequent peritonitis develop, there is a reported fetal mortality rate of more than 30% and even a maternal mortality rate of 1% to 2%. Appendectomy for nonperforated acute appendicitis has a low fetal mortality rate and negligible maternal mortality rate. Hence, once the diagnosis of appendicitis has been made in the pregnant patient, urgent exploration should be accomplished. In addition, some advocate a liberal approach and justify a negative appendectomy rate of 20% to 40% to minimize the risk of perforation. Appendicitis remains the most frequent nonobstetric indication for laparotomy during pregnancy.

Differential Diagnosis[21,22,26]

The differential diagnosis for appendicitis is lengthy. Stated differently, appendicitis is in the differential diagnosis of virtually any patient with acute abdominal pain. Certainly, any inflammatory process that localizes or is referred to the right lower quadrant is in the differential diagnosis of appendicitis. It useful to consider alternative diagnoses for appendicitis based on the patient's age and gender.

In children, it is helpful to remember that appendicitis is very unusual in children younger than 5 years. Extra-abdominal childhood illnesses such as otitis media, pneumonia, or meningitis may manifest with abdominal discomfort, nausea, and vomiting. Careful attention to a thorough physical examination often aids in identifying extra-abdominal diseases. Although diarrhea does not exclude the diagnosis of appendicitis, it is an unusual accompaniment to the disease. Diarrhea, especially in large amounts, and abdominal pain are more characteristic of viral gastroenteritis. A prodrome of fever, myalgias, and easy fatigability suggest a viral etiology for the patient's symptoms. Mesenteric lymphadenitis may also be confused with appendicitis. Frequently, an antecedent history of respiratory tract infection can be elicited to support the diagnosis of mesenteric lymphadenitis. Meckel's diverticulitis can be indistinguishable from appendicitis based on the preoperative history and physical examination. Intussusception typically manifests with episodic abdominal pain and distension. Physical findings of a tender, abdominal mass and hemoccult-positive stool also support the diagnosis. In the neutropenic child with right lower quadrant tenderness, typhlitis or acute inflammation of the cecum is a consideration. Systemic antibiotics are the mainstay of therapy and CT imaging may be useful in distinguishing typhlitis from appendicitis especially if there is evidence of pneumatosis intestinalis of the colonic wall.

The highest percentage of misdiagnosis in patients who appear to have appendicitis occurs in women of childbearing age. Gynecologic problems are frequently mistaken for appendicitis and the negative appendectomy rate in young women ranges from 15% to 40%. Salpingitis can manifest in a remarkably similar pattern to appendicitis. Patients with salpingitis may have a more prolonged course of illness before presentation and on physical examination, cervical motion tenderness may suggest the diagnosis. A ruptured ovarian follicle can cause abdominal pain that localizes to the lower quadrants. Its occurrence at mid-cycle, or mittelschmerz, along with the absence of systemic symptoms or signs and a history of recurrent pain suggest this diagnosis. Symptoms that occur in association with menses are consistent with endometriosis especially when pain occurs in the absence of other symptoms and signs of inflammation. A ruptured ectopic pregnancy is in the differential diagnosis of appendicitis. Hemodynamic changes consistent with hemorrhage, a tender, painful mass on pelvic examination, and a positive pregnancy test, all suggest this diagnosis. Traditionally, culdocentesis of nonclotted blood was diagnostic, but more recently, imaging studies such as ultrasound examination have proven to be very helpful. Urgent exploration should not be delayed if there is evidence of uncontrolled hemorrhage.

In young men, the diagnosis of appendicitis is most readily apparent. Testicular torsion or epididymitis may manifest with right lower quadrant pain, but they are usually easily distinguished from appendicitis on physical examination. Symptomatic nephrolithiasis or urinary tract infection may manifest in either gender with right lower quadrant pain. The presence of flank or back pain along with hematuria or pyuria suggests a diagnosis associated with the genitourinary tract. Crohn's disease often manifests in young patients and, on occasion, can be confused with appendicitis. Typically, the patient will have a history of recurring symptoms, alteration in bowel habits, and possibly blood in the stool. It is always worthwhile to elicit a travel history from the patient with acute abdominal pain. Recent travel to a foreign country along with a history of diarrhea should raise the suspicion of infectious enteritis or colitis. Infarcted appendicae epiploica usually manifests with sharp pain that is highly localized. The diagnosis is suggested by point tenderness in the absence of other inflammatory signs such as fever or leukocytosis. Before CT, it was very difficult to make the diagnosis, but now CT can often identify the offending focus.

In the elderly patient, colonic diverticulitis should be in the differential diagnosis of appendicitis. Cecal diverticulitis is unusual, but may be indistinguishable from appendicitis. There may be a longer prodrome and CT may help to distinguish the 2 diagnoses, but it is often determined at the time of exploration. Sigmoid diverticulitis, of course, is usually manifest in the left lower quadrant. However, a redundant sigmoid colon may "flop over" to the right lower quadrant and lead to a presentation similar to appendicitis.

Diagnostic Imaging

Several radiologic modalities have been used in the diagnosis of appendicitis. Ultrasonography and CT have proven extremely useful in clinically equivocal cases of appendicitis. However, routine use of these modalities in all patients suspected of having appendicitis is not well-established. If the diagnosis is apparent from the history, physical examination, and laboratory studies, immediate operation without imaging is justified.

Plain Radiography

Plain radiography has been used in evaluating gastrointestinal disease since the early 1900s. This modality has been invaluable in diagnosing many gastrointestinal disorders, but it has not been very useful in diagnosing patients with appendicitis. The appearance of an opaque fecalith in the right lower quadrant is often quoted as being the hallmark radiographic finding in appendicitis, but fewer than 5% to 8% of patients present with this finding.[35,80] Other commonly described but nonspecific findings include gas in the appendix, localized paralytic ileus, loss of cecal shadow, blurring or obliteration of the right psoas muscle, rightward scoliosis of the lumbar spine, haziness over the right sacroiliac joint, and free intraperitoneal air or fluid.[33] In a study of 821 consecutive patients hospitalized for suspected appendicitis, no individual radiographic finding was highly sensitive or specific.[81] In patients with equivocal clinical findings, plain abdominal films may be indicated when other conditions such as perforation, intestinal obstruction, or ureteral calculus are suspected.[82] Overall, plain radiographs lack sensitivity and specificity in diagnosing appendicitis and are not cost-effective in the diagnosis of appendicitis.

Barium Enema

The use of barium enemas as a primary modality to diagnose appendicitis is largely of historical interest only. Most of the clinical studies that advocated the use of barium enemas to diagnose appendicitis were before CT came into wide use. The radiographic findings suggestive of appendicitis include incomplete filling of the appendix, irregularities of the appendiceal lumen, mass effect on the cecum or terminal ileum, and most importantly, nonvisualization of the appendix.[33,83] Diagnostic problems in using barium enemas include the fact that the appendix cannot be visualized in 10% of normal patients. In addition, the appendix has been reported to fill with barium in patients with perforation, resulting in spillage of barium into the peritoneal cavity.[35] Finally, barium enemas are uncomfortable and time-consuming, and their diagnostic accuracy is less than other noninvasive imaging modalities. For these reasons, barium enema is now used infrequently in the diagnosis of appendicitis.[33]

Ultrasonography

Ultrasound was first used as a diagnostic modality in the early 1950s. However, it was not until 1981 that Deutsch and Leopold[84] reported the first ultrasonic visualization of the appendix. Following this initial publication, ultrasound studies of appendicitis began to appear in the literature over the next 10 years. The late introduction of ultrasound as a diagnostic modality for appendicitis was largely due to the interference of bowel gas and the lack of a transducer with enough spatial resolution to pick up small structures such as the appendix. Introduction of the graded compression technique in ultrasound improved the ability to visualize the appendix. It decreases the distance between the transducer and the appendix, and compresses overlying bowel that eliminates gas artifacts and enables clearer visualization of retroperitoneal structures for comparison. The technique involves applying gradual, moderate pressure over the right lower quadrant in an effort to collapse the normal bowel and visualize the distended appendix.

The inflamed appendix on ultrasound has been described as an immobile, noncompressible, blind-ending structure consisting of an anechoic lumen surrounded by an echogenic mucosa and hypoechoic thickened wall adjacent to the cecum.[85] The diagnostic accuracy of graded compression ultrasound has been reported to range from 71% to 97%, with sensitivities and specificities in the 76% to 96% and 47% to 94% ranges, respectively.[33,80,86,87] This wide range of findings is not surprising for a modality in which the diagnostic images and their interpretation are highly dependent on operator clinical and technical skills.

When the appendix is visualized, the criteria for diagnosis of acute appendicitis by ultrasonography are well-described.[84,88] The most useful ultrasound finding that is suggestive of appendicitis is reported to be a transverse appendiceal diameter of 6 to 7 mm or greater.[33] The difficulty with this criterion for diagnosing appendicitis is that the normal appendiceal diameter ranges from 3 to 13 mm. However, 1 study showed that only 9% of patients had an appendiceal diameter of 7 mm or more.[89] Overall, this finding has been reported to have a sensitivity of 100%, but a specificity of only 64%.[90]

The ultrasound finding of a "target" appearance of the inflamed appendix, namely, a lumen surrounded by a thickened wall, has also been described as a characteristic finding of appendicitis.[85] Inflammatory fat changes have been described on ultrasonography in patients with acute appendicitis, but this finding is reported to have a low sensitivity of 50%.[89] The ultrasound findings of appendiceal perforation include loculated pericecal fluid, a phlegmon, prominent pericecal fat, and circumferential loss of the submucosal layer. Other findings include an appendicolith and the absence of gas in the appendiceal lumen.

Despite these well-described ultrasound findings, there does not appear to be an evidence-based standard on how they are used and there is variability in terms of which findings an individual radiologist will use in making the diagnosis of appendicitis. In a recent prospective ultrasound study of 457 patients in which the appendix was visualized (239 control patients, 138 with right lower quadrant pain without appendicitis, and 80 with appendicitis), the investigators used the following criteria to differentiate an acutely inflamed appendix from a normal one: 1) proof that the point of maximal tenderness was located at the appendix, 2) an outer appendiceal diameter of 6 mm or more, 3) noncompressibility of the appendix, 4) rounded transverse section of the appendix, 5) increased blood flow in the appendiceal wall on color Doppler, and 6) echogenic periappendiceal inflammatory fat changes.[91] Unfortunately, the investigators did not state whether all 6 findings had to be present at the same time to diagnose appendicitis or if 1 or 2 of the findings were definitive for their purposes. In contrast, in a prospective, randomized comparison of CT with ultrasound to diagnose appendicitis in 89 patients, the authors used the following criteria to differentiate an acutely inflamed appendix from a normal one: 1) visualization of the appendix, and 2) an outer diameter of 6 to 7 mm or more.[92] These studies clearly underscore the need to gain a better understanding of the various ultrasound findings and the ongoing need to have some level of agreement in their use among radiologists.

Difficulties with ultrasonography include the fact that a normal appendix must be identified to rule out acute appendicitis, leaving some to conclude that ultrasound is more useful in detecting appendicitis than ruling it out.[93] The rates of detecting a noninflamed or normal appendix have been reported to be between 60% and 82%.[90] Visualization of a normal appendix is more difficult in patients with a large body habitus or if there is an associated ileus that produces shadowing due to overlying gas-filled loops of bowel. The accuracy of ultrasonography also decreases with a retrocecal location of the appendix.[94] Moreover, perforation significantly decreases the sensitivity of graded compression ultrasound to as low as 28.5%.[33] Common false-positive diagnoses include Meckel's diverticulitis, cecal diverticulitis, inflammatory bowel disease, pelvic inflammatory disease, endometriosis, and various ovarian pathologies.

The use of ultrasound as a diagnostic modality for appendicitis has several advantages and disadvantages. The disadvantages include the relatively low specificity of many of the findings on ultrasound and a lack of evidence-based procedures for conducting and interpreting appendiceal ultrasounds. Another disadvantage is that patients often complain of the discomfort evoked by the transducer pressure during ultrasound evaluation. As for the advantages, ultrasonography is relatively inexpensive, safe, and widely available. Other advantages include noninvasiveness, short acquisition time, lack of radiation exposure, and the potential for discovering other causes of abdominal pain. For these reasons, it is especially useful in pregnant women and children. It is also useful in women of childbearing age since ultrasound is an excellent modality for imaging of the reproductive organs.

Computed Tomography (CT)

CT was invented in 1972 by British engineer Godfrey Hounsfield. The original systems were dedicated to head imaging only, but "whole body" systems with larger patient openings became available in 1976 and CT was widely prevalent by the early 1980s. The prototype CT scanners required roughly 4 minutes of lapsed time to acquire a single slice or image, but modern units produce images in less than 0.5 seconds and a complete body scan can be performed in just a few minutes. Since the introduction of spiral CT in the 1990s, the scan times are even shorter compared with sequential CT and the patient radiation dose is reduced.

As a diagnostic modality for appendicitis, the accuracy of CT has been reported to be as high as 93% to 98% with sensitivity and specificity in the 87% to 100% and 95% to 99% range, respectively.[80,95-97] The accuracy of CT relies in part on its ability to reveal a normal appendix more reliably and with greater consistency than ultrasonography. In a study of 210 helical appendiceal CT examinations in patients with oral and rectal contrast, an enlarged appendix with periappendiceal fat stranding was observed in 93% of patients with appendicitis.[96] In another study of 238 CT examinations with intravenous contrast, several CT characteristics of appendicitis were described. These findings include: 1) enlarged appendix (diameter ≥6 mm) (sensitivity, 93%; specificity, 92%), 2) appendiceal wall thickening (sensitivity, 66%; specificity, 96%), 3) periappendiceal fat stranding (sensitivity, 87%; specificity, 74%), and 4) appendiceal wall enhancement (sensitivity, 75%; specificity, 85%).[97] Other reports have also supported appendiceal diameter, wall changes, and fat stranding as being the top 3 CT findings suggestive of appendicitis.[98]

Although many studies have found CT to be an accurate modality for the diagnosis of appendicitis, there is continued controversy regarding the optimal CT technique for patients with suspected appendicitis.[97] Three major approaches have been advocated: 1) unenhanced CT of the abdomen and pelvis, 2) addition of oral and/or intravenous contrast media, and 3) focused appendiceal CT (imaging only the right lower quadrant) using rectally administered contrast media.

Unenhanced CT has been used with some success in children and adults.[95,99] The benefits of this approach include a shorter time for CT acquisition with maintenance of sensitivity (96% to 97%), specificity (99% to 100%), and accuracy (97% to 99%) when compared with traditional CT scans. Although these studies showed that appendicitis could be diagnosed accurately without contrast, another study showed that intravenous contrast significantly improves the diagnostic accuracy of helical CT.[100] As for focused appendiceal CT, studies using either oral only or oral plus rectal contrast show that focused appendiceal CT yields high levels of accuracy (96% to 98%) in clinically equivocal cases.[101,102] Moreover, studies using focused appendiceal CT with rectal contrast only yielded high levels of accuracy in the 96% to 98% range.[101,103,104]

In assessing the overall utility of CT, several authors have attempted to document its impact on the negative appendectomy and perforation rates for appendicitis. One study involving 908 patients noted a drop in the negative appendectomy rate from 20% to 7% and a drop in the perforation rates from 22% to 14%.[104] The authors concluded that CT should be performed in nearly all female and many male patients. However, the high CT accuracy rates in literature reports are not duplicated at all hospitals.[105] Naturally, decreased CT accuracy would reduce its potential impact on perforation and negative appendectomy rates. Thus, there is some controversy as to whether CT has positively impacted the perforation and negative appendectomy rates.[106,107] In particular, Flum and colleagues[108] showed no changes in the population-based incidence of negative appendectomy and perforation rate after the widespread use of CT and ultrasound imaging.

The advantages of CT over ultrasound include its higher diagnostic accuracy and operator independence. Additional advantages relating to accuracy include greater ability to detect the normal appendix, phlegmon, and abscess. In fact, CT is often used when ultrasound yields suboptimal or inconclusive results. The disadvantages of CT include possible iodinated contrast media allergy, patient discomfort from administration of contrast media (especially if rectal contrast media is used), exposure to ionizing radiation, and costs that generally range 3 to 4 times the cost of ultrasound.

Radioisotope and Magnetic Resonance Imaging (MRI)

Radioisotope imaging with labeled white blood cells is being investigated in patients with acute appendicitis. In the fall of 2004, the U.S. Food and Drug Administration approved a new product that utilizes a monoclonal antibody to label white blood cells in vivo. The product, technetium fanolesomab (NeutroSpec), is specifically indicated for "scintigraphic imaging of patients with equivocal signs and symptoms of appendicitis who are 5 years of age or older."[80] The utility of this technique is yet to be established.

Magnetic resonance imaging (MRI) is also being investigated as a potential diagnostic modality for appendicitis. At least 1 study has indicated MRI to be superior to ultrasound in revealing acute appendicitis.[109] Its role as an adjunct to evaluating patients with acute abdominal pain remains to be determined.

Imaging Summary

The optimal imaging technique for acute appendicitis should have several key characteristics. It must be accurate, quick, safe, technically nonchallenging, readily available, cost efficient, and capable of being performed with little risk or discomfort for the patient. Imaging procedures, specifically ultrasonography and CT, have been very useful especially in clinically equivocal cases. However, the routine use of ultrasonography and CT in the diagnosis of appendicitis in all patients is not well-established.[80] The results of several studies are conflicting in demonstrating improvement in the negative appendectomy rate or perforation rate.[104,106-108] For now, the use of imaging modalities in atypical presentations of suspected cases of appendicitis is very helpful. The use of imaging in patients with typical presentations is not clearly indicated, but if elected, then it should complement, not replace clinical assessment and judgment.

Antibiotic Therapy

Anderson and colleagues performed a meta-analysis of randomized or controlled clinical trials investigating the use of antibiotic therapy versus placebo for patients with suspected appendicitis who underwent appendectomy. These investigators evaluated 45 studies with 9576 patients.[110] Outcome measures were wound infection, intra-abdominal abscess, hospital length of stay, and mortality rate. Their overall conclusion is that the use of antibiotics is superior to placebo in preventing wound infection and intra-abdominal abscesses regardless of the pathologic state of the appendix. The optimal duration of treatment is unclear, although it is best to administer the first dose of antibiotics preoperatively. Finally, the choice of antibiotics should be governed by the bacteriology of appendicitis. Hence, it is best to use antibiotics that provide coverage for Gram-negative and anaerobic organisms.

Surgical Management[21-23]

In general, the best treatment for appendicitis is appendectomy. There are a handful of circumstances in which appendectomy may be delayed. If the episode has resolved by the time the patient has sought medical attention, then it is safe to advise elective or interval appendectomy to prevent recurrence. If the patient has a periappendiceal abscess without peritonitis, then it is appropriate to achieve percutaneous drainage first, allow the inflammation and abscess to subside, and then perform an interval appendectomy in 6 to 8 weeks. If the patient is in a remote location such as traveling on a ship at sea where a standard operation cannot be performed, then it is appropriate to treat the patient with analgesics, antibiotics, and supportive therapy until it is safe to transport the patient to a facility that can provide surgical care. However, notwithstanding these exceptions, appendectomy is the treatment of choice for appendicitis.

Once appendectomy has been planned, supportive measures for the patient should be accomplished expeditiously. Hypovolemia and electrolyte abnormalities should be corrected even if this takes several hours. If there is a significant ileus with abdominal distension, then a nasogastric tube should be placed. Comorbid illnesses, especially cardiopulmonary disease, should be addressed. Central venous, pulmonary artery, or arterial catheters should be placed if necessary to optimize the patient's condition preoperatively. Broad spectrum antibiotic coverage that covers anaerobic and Gram-negative organisms should commence before operation. Although appendectomy should not be delayed indefinitely, it is entirely appropriate to spend time to optimize a patient's medical condition to reduce the anesthetic and operative risk.

Open Appendectomy

After satisfactory induction of general anesthesia, careful palpation of the abdomen should be accomplished. If a mass is detected, then the incision should be made directly over the mass to facilitate drainage of the underlying abscess. Typically, no mass is appreciated and then, a right lower quadrant muscle-splitting incision is preferred. The skin incision can be made either transversely or at an oblique angle as described by McBurney. The incision should be centered at McBurney's point, approximately two thirds of the distance in a line drawn from the umbilicus to the anterior superior iliac spine. This incision can be extended medially if necessary, but initially, it should extend only slightly over the right rectus muscle. After skin and subcutaneous tissue are divided, the external oblique fascia is incised in the direction of its muscle fibers. The underlying oblique muscles can then be separated bluntly in the direction of their fibers without transection. The muscle fibers are retracted to expose the peritoneum that is incised transversely to gain access to the abdominal cavity. It is often possible to identify the peritoneum easily at a point just lateral to the right rectus muscle. Access to the abdomen at this location can be accomplished with minimal separation of the oblique muscles and no division of the rectus muscle.

Although a paramedian incision has been employed in the past, this technique has fallen into disfavor and it is not recommended. Even if the diagnosis of appendicitis is proven false, it is possible to extend a right lower quadrant incision medially to perform most operations on the right side of the abdomen including a right hemicolectomy. Sometimes the patient will present with an acute abdomen and peritonitis. Although acute appendicitis may be in the differential diagnosis, it may not be regarded with a high index of suspicion. A midline incision is entirely appropriate under these circumstances and it is certainly possible to remove the appendix easily through a midline incision. However, in patients in whom the diagnosis of acute appendicitis appears likely, a right lower quadrant incision is preferable. On occasion, a right lower quadrant incision may be employed for suspected appendicitis, and an acute abdominal condition is encountered that is truly out of reach of the incision such as a perforated duodenal ulcer. The surgeon should proceed with the correct incision to treat the emergency at hand, and then close both incisions at the end of the laparotomy.

Once the peritoneum is opened, any purulent fluid that is encountered should be aspirated and cultured. Retractors are positioned to separate the peritoneal opening and many surgeons perform a sweep of the abdomen with their finger. In patients with an appendix that is positioned in the pelvis, toward the sacral promontory, or toward the ileum, the surgeon's finger may be able to elevate the appendix into the wound easily where it can be grasped with a forceps or noncrushing clamp. However, caution should be exercised in performing the finger sweep. It is possible to fracture a gangrenous appendix if performed vigorously so a gentle approach should be adopted. In many patients, this maneuver may be unsuccessful. It is still worthwhile to gently palpate the area and often, it is still possible to feel a thickened, indurated appendix that directs the surgeon to the inflamed organ. If the appendix is not readily palpable, then there should be no hesitation to extending the incision to gain better exposure to the abdomen. The Fowler-Weir extension refers to division of the anterior and posterior right rectus sheath with medial retraction of the muscle. In addition, if it is not possible to feel the appendix, then tracing the tenia coli to their confluence helps to identify the base of the appendix and is a particularly useful maneuver in identifying a retrocecal appendix that is not easily palpable. If necessary, division of the lateral attachments of the cecum permits its mobilization into the field and enhances exposure to its posterior surface. A manual rocking action of the cecum after division of its lateral attachments is frequently successful in bringing the cecum and appendix anteriorly into the operative field.

Once identified, the appendix is elevated and mobilized by dividing the mesoappendix between clamps. The mesoappendix may be thickened or edematous and care should be taken as the friable mesoappendix is divided. Care must be taken to securely ligate the appendiceal artery that is located in the mesoappendix near the base of the appendix. If the appendiceal tip is retroperitioneal or retrocecal and there is significant inflammation, the appendix may need to be approached in a retrograde fashion after first dividing the base of the appendix.

There are several methods for approaching the appendiceal stump. By tradition, many surgeons crush and ligate the appendiceal stump before inverting it with a pursestring or Z-stitch. In this situation, the stump is ligated or double ligated with a sturdy suture and the pursestring or

Z-stitch is placed approximately 1 cm from the stump. These techniques have the potential to create a mucocele of the appendiceal stump and may result in a cecal mass defect that confounds diagnosis in later life. This is generally avoided by destroying the residual distal mucosa, often with electrocautery. Stump inversion may be necessary in the rare case in which appendiceal necrosis extends to the stump, but simple ligation with a sturdy, absorbable suture is adequate in most patients. Engstrom and Fenyo[111] performed a randomized trial of ligation and double invagination versus simple ligation alone. There were no differences in wound infection, hospital length of stay, or other outcomes in this study with the exception of a higher rate of early small bowel obstruction in the invaginated group.

Alternatively, a stapling device also works quite well in terms of amputating the appendix and providing a secure closure of the cecum adjacent to its base. In this circumstance, a short "cuff" of the cecum is removed along with the appendix to ensure that the entire appendix is removed. The surgeon may wish to invert the cecal staple line with interrupted Lembert sutures, but this is not absolutely necessary. If a stapling device is used, the surgeon must be careful not to remove too much of the cecum and potentially, impinge on the ileocecal valve. This can be avoided by carefully and completely dissecting all attachments of the appendiceal base from the cecum so that the entire length of the appendix is clearly identified before amputation and also tracing the terminal ileum directly into the cecum to identify the ileocecal valve. After the appendix is removed, the operative site and wound may be irrigated and followed by closure of the abdominal wall in layers. Drainage is not necessary unless there is an abscess cavity and then, drainage is indicated. Even if the appendix is gangrenous or perforated, drainage is unnecessary if there is no clearly defined abscess cavity.

If the appendix appears normal, then a thorough inspection of the abdomen is necessary. The cecum, sigmoid colon, and ileum should be inspected for diverticular disease. In particular, a Meckel's diverticulum should be sought that is likely to reside within 2 feet of the ileocecal valve. Signs of inflammatory bowel disease should be sought. The gallbladder should be visualized, especially in an older patient. If purulent material is evident that seems to originate from the upper abdomen, then evaluation of the duodenum for perforation should be accomplished. Mesenteric lymphadenopathy should be evaluated and if present, cultures should be obtained. In a female patient, both ovaries and Fallopian tubes should be inspected for evidence of pelvic inflammatory disease, ruptured follicular cysts, ectopic pregnancy, or other pathology. Again, there should be no hesitation to enlarge the incision to accomplish a thorough abdominal exploration. If purulent fluid or particulate matter is present in the abdomen, then complete exploration must be accomplished until the source is identified since virtually all patients with this finding will have a surgically treatable lesion.

In patients who have a normal appendix, appendectomy is still advised. The morbidity of performing an appendectomy in this circumstance is negligible. Furthermore, since the patient likely has a right lower quadrant incision, then leaving the appendix behind may cause diagnostic confusion in the future as clinicians are likely to consider the appendix absent in the context of an "appendectomy" incision. The exception to this recommendation is if the cecal wall at the base of the appendix is diseased, most notably with Crohn's disease. The appendix must be left in situ in that situation since there is a significant risk of stump failure with subsequent development of a fecal fistula.

Drainage of Periappendiceal Abscess

If a periappendiceal abscess is diagnosed preoperatively either by physical examination or imaging studies, then percutaneous catheter drainage is the preferable initial treatment.[112] Catheter drainage using CT or ultrasound guidance is usually successful in controlling the infectious process and permitting the abscess cavity to collapse. Generally, 7 to 10 days of catheter drainage is necessary. An interval appendectomy may be performed after the abscess and surrounding inflammation have resolved, usually approximately 6 to 8 weeks after initial drainage.

If the patient has peritonitis, then exploration is warranted. The abscess should be opened, cultured, and evacuated. Loculations should be broken up and closed suction drains should be placed into the cavity. Appendectomy should be accomplished if technically feasible. However, extreme caution should be exercised in proceeding with appendectomy. If the cecal wall adjacent to the appendix is especially edematous or friable, then appendectomy should be delayed. If the appendix is not removed, patients have a 10% to 80% risk of developing appendicitis again, so interval appendectomy should be performed.

Laparoscopic Appendectomy

Laparoscopic appendectomy was first reported by Kurt Semm, a German gynecologist, in 1983, but it was not until the early 1990s that this approach gained wide acceptance.[113] Since that time, there have been multiple prospective, randomized controlled trials, several meta-analyses, and nationwide database reviews comparing open to laparoscopic appendectomy.[114-129] Despite the plethora of data, there is still controversy regarding laparoscopic vs. open appendectomy. However, there appears to be an increasing trend in the utilization of laparoscopic appendectomy. Nguyen and colleagues[128] showed that the utilization of laparoscopic appendectomy in the United States has more than doubled, from 20% of cases in 1999 to 43% of cases in 2003. In practice, the decision to perform appendectomy open or laparoscopically often depends on surgeon expertise and the availability of operative and hospital resources.

Indications

The indications for laparoscopic appendectomy are the same as those for open appendectomy.[130] A laparoscopic approach provides the surgeon with a tool not only to rule out appendicitis but also to inspect other organs simultaneously to determine the true cause of the patient's symptoms. The visualization is often superior to the limited exploration that can be accomplished through a right lower quadrant incision. This is particularly important in the patient in whom the diagnosis is not clear and in women of childbearing age.

The indication for laparoscopic appendectomy in complicated or perforated appendicitis is controversial. There have been several studies that have examined the role of laparoscopic appendectomy in this setting and they suggest that laparoscopic appendectomy can be performed safely in these patients.[131-134] The overall complication rates are comparable and several studies suggest a lower wound infection rate and reduced hospital length of stay. As expected, the conversion rate in these patients typically ranges from 20% to 30%.

Given that a laparoscopic approach may be technically more challenging than an open approach, we believe that surgeons should exercise caution in performing laparoscopic appendectomy in the absence of sufficient training or expert assistance. Likewise, as with any laparoscopic procedure, conversion to an open operation should be not be considered a complication, but rather an exhibition of sound surgical judgment.

Contraindications

The number of absolute and relative contraindications to performing laparoscopic appendectomy have decreased over the past 10 years as minimally invasive surgical equipment and surgical skills have improved. Perhaps the most common contraindication to performing laparoscopic appendectomy is lack of surgeon experience. As surgeons gain confidence in their laparoscopic skills and as the procedure becomes more common

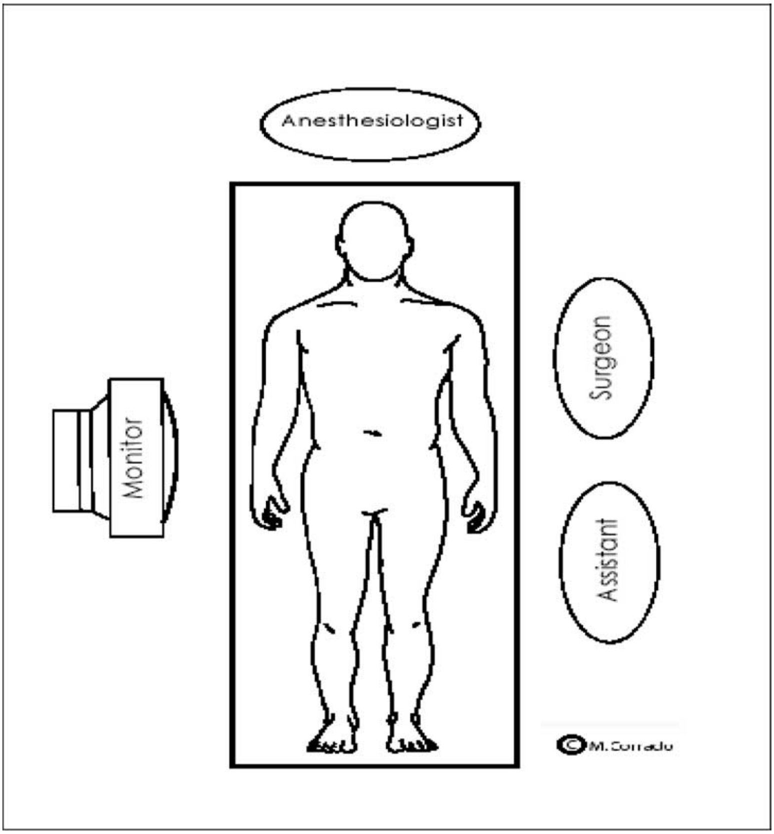

FIG 1. Room setup for laparoscopic appendectomy.

in residency training programs, this should not be a significant factor in the future.

Absolute contraindications include the inability to tolerate general anesthesia, refractory coagulopathy, and diffuse peritonitis with hemodynamic compromise. Diffuse peritonitis with hemodynamic compromise represents a surgical urgency in which attempted laparoscopy is not prudent. Open laparotomy allows rapid determination of the etiology and more expeditious management of the disorder. Relative contraindications include previous abdominal surgery with extensive adhesions, portal hypertension, severe cardiopulmonary disease, and advanced pregnancy.

Operative Technique for Laparoscopic Appendectomy

After the induction of general anesthesia, a urinary catheter and an orogastric tube are placed. The surgeon and the first assistant may stand

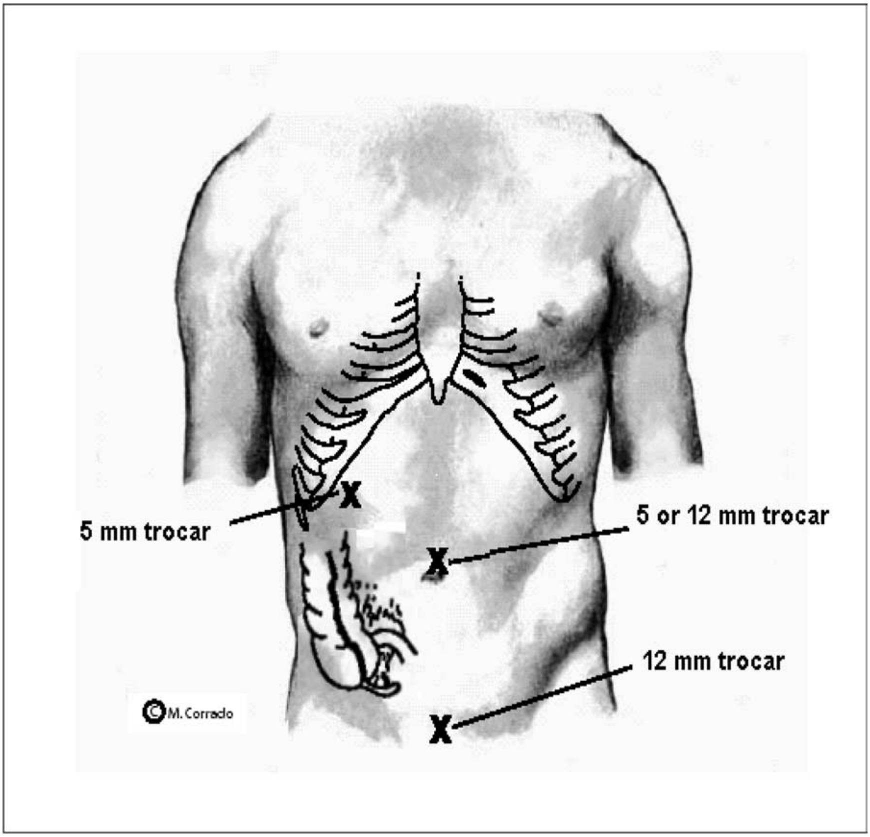

FIG 2. Trocar placement for laparoscopic appendectomy.

on the patient's left side. A single video monitor is used on the right side of the operating table (Fig 1).

Pneumoperitoneum is created with CO_2 insufflation into the abdominal cavity. The initial umbilical trocar can either be a 5 mm or a 10 mm trocar, depending on the diameter of the laparoscope being used. An angled laparoscope, either 30° or 45°, is especially helpful. The additional trocars are then placed under direct visualization (Fig 2). A 12 mm trocar is used in the suprapubic area to accommodate a laparoscopic linear stapling device and also to facilitate removal of the specimen. The larger incisions at the umbilicus and at the suprapubic area in the hairline allow for excellent cosmetic results. The third trocar should be a 5 mm trocar in the right side of the abdomen over the right colon. The reason for

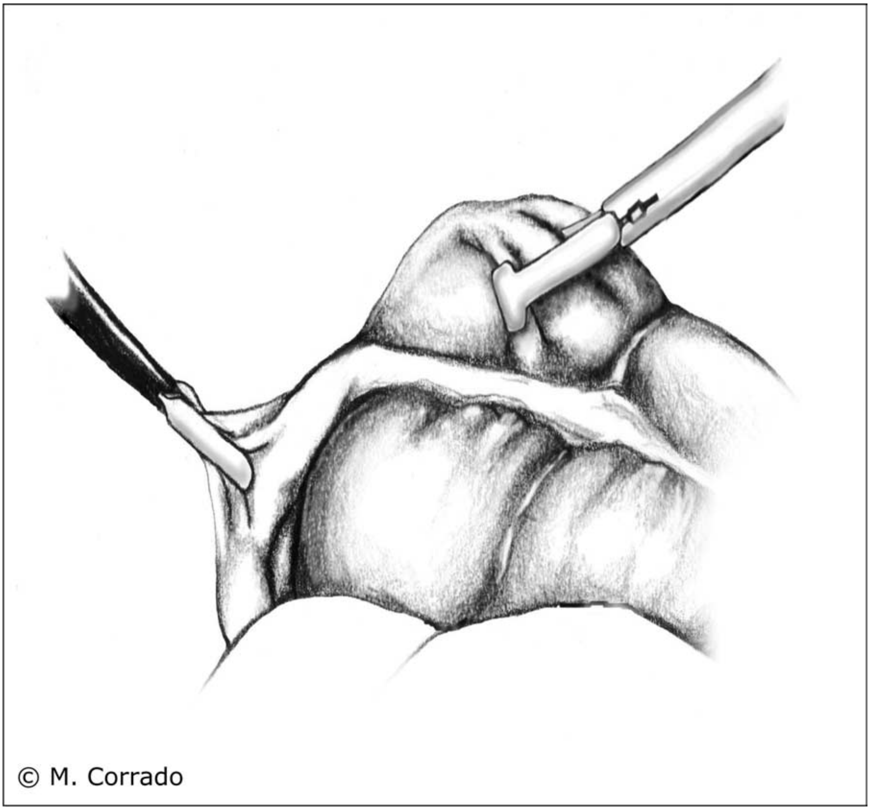

FIG 3. Exposure of the appendix.

choosing this trocar placement is to allow adequate distance from the first 2 trocars and to allow for "triangulation" toward the appendix.

After exploration of the abdomen, attention is focused on the appendix. It is helpful to place the patient in the Trendelenburg position with the bed rotated toward the patient's left side. Using an atraumatic grasper via the right abdominal port, the cecum is retracted superiorly and medially. In most cases, this maneuver will elevate the appendix into the field of view. If the appendix is retrocecal, the cecum should be mobilized medially by incising the lateral peritoneal attachments of the cecum. In patients with substantial inflammation, the appendix may be difficult to locate and technical maneuvers described previously should be employed to mobilize the cecum to facilitate identification of the appendix. Once the appendix is identified, it is grasped and elevated toward the anterior abdominal wall with

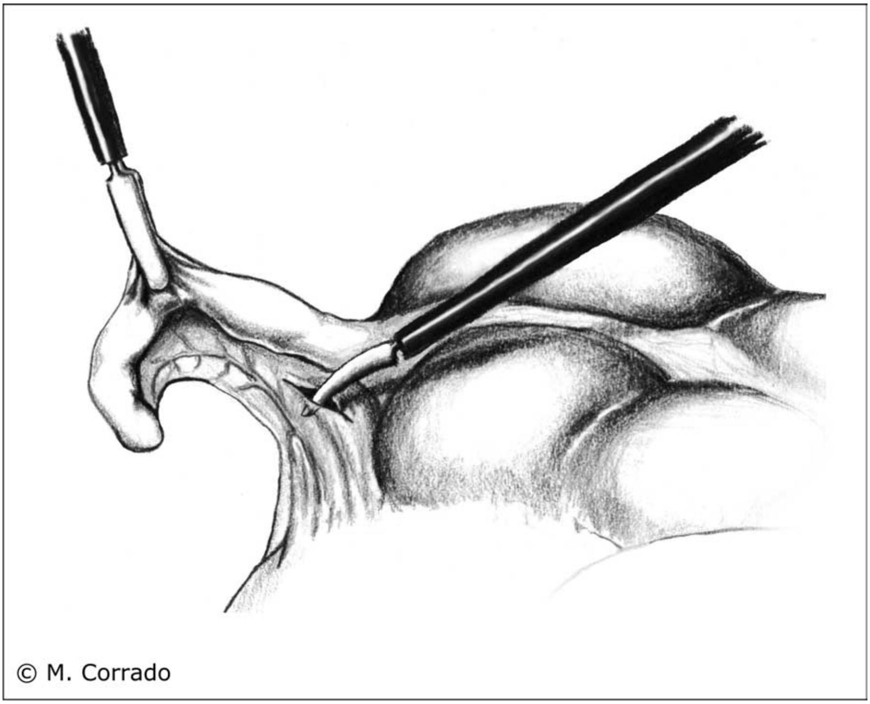

FIG 4. Dissection of the mesoappendix to create a window near the base of the appendix.

an atraumatic grasper (Fig 3). Using a curved dissector a mesenteric window is created in an avascular area of the mesentery near the base of the appendix (Fig 4). The mesoappendix can be divided with ultrasonic energy, a laparoscopic linear stapling device, or with surgical clips. We prefer to use a linear stapling device with a 2.5 mm staple cartridge to assure hemostasis (Fig 5). Once the mesoappendix is divided, any attachments at the appendical base are dissected to clearly identify the site of transection. The appendix is transected with a laparoscopic linear stapling device with a 2.5 mm staple cartridge removing a short cuff of cecum to ensure complete removal of the appendix (Fig 6). An alternative technique of performing the appendectomy involves placing 3 ligating loops at the base of the appendix and dividing the appendix between the distal and the middle loop. The appendiceal stump does not need to invaginated. The appendix is placed into a specimen bag and retrieved from the intra-abdominal cavity via either the umbilical or the suprapubic trocar site.

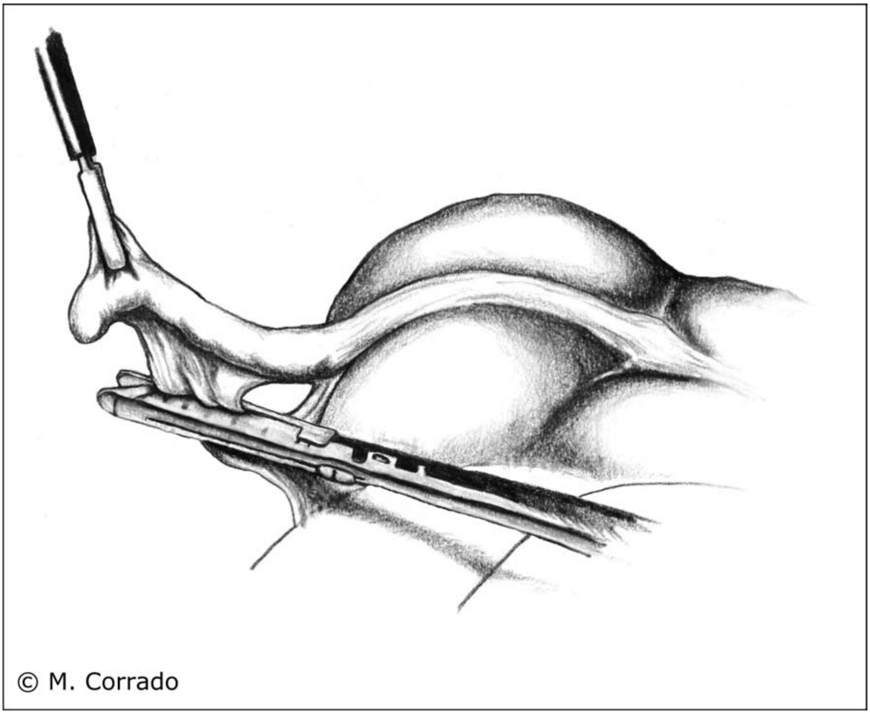

FIG 5. Transection of the mesoappendix with a linear stapling device.

Results of Laparoscopic Appendectomy

Multiple prospective, randomized trials (Table 4) and meta-analyses have been conducted to assess the value of laparoscopic appendectomy compared with open appendectomy.[114-127] There is some variability in the results of these studies, but several generalizations can be drawn. Laparoscopic appendectomy was associated with longer operative times, usually about 15 to 20 minutes. Conversion rates to an open approach ranged from 5% to 25%, often depending on the presence of perforation or complicated appendicitis. Hospital length of stay was either not significantly different or favored a laparoscopic approach. In studies that demonstrated a significantly reduced length of stay for laparoscopic appendectomy, the advantage was typically 1 day. Most investigators observed a faster return to normal activities by approximately 5 to 7 days in patients who underwent laparoscopy. The results for overall complication rates were decidedly mixed, with no clear advantage for either

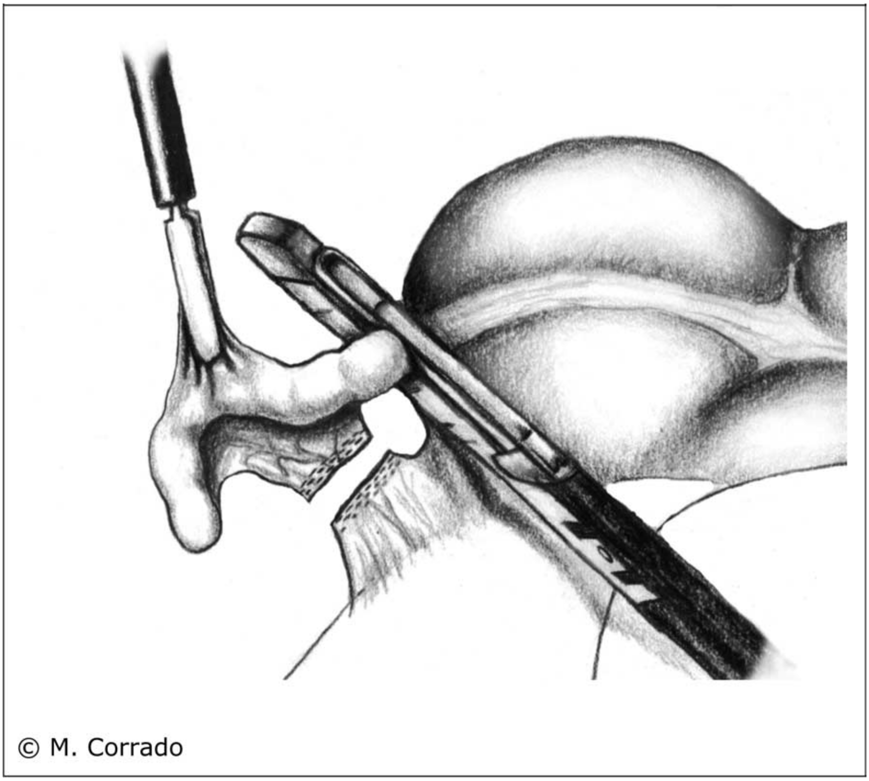

FIG 6. Transection of the appendix with a linear stapling device.

approach. However, most studies demonstrated a reduced wound infection rate for patients who underwent laparoscopic appendectomy.

Several studies have accomplished cost comparison and the results are mixed.[114,116,122] Some have demonstrated cost savings with laparoscopic appendectomy due to the reduced length of stay whereas others suggest that laparoscopic appendectomy is associated with higher costs due to longer operative times and equipment costs. In 1 study of a large, nationwide administrative database, there was no significant difference in cost between the 2 approaches.[128]

Despite the rapid acceptance of laparoscopic cholecystectomy and other laparoscopic intra-abdominal procedures, there is no clear consensus regarding the use of laparoscopic appendectomy. The results of open appendectomy are reliable across the spectrum of hospitals and associated with highly satisfactory outcomes. The proponents of open appendectomy interpret the results of recent studies with the admonition that statistically

TABLE 4. Selected randomized trials of laparoscopic versus open appendectomy

Reference	n		OR Time (min)		Conversion rate (%)	LOS (days)	
	L	O	L	O		L	O
Long et al (2002)	93	105	107	91	16	2.6	3.4
Pedersen et al (2001)	282	301	60	40	23	2	2
Ozmen et al (1999)	35	35	28	38	—	1.6	3.7
Hellberg et al (1999)	244	256	60	35	12	2	2
Heikkinen et al (1998)	19	21	31	41	5.3	2	2
Klinger et al. (1998)	87	82	35	31	0	3	4
Reiertsen et al (1997)	42	42	51	25	0	3.5	3.2
Minne et al (1997)	27	23	82	67	7.4	1.1	1.2
Macarulla et al (1997)	106	104	55	45	8.3	3.4	4.8
Ortega et al (1995)	167	86	68	58	6.5	2.6	2.8

L = Laparoscopic appendectomy; O = open appendectomy; OR = operating room; RTNA = return to normal activity; LOS = hospital length of stay.

significant differences are not necessarily clinically significant and in the case of appendectomy, there is no clear indication that laparoscopy is the approach of choice. The proponents of laparoscopic appendectomy point out that multiple studies demonstrate an advantage in reduced morbidity and length of stay. Although the differences may not appear clinically significant to some, they are significant in light of the large number of patients who undergo the procedure annually in the United States. It is possible that eventually laparoscopic appendectomy may become the procedure of choice for appendicitis, but for the near future, open appendectomy is likely to predominate.

Surgical Audit and Outcomes

There have been several large administrative database reports on appendectomy that provide valuable insight into the current state of surgery for appendicitis. Guller and colleagues[129] studied 43,757 patients using the Nationwide Inpatient Sample. This sample is derived from the Healthcare Cost and Utilization Project, which contains more than 8 million procedures in 1997 from 1000 nonfederal, community hospitals in 22 states. The average age of patients was 30.7 years and the male:female ratio was approximately 3:2. Perforated appendicitis was present in 29.2% and appendiceal abscess was present in 12.7% of patients. The mortality rate was 0.24%, the complication rate was 10.7%, and the wound infection rate was 1.7%. In part, this study was designed to assess laparoscopic vs. open appendectomy. Laparoscopic appendectomy was performed in 17.4% of patients. The investigators found that after risk

TABLE 4.

RTNA		Wound Infection (%)		Complications (%)	
L	O	L	O	L	O
14	21	18.2	16.2	28	28
7	10	2.8	6.9	10.3	9.0
—	—	5.7	8.6	18	52
13	21	—	—	4.9	6.2
10	19	0	4.8	—	—
14	15	6	7	—	—
15	19.7	2.4	0	40.5	28.6
14	14	—	—	18.5	4.3
—	—	0.9	4.8	5.6	7.7
9	14	2.4	12.8	4.2	20.9

adjustment, laparoscopic appendectomy was associated with a reduced infection rate and reduced overall complication rate. They also found that median length of hospital stay for laparoscopic appendectomy was 2.06 days compared with 2.88 days for open appendectomy ($P < 0.0001$).

Nguyen and colleagues[128] studied outcomes of 60,236 patients who underwent open (68%) or laparoscopic (32%) appendectomy from 1999 to 2003. These patients were registered in the University Health System Consortium Clinical Database, a collection of discharge data from 129 academic health centers and affiliate community hospitals across the United States. The intent of their study was to compare the outcomes of laparoscopic vs. open appendectomy. The noteworthy findings were that laparoscopic appendectomy was associated with a shorter length of hospital stay, lower rate of 30-day readmission, and lower rate of overall complications.

Both of these studies suggest an advantage in outcomes for laparoscopic vs. open appendectomy. Although both investigator groups attempted risk adjustment in their analyses, a retrospective review of large administrative database results must be interpreted with caution. However, the collective results of both studies indicate that regardless of approach, appendectomy is currently performed with negligible mortality, an overall complication rate less than 10%, a wound infection rate less than 2%, and an average hospital length of stay of 2 to 3 days.

Margenthaler and colleagues[135] sought to define risk factors for adverse outcomes in patients undergoing surgery for appendicitis in the Department of Veterans Affairs Medical Centers. All patients who underwent surgery for appendicitis from 1991 to 1999 and were registered in the National Surgical Quality Improvement Program were selected for study.

There were 4163 patients who were identified. The 30-day mortality rate was 1.8%. The 30-day morbidity rate was 16% and the most frequent complications were prolonged ileus, failure to wean from the ventilator, pneumonia, and both superficial and deep wound infections. Preoperative risk factors that predicted a high risk of mortality included “completely dependent” functional status, bleeding disorder, steroid usage, and current pneumonia. A greater than 10% weight loss in the preceding 6 months and “moribund” American Society of Anesthesiologists (ASA) classification were also associated with a high risk of complications. Although the patient population that they studied is not representative of patients who undergo appendectomy in general, their findings underscore that appendectomy is not a routine procedure in older patients and is associated with significant mortality and morbidity, especially in the presence of the aforementioned risk factors.

Summary

Appendicitis is a common condition, occurring in 250,000 patients every year in the United States and accounting for an estimated 1 million hospital days per year. Acute appendicitis is the most common cause of an acute abdomen that requires surgical treatment. A diagnosis can be made on clinical grounds in most patients, but imaging studies are useful in patients with equivocal findings. Prompt diagnosis and surgical treatment are the cornerstones of therapy to preempt progression of the disease to perforation that is associated with increased morbidity. Both laparoscopic and open appendectomy are viable surgical options, with most recent studies suggesting more favorable outcomes with a laparoscopic approach. In practice, the choice for either is usually based on the expertise of the surgeon along with the availability of hospital resources.

The precise etiology of appendicitis is unclear. Accordingly, surgeons will continue to evaluate and treat patients with appendicitis for the foreseeable future. The liberal use of imaging modalities to improve the accuracy of preoperative diagnosis and minimize the negative appendectomy rate is a trend that is likely to continue. Operating on a patient without an imaging examination may often be appropriate, but will be the exception, not the rule. Finally, the trend toward laparoscopy is relatively slow compared with its adoption for the surgical treatment of other diseases, but inexorable. It would not be surprising if laparoscopic appendectomy becomes the most popular treatment for appendicitis in the future.

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