



# Management of appendicitis: appendicectomy, antibiotic therapy, or both?

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**Introduction:** Appendicitis is a global disease with an incidence of 7–12% in the population of the USA and Europe but is low and rising in the developing world. It is the most common acute general surgical emergency, but as no investigation is accurate, the diagnosis has to rely on clinical symptoms and signs and, thus, frequently misdiagnosed. The aim of the study was to debate the arguments for managing appendicitis (operative, nonoperative, or both).

**Patients and methods:** Electronic searches of the MEDLINE (PubMed) database, Cochrane Library, and Science Citation Index were performed to identify original published studies on appendicitis and the pre-COVID-19 (coronavirus disease 2019) and post-COVID-19 management. Relevant articles were searched from relevant chapters in specialized texts, and all have been included.

**Discussion:** There are indications for operative (surgery), nonoperative (antibiotics), or both in the management of acute appendicitis. Although laparoscopic appendicectomy is becoming the gold standard of treatment, knowledge of the pros and cons of this approach versus the open approach is important. The controversy in the management of the appendix mass/abscess between an expedient appendicectomy or a combination of conservative management (antibiotics) and interval appendicectomy remains.

**Conclusion:** Laparoscopic appendicectomy is becoming the gold standard for the treatment of appendicitis. However, the advantages of the innovations in minimally invasive and endoscopic surgery are unlikely to render formal open appendicectomy obsolete. Nonoperative management with antibiotics may suffice in selected cases with uncomplicated appendicitis. It is imperative that patients are counseled appropriately if primary antibiotic treatment is to be routinely offered as first-line therapy.

**Keywords:** appendicectomy, appendicitis, antibiotic therapy, interval appendicectomy

## Introduction

Appendicitis is the most common acute intra-abdominal emergency, and the presentation varies from subclinical and self-resolving to overwhelming sepsis and death. As no investigation is accurate, the diagnosis has to rely on clinical symptoms and signs or clinical scoring systems and, as a result, frequently misdiagnosed. Blockage of the appendiceal lumen by faecolith is assumed to be the mechanism in many cases. If appendicitis is untreated, the progression of the disease depends on the interplay of several factors (Table 1). Progression from intramural inflammation through the luminal obstruction to gangrene and perforation is not inevitable. Inflammation follows a variable

pattern which may be aborted or delayed by host defenses at any time<sup>[1]</sup>. Children less than 3 years of age have an 80% perforation rate because of delay in diagnosis and host defenses, including the omentum, are not fully developed<sup>[2]</sup> Appendicitis has a more rapid course in the elderly because of atherosclerosis, gangrene, and perforation are common<sup>[3]</sup>. The perforation rate of 25% in patients with a history of pain of less than 24 h is not much lower than the 35% rate of perforation in patients with a history of over 48 h<sup>[4]</sup>. These may indicate that uncomplicated and complicated appendicitis are distinct diseases. An alternative outcome is that the appendix becomes surrounded by a mass of omentum which walls the inflammatory process and prevents inflammation from spreading to the abdominal cavity (appendix mass), yet the resolution of the condition is delayed. If the appendix becomes walled off by the omentum but has perforated, an abscess will develop localized to the periappendiceal region in the right paracolic gutter or the subcecal area of the pelvis. However, there is no evidence to indicate the proportion of patients likely to

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**Table 1**

### Factors determining progression of inflammation in appendicitis

Systemic	Local
Extremes of age	Site of appendix
Coincidental systemic disease (e.g. rheumatoid arthritis, morbid obesity)	Speed of development of inflammation
Immunosuppression (e.g. as a result of HIV/AIDS, corticosteroids, chemotherapy)	Presence of faecolith
	Vascular impairment
	Mobility of omentum (less in children)

develop diffuse sepsis because the antibiotic treatment alters the pattern of disease by replacing the risks of perforation with the lesser risk associated with surgery. In addition, there is inter-individual variation between the host (patient) defense mechanisms and the disease<sup>[4,5]</sup>. The indications for operative (surgery), nonoperative (antibiotics), or both in management are discussed. Laparoscopic appendectomy has become the gold standard of treatment, but nonoperative management with antibiotics may suffice in selected cases with uncomplicated appendicitis. The management of the appendix mass/abscess may entail an expedient appendectomy or a combination of conservative management and interval appendectomy.

### Arguments for primary antibiotic treatment

The fact that only few patients progressed to the potentially lethal complications provides the argument for conservative antibiotic treatment. The role of antibiotic treatment in early uncomplicated appendicitis using broad-spectrum third-generation cephalosporins such as *i/v* ceftriaxone and *i/v* metronidazole for anaerobes, is well known<sup>[5-7]</sup>. Typically, patients who develop appendicitis in isolated settings (e.g. on ships, submarines, saturation dives, or in remote areas) are treated conservatively with antibiotics, and, in most cases, the appendicitis is resolved without surgery<sup>[5,6]</sup>. There is a reasonable body of evidence to support nonoperative treatment of appendicitis predating the coronavirus disease 2019 (COVID-19) pandemic with low failure rates and minimal recurrence, especially in the 5–16 year olds<sup>[5,7-18]</sup>. Conservative treatment with later drainage of any abscess had been the standard, although diffuse peritonitis was usually fatal. Surgery for appendicitis only evolved when the mortality associated with perforated appendicitis was significant (>5%). The mortality was associated with the age of the patient and delayed diagnosis resulting in perforated appendicitis<sup>[1-6]</sup>. In addition, advances in interventional radiological techniques for peritonitis have also significantly reduced the morbidity and mortality of physiologically severe complicated abdominal infections, including appendix abscesses<sup>[19]</sup>. Salminen *et al.* demonstrated in 257 patients between 16 and 60 years old in Finland that by using *i/v* ertapenem for 3 days followed by 7 days of oral levofloxacin and metronidazole, 75% required no surgery in 1 year and there was no progression to complicated disease. The recurrence rate was 27% (1 year), 34% (2 years), 35% (3 years), 37% (4 years), and 39% (5 years)<sup>[12]</sup>. Thus, even with long-term follow-up, the initial treatment with antibiotics is still a safe alternative approach to appendectomy. Recent studies, particularly during the COVID-19 lockdown, have re-demonstrated the fact that although there is a 20% risk of recurrent attacks, simple appendicitis may be treated with antibiotics only<sup>[6,20]</sup>. This may explain the decreased incidence of acute appendicitis during the COVID-19 pandemic following antibiotic treatment for right iliac fossa pain. However, there was a higher incidence of complicated appendicitis in patients who underwent appendectomy when compared to those in the prior year, which mostly must have been due to the ‘stay at home’ message<sup>[20,21]</sup>. Although there is greater reliance on computer tomography imaging, it was suggested as a reasonable alternative option for carefully

selected patients in the early stages of the COVID-19 pandemic<sup>[20,22]</sup>. Antibiotics, as definitive therapy, may act in synergy with the host defense mechanisms and thus be most useful in the acute catarrhal phase of appendicitis, which usually spontaneously resolves<sup>[5,23]</sup>. Thus, uncomplicated appendicitis may be a distinct entity. Primary antibiotic therapy avoids the complications of open appendectomy and the generally 10% negative appendectomy rates. The use of antibiotics may also convert acute appendicitis into a semiselective procedure. During the ‘lockdown’ period of the COVID-19 pandemic, it allowed time to obtain the COVID-19 test result and, by so doing, excluded COVID-19 as the cause of the abdominal symptoms, which is an important differential diagnosis of appendicitis<sup>[20,22,24,25]</sup>. However, a much more recent study in Amsterdam showed that about half of the average population preferred antibiotics over surgical treatment of uncomplicated appendicitis and was willing to accept a high recurrence risk to avoid surgery initially. Participants who preferred surgery tolerated only a very low recurrence risk with antibiotic treatment<sup>[26]</sup>. This was similarly reproduced in the USA<sup>[27]</sup>. It is also interesting to note that the effects of widespread antibiotics, such as drug resistance and opportunistic infections, both the individual patient and the population at large, are poorly considered in the literature<sup>[28,29]</sup>.

### Argument for appendectomy

Although it is clearly advantageous to spare patients from unnecessary surgery, the morbidity and mortality from failing to diagnose appendicitis until perforation has occurred are greater than that associated with the removal of a normal appendix<sup>[4,5]</sup>. Thus, early surgery for all patients with suspected appendicitis gradually became the definitive method of preventing severe peritoneal sepsis. It is important to note that the earlier optimism regarding the benefit of antibiotic therapy for uncomplicated acute appendicitis was not demonstrated in Herrod *et al.*<sup>[30]</sup> meta-analysis of further large trials. They showed a primary antibiotic treatment efficacy of 63% at 1 year compared with an efficacy of 92% for appendectomy. Antibiotic therapy carries a significantly increased risk of readmissions, complicated appendicitis following treatment failure or recurrent appendicitis. It is imperative that patients are counseled appropriately if primary antibiotic treatment is to be routinely offered as first-line therapy. Since the incidental removal of an inflamed appendix through a groin incision for a scrotal hernia by Amyand in 1735 and the first appendectomy for appendicitis by the French surgeon Mesteivier in 1759, open appendectomy through a standard right iliac fossa (modified McBurney’s gridiron/Lanz) incision at the earliest possible time after the onset of symptoms is the standard treatment of choice. Diffuse peritonitis, which has been diagnosed preoperatively, should be dealt with by formal laparotomy to allow thorough peritoneal toilet and lavage<sup>[4,31,32]</sup>. Modern minimally invasive techniques have equal efficacy, minimal postoperative pain, decreased negative appendectomy rate, decreased surgical site infection, and early return to normal activities. They include conventional laparoscopic appendectomy, single incision (port) laparoscopic appendectomy, and transluminal [Natural orifice transluminal endoscopic surgery (NOTES)] appendectomy via a transgastric, colonic, or vaginal

approach<sup>[33,34]</sup>. NOTES have the advantage of markedly decreasing surgical site infection, hernias, and postoperative pain<sup>[35,36]</sup>. However, the cost and technical expertise required in these novel techniques, including the numerous limitations of NOTES, should be taken into consideration. Recent guidelines stipulate that appendicectomy should be performed laparoscopically unless this is contraindicated<sup>[6,31]</sup>. Although conventional laparoscopic appendicectomy has become the gold standard, these innovations are unlikely to render formal open appendicectomy obsolete<sup>[33]</sup>. In 2012, in the UK, one-third of patients underwent open appendicectomy<sup>[37]</sup>. Open appendicectomy provides all the valuable skills of abdominal incision, dissection, resection, and abdominal wall closure required by a trainee surgeon. The skills will be useful following conversion of laparoscopic to open surgery<sup>[37,38]</sup>. However, unlike laparoscopic surgery, open procedures typically commit the surgeon to proceed to appendicectomy even if the appendix is macroscopically normal on visualization. Thus, the increased take-up of laparoscopy would hypothetically decrease the negative appendicectomy rate<sup>[31,33,34]</sup>.

### Arguments for interval appendicectomy

The results of the surgical treatment of appendicitis have improved dramatically during the past decades because of the introduction of more effective antibiotics against both aerobes and anaerobic organisms if peritonitis develops. Prophylactic use of antibiotics (short course *i/v* metronidazole) perioperatively halved the incidence of surgical site infection with important clinical and economic consequences<sup>[39]</sup>. A single perioperative dose of antibiotic is sufficient for low-risk cases, but a therapeutic 3-day course is necessary when peritonitis is present. There is controversy in the management of the appendix mass/abscess. Some authors believe that the condition is best managed conservatively as the risk of perforation has passed, and the removal of the appendix at this late stage can be difficult. Patients with a mass which does not diminish within a short time should be submitted to full intestinal investigations. In older patients, a diagnosis of carcinoma of the cecum, which has obstructed the appendix, must be considered and excluded by a computed tomography scan or colonoscopy<sup>[3]</sup>. However, conservative management of an appendix mass risks a 30% recurrence of acute inflammation<sup>[4,32]</sup>. Subacute obstruction may occur and the appendix mass may be confused with a cecal carcinoma in the elderly, Crohn's disease, ileocecal tuberculosis, or an ovarian tumor. Appendix abscess is characterized by a swinging pyrexia, tachycardia, undulating mass and being systemically unwell. It is best treated by surgical intervention through a standard right iliac fossa incision. The residual necrotic appendix is usually found and resected. Tissues and organs adjacent to the abscess cavity will be friable with a tendency to bleed and should be handled with care. In the author's experience, differentiating between a preoperative palpable phlegmonous mass from an abscess is not a practical problem because surgery is the correct management for both. In addition, a mass is often detected only after the patient has been anaesthetized and paralyzed. Such a policy renders any debate on interval appendicectomy redundant<sup>[31,32]</sup>. The operation, which may be an appendicectomy, an ileocecal resection or a hemicolectomy if indicated during the first admission, is expeditious and safe, provided steps are taken to minimize postoperative

sepsis. An expedient appendicectomy is the practice of the author. The serious consequences of missing a carcinoma in the elderly patient or other pathological lesions such as Crohn's disease, ileocecal tuberculosis, and schistosomiasis are abolished<sup>[3,4,32,40]</sup>. The controversies with conservative antibiotherapy and drainage of appendix abscess include the optimal timing of the interval appendicectomy, which is usually 6–12 weeks<sup>[25,41,42]</sup>. There are reports of recurrent appendicitis and increased neoplasms within that interval. Reoperation is associated with a significant incidence of postoperative complications, and most patients are not treated by operation unless they develop further trouble. There is no evidence of the benefit of lavage over suction alone for postoperative infective complications<sup>[43]</sup>, and the insertion of a drain in the abscess cavity is controversial. In fact, there is a significantly longer operative time and a higher postoperative complication rate (surgical site infection/intra-abdominal abscess) in the irrigation group than in the suction-only group after laparoscopic appendicectomy for uncomplicated appendicitis<sup>[44]</sup>. Peritoneal and wound drains are of no use. Delayed or nonclosure of the skin is not necessary. Apart from the problem of the drain type (open vs. close), the size of the abscess cavity (small vs. large) and the removal time (early vs. late), abdominal drains may cause more problems than they solve. The adhesions that occur in the healing process of the stump or general peritoneal cavity will attract the peritoneal drain (foreign body), prevent adhesions to vascular structures and physically damage the small bowel or stump, causing an enterocutaneous fistula<sup>[45,46]</sup>. Drains can mislead the surgeon as they easily get blocked. They are portals for the entry of exogenous bacteria causing surgical site and wound infection<sup>[45]</sup>. Large bore drains are useful in sepsis following inadequate peritoneal lavage in generalized peritonitis or residual sepsis but should be placed in the appropriate dependent areas of the abdominal cavity such as the paracolic gutters, pelvis away from the intestine<sup>[47]</sup>.

### Postoperative complications

Postoperative peritoneal sepsis may be diffuse and result in intestinal obstruction or a localized, usually pelvic, abscess requiring protracted convalescence. Both complications are the result of poor surgical technique. Untreated pockets of infected peritoneal fluid and failure to remove faecoliths cause postoperative sepsis. If obstruction and sepsis persist, reoperation is indicated. Leakage from the stump of the appendix is an uncommon but serious complication as it causes a high-pressure, large output fecal fistula which will require an ileocecal resection or a right hemicolectomy<sup>[48]</sup>. Although pelvic abscesses could be drained via the rectum, other well-defined abscesses should be drained percutaneously under radiological or ultrasonic guidance followed by a microbiologically-guided therapeutic course of antibiotics for 2 weeks<sup>[19,47]</sup>. Ruptured appendicitis has been implicated in causing scarring, which can lead to infertility and/or ectopic pregnancy. Appendicectomy is not associated with future infertility in women from scarring, but with an increased risk of ectopic pregnancy<sup>[49]</sup>. Although, a nationwide cohort study in Finland in 2021 showed no association between complicated appendicitis on the risk of later *in-vitro* fertilization treatment requirement and ectopic pregnancy<sup>[50]</sup>, the argument for early laparoscopic appendicectomy in childbearing age to diagnose

and treat appendicitis or complicated salpingitis is still favoured over nonoperative management.

## Conclusion

Laparoscopic appendectomy is becoming the gold standard for the treatment of appendicitis. The advantages of the innovations in minimally invasive and endoscopic surgery are unlikely to render formal open appendectomy obsolete. Nonoperative management with antibiotics may suffice in selected cases with uncomplicated appendicitis. It is imperative that patients are counseled appropriately if primary antibiotic treatment is to be routinely offered as first-line therapy. The controversy in the management of the appendix mass/abscess remains.

## Ethical approval

The research did not involve patients directly. Thus there was no need for ethical approval.

## Consent

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## Author contribution

E.P.W.: main author and contributed to the conception, design, and literature search; A.V.Z.: contributed to the literature search; E.N.: contributed to the literature search.

## Conflicts of interest disclosure

There are no conflicts of interest.

## Guarantor

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