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# Pathogenic Bacteria Associated With Acute Appendicitis: A Review Article

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**ABSTRACT:** Acute appendicitis is one of the most common abdominal emergencies, yet the cause is still not clearly understood. The most accepted theory is based on luminal obstruction, but obstructive fecaliths are found in only a portion of the patients. In fact, the bacterial etiology of appendicitis may be more common than fecal-foreign body. Literature was searched for studies that isolated bacteria from the appendix using either culturing techniques or molecular techniques and were case-control in nature. The main scope of this review is to provide an overview of the studies conducted regarding the role of bacteria in the causation of appendicitis, as well as to review recent molecular studies.

## 1. INTRODUCTION

In a modern life with rapidly changing bacterial resistance and surgical techniques, the picture of appendicitis has changed. Pathogenic bacteria associated with appendicitis in the previous review article might have changed. The Western Surgeon Society has proposed antibiotic treatment as the first-line treatment for appendicitis. The author concluded that antibiotic treatment could be an alternative when the patient or institution prefers conservative treatment. Otherwise, acute appendicitis is still the most common situation today in an emergency visit. A histopathological report after appendectomy and colonization of bacteria from appendectomy might support the treatment of acute appendicitis in each center (Hansson et al., 2012). The author aims to review pathogenic bacteria associated with appendicitis in the above specimens and compare them with the previously published data.

The authors searched for articles related to "bacterial colonization of appendicitis" and "pathogenic bacteria of appendicitis from the histopathological analysis of the appendix," which were published from the year 2007 in the PubMed database. Five articles in four studies were summarized from a review of these studies. The rate of incidence of appendicitis was 22.72, 13.57, and 2.92 per 10 000 population per year. It was concluded that the most common pathogenic bacteria related to acute appendicitis were Escherichia coli (38.7%−86.7%) followed by Bacteroides species (10.3%−21%). E. faecium and E. faecalis rates were increasing in the last decade in North America. It can be an interesting portion for a surgeon to propose an antibiotic with coverage in the combination of the two enterococcal organisms for a patient suspected of appendicitis. In some papers, the concern of compounds of pathological findings and bacterial colonization might increase the severity of acute appendicitis was proposed (Chen et al., 2012)

## 2. AIM AND SCOPE OF THE REVIEW

The main scope of this review is to provide an overview of the studies conducted regarding the role of bacteria in the causation of appendicitis, as well as to review recent molecular studies. Acute appendicitis is one of the most common abdominal emergencies, yet the cause is still not clearly understood. The most accepted theory is based on luminal obstruction, but obstructive fecaliths are found in only a portion of the patients. In fact, the bacterial etiology of appendicitis may be more common than fecal-foreign body. Literature was searched for studies that isolated bacteria from the appendix using either culturing techniques or molecular techniques and were case-control in nature.

## 3. APPENDICITIS: ETIOLOGY AND PATHOPHYSIOLOGY

Appendicitis is the most common cause of an acute abdomen and is defined as the inflammation of the vermiform appendix. It can be classified as acute, recurrent or chronic, or in the form of a mass or complicated (like ruptured appendix), and subacute. The exact pathophysiology of appendicitis is still under debate between fecalith and infection, and some of the recent studies show that appendicolith is seen in fewer cases of acute appendicitis, and they are more likely to be on the right side of the abdomen instead of the left side. For years, the misleading idea of appendicitis was conceived as a disease that results from the obstruction of its lumen with fecal materials or appendicoliths. According to this, the condition results in the rise of intraluminal pressure, the decline of blood flow, and the weakening of defense mechanisms within the wall. As a consequence of a decrease in the defense mechanisms of the ileocecal area, the bacteria in the lumen would penetrate the mucosa and cause inflammation. However, recent studies have refuted this idea (Vaos et al., 2019).

Several hypotheses have been proposed to identify the underlying mechanism of appendicitis, although all of them converge towards the involvement of bacteria. People have different sizes of appendices, and in most patients, fecal materials are accumulated in the appendix. Hence, the frequently asked question is why there are not historically significant data available on appendicitis, and why do we rarely encounter appendicitis in patients who have complicated fecaloma without significant inflammation? The bacteriologic pathology is then believed to be the missing part of the puzzle. Several studies carried out on patients who underwent appendectomy, whether they showed an acute inflammatory process or were appendicitis-free, identified the presence of bacteria. In appendicitis, and even in patients with fecaliths on colonoscopy, there is no definite bacterial type linked to acute appendicitis. Some studies demonstrated that viridans streptococci and Enterobacteriaceae were the predominant remaining bacterial types (Ucar Karabulut et al., 2022).

### 3.1. PATHOPHYSIOLOGY OF APPENDICITIS

The most precise portion of the appendicitis pathophysiology happens to be one of the most historically mysticated. Appendicitis is recognized whereby a combination of intra-luminal obstruction, mucosal barrier disruption, and secretions are overproduced distally, causing subsequent inflammation. The theory of obstruction as the initiator of appendicitis has been proposed in the early 1800s by two multiple groups, both disdaining or neglecting experimental evidence and subsequently falsifying each other's work. Internal hernias, drug bezoars, and retained foreign material are all potential sources of obstruction. The more common processes identified to be involved in the overgrowth of secretions; however, some authors hesitate to employ the term obstruction. Short acute aperistaltic segments of the appendix are frequently present, and the fecalith or inflamed appendiceal orifice can limit motility, infold luminal structures such as lymphoid follicles, and partially obstructie opening. Regardless of the definition, this mechanical event is thought to increase intramural and intraluminal pressures, leading to vascular congestion, ischemia, and subsequent transmural inflammation. Involving the hollow viscus: dilation-leading-to-thickening models, on the other hand, vary in their mechanisms of intraluminal pressure elevation. Inflammation-producing dilation is attributed to drainage obstruction rather than the more active inflammation; nonetheless, there is still redundancy in the initiating processes. The supposed role of serosa involved in peroral wound contamination has been challenged, but the 'sufficient' vessel occlusion leading to gut ischemia is crucial within such diversion models (Nguyen et al., 2023).

The precise role of bacteria in the appendicitis pathway is ill-defined, but their participation has likely been underestimated historically. Gastrointestinal ailments unlikely to be influenced by bacterial growth include mucosa-driven dysmotilities, secretory imbalances such as hyperchlorhydria, and bile acid changes. Gastroenteritis and other extrinsic or systemic factors are largely managed by the time they reach the cecum. The anti-pathogen layer of glycoproteins and immunoglobulins generally prevents enteric bacterial penetration, although some processes may promote this. For instance, increased apoptotic bodies were present in the base of crypts of unprepared colorectal mucosa and serving bacterial taxis in the normally prepared mucosa. Transepithelial edema may also be the consequence of mucosal shedding and/or neutrophilic inflammation, leading to increased polyethylene glycol flux in histamine-stimulated guinea pigs. Mucus clearance of inflammatory cells is best characterized in the respiratory system, but depicted in gut images. Potential vaso- and hence serosal response perturbant-in-ulcerative-coli properties facilitate potential mucus penetration. Furthermore, once in the muscle, bacterial signaling among smooth endoplasmic reticulum and other peristaltic cell influencing S-nitrosylation has been proposed. Thus, while there remains no direct evidence for the role of enteric bacteria in appendiceal pathophysiology, there is still circumstantial reasons to believe that obstruction, inflammation, and bacterial seeding are robust during appendicitis (Carr, 2000).

## 4. COMMON PATHOGENIC BACTERIA IN APPENDICITIS

Escherichia coli and Bacteroides fragilis are the most commonly encountered pathogenic bacteria in appendicitis, irrespective of the setting. The former, along with Aeromonas hydrophila, are more common in developing countries because they have evolved to counter so many of the conventional antibiotics. Some studies found that the most frequent aerobic bacteria were E. coli, which was found in 85.47% of patients who had confirmedly diagnosed acute appendicitis. Less frequently reported bacteria have been: Pseudomonas aeruginosa (18 out of 117), Enterococcus spp. (21 out of 117), Streptococcus spp. (29 out of 117, and Klebsiella pneumoniae (30 out of 117), as reported by Chen et al. (2012). Another study conducted by Bazzaz et al. (2018) found that the pathogenic bacteria accountable for appendicitis, include: Staphylococcus xylosus (2%), Staphylococcus epidermides (2%), Enterococcus faecium (1.9%), Serratia fonticola (2%), Enterrobacter cloacae (2%), Pseudomonas aeruginosa (3.9%), Raultella terrigena (3.9%), Citrobacter youngae (3.9%), Klebsiella pneumonia (5.9%), Enterococcus faecalis (5.9%), Escherichia coli (66.7%).

### 4.1. ESCHERICHIA COLI

Escherichia coli (E. coli) is a common member of the normal lower sigmoid colon flora in humans, found in more than two-thirds of the global population and also the major organism of the gastrointestinal area. It is estimated that 95-99% of normal human fecal flora comprises E. coli. Although most E. coli serotypes are commensals and are commonly present in the human host, many are found to be associated with infections such as bacteremia, urinary tract infections, meningitis, and septicemia. There are at least six pathogenic categories of E. coli with strains variously referred to as "uropathogenic," "enterotoxigenic," or "shiga-toxin-producing" according to a wide variety of virulence mechanisms employed by these microorganisms. Certain types of E. coli strains are recognized to cause peritonitis, either directly or indirectly via perforation of intraabdominal hollow viscus (Ruff et al., 1994).

In clinical circumstances of left colonic adenocarcinoma, terminal ileal or appendicular carcinoid, localized peritonitis, or appendiceal mucocele produces a sequestered microenvironment for prolonged bacterial growth, which can eventually lead to the development of acute appendicitis. Infections can be of diverse etiology, ranging from fungal candidiasis to viral Herpes Simplex infection, Actinomycosis, Mycobacterium, Streptococcus, and Helicobacter. E. coli is the commonest member of the colonic flora, with an infrequent tolerance to thermodynamic properties of the mucoid environment and is restricted from accessing the appendiceal lumen. For this study, the prevalence of microbes in appendicitis that was included in our research has been described earlier (Rakovich & Larue, 2007).

### 4.2. BACTEROIDES FRAGILIS

B. fragilis is an anaerobic, non-spore-forming bacterium that is often found in the colon and is responsible for bile resistance and mucinase production. This makes B. fragilis a leading cause of intra-abdominal infection with greater virulence and mortality from peritonitis and abscess formation. It has been found to be present in 25-80% of patients with or without perforated appendicitis. It was also shown that rates of perforation were significantly higher in patients with appendicitis due to B. fragilis and E. coli. Related virulence factors include capsular polysaccharide, which is partially responsible for preventing phagocytosis and endotoxin production with a pro-inflammatory effect mediated by blood macrophages and suppressed lymphoproliferative response role of platelets. This polymicrobial origin was confirmed after surgically treating 134 patients with perforated appendicitis, in whom Escherichia coli was present in 92.5% of the patients and B. fragilis in 17.9% of the cultures, which was a major cause of perforation (Pieper et al., 1979).

Bacteroides fragilis has been identified as part of the fecal flora and is associated with the development of appendicitis, with a prevalence of 17.3% according to a prospective cohort study from Asia. However, the association of Bacteroides fragilis and appendicitis has not been established as the stool of the Bacteroides fragilis-infected patients with high B. fragilis count exceeds the minimum criteria for developing appendicitis (Téoule et al., 2020).

### 4.3. ENTEROCOCCUS SPECIES

Enterococcus is an oxalidase and catalase negative, non-sporing, and non-motile Gram-positive coccus. Enterococcus exhibits a polymorphic cell grouping but can form short chains and pairings. They are facultative anaerobes with a respiratory metabolism possessing an F1F0 proton-translocating ATPase (ATP synthase) making them able to grow in host tissues in response to a gram-positive human antimicrobial peptide LL-37. E. faecalis can also be described phenotypically by biochemical tests, showing a negative result for bile and high salt but a positive result for sorbitol, PGM, and pyroglutamate a-reductase, during a carbohydrate fermentation test E. faecalis is positive for mannitol and sorbitol but negative for arabinose and trehalose also showing negative growth at both 10°C and 45°C. With current advances, most if not all Enterococcus species are involved in human disease including skin ulcers, infected surgical wounds and nosocomial urinary, pelvic, and biliary (Zachos et al., 2023).

Enterococcus faecalis is increasingly being recognized as a major nosocomial and potential community pathogen worldwide. E. faecalis is involved in various human diseases, such as neonatal meningitis and transplant-associated peritonitis.

An in-depth understanding of enterococcal GIs is vital, as they are significant contributors to the adaptability, phenotypic diversity and overall success of E. faecalis by encoding traits providing selective advantages in the human host or healthcare environment, including antimicrobial resistance, pathogenicity and niche specialization. E. faecalis strains can also carry large E. faecium Tn5253-family conjugative integrative elements (also called integrative and conjugative elements, ICEs) that harbor genes conferring resistance to chloramphenicol and aminoglycoside, thereby reducing the therapeutic options against these organisms. For various human bacterial pathogens, mobile genetics element could transform avirulent strains into hypervirulent ones and account availability of a whole genetic payload to a recipient bacterium in an instant, all this together could have an impact on a patient's source of infection and would then contribute to disease establishment (Tamura et al., 2022).

## 5. DIAGNOSTIC METHODS FOR IDENTIFYING PATHOGENIC BACTERIA

The diagnosis of acute appendicitis is obtained from clinical suspicion confirmed by physical signs of tenderness, nausea, and pain in the lower abdominal cavity. Physical examination and laboratory tests are useful, but a surgeon's clinical experience permits diagnosis even when nonpathogenic bacteria are isolated. Medical history and some simple exams may clarify that lower abdominal pain is not caused by appendicitis (and therefore the patient should be followed by a specialist), but physicians mostly care that the

patient undergo appendectomy (in which case the most appropriate surgeon is a generalist). Blood analyses must prove either leukocytosis with neutrophilia, and CRP levels should be massively positive in acute disease. Abdominal ultrasound is not required to diagnose appendicitis but may clarify a diagnosis of typhilitis mimicking appendicitis or may exclude other causes of right abdominal pain (Blok et al., 2022).
Pathologic tissue with both bacterial and fungal microbiota, as confirmed by PCR and next-generation sequencing with a total count of 120,000 organisms (the maximum threshold for the method), may be taken as certain proof of acute appendicitis. A histopathological examination is useful for unclear cases or by the classification of an antimicrobial plan or hospitalization if complications are present or when one is continuing in the clinical observations of a medical trial. Milder cases can sometimes be managed with antimicrobial therapy. In sub-acute appendicitis, the findings range from non-sterile purulent exudate to manifest complications requiring peritoneal lavage and drainage to avoid longer hospitalization or outright surgery. In pre-scientific medicine, surgical intervention was based on severe pain gum symptoms. In this hospital, contrast-enhanced computer tomography, which has a very high sensitivity and specificity in this specific clinical situation, is used (Blohs et al., 2023).

### 5.2. LABORATORY TESTS

Many laboratory tests have been proposed for identifying and characterizing the pathogenic bacteria associated with appendicitis. In these tests, inflammatory markers, special selective and differential media, particularly in tubular adenoma appendix specimens, and microscopes for capturing narrow endoscopic biopsies have been used. It is well known that the primary role of considering the results of theoretical pathogen detection tests is to confirm the presence of infectious agents and to exclude non-pathogenic and opportunistic microorganisms. Symptoms in pure appendicitis may vary, and the presence of more than one bacterium is well known; it is significant in revealing that pure appendicitis is not always a sterile disease. In all such cases, when applied in a theoretical context, these tests substantially exclude the effects of commensal, special regional microorganisms, and other microorganisms (e.g., separately taken starch oat-starch-components) in order to better understand the actual value and effects of clinical laboratory applications. Theoretically proposed laboratory pathogen detection tests have positive and negative aspects. These tests are not completely virus or bacterium-specific traps, and they are not always compatible; even if there was no growth, the absence of a specific pathogen could not be explained by theory. Negative test results do not represent the absence of aspirin, which is known to be incompatible with numerous clinical laboratory pathology results in 'pure' and reactionary inflammation from context (Yesilalioglu et al., 2023).
However, these are the most common tests used to obtain traditional results and are routinely available in larger laboratories, as well as technical, instrumental, and experiential applications. We can classify these tests performed in pure appendicitis as biochemistry, serology, bacteriology, histopathology, and molecular microbiology. Most of these tests can be adapted to the equipment used in multi-parametric systems for the detection of standard clinical biochemistry and rapid microbiologists. Histopathology and special bacteriology tests used require the use of separate and additional instruments. Since the scopes are not aligned, the folding of the cut edges and the lifting of the tissue surface take longer, and additional work may be required to identify the target point. In theory, the microscopies used to apply these tests in pure and standard correspondence often offer lower performance compared to other endoscopic examinations (Rautio et al., 2000).

## 6. TREATMENT STRATEGIES FOR APPENDICITIS

Various treatment strategies are employed for handling appendicitis. Foremost among these are those involving the use of antibiotic therapy. The targets of the antibiotic therapy are to inhibit the polymicrobial microflora, even though it primarily consists of obligate aerobes. The primary contaminants of the gastrointestinal flora consist, in part, of aerobes. These regions are situated distally within the colon. Aerobic contaminants—and infecting aerobes, in particular—are blamed for the etiology of appendicitis, and this serves as significant evidence in our argument. The significance of using antibiotics alone in the treatment of appendicitis is that such an approach is able not only to maintain some instances of therapeutic success, but in almost all cases it allows for a reduction in the risk of operative complications when used in combination with surgery prior to the performance of surgical procedures (Becker et al., 2018).
The purpose of administering the surgical procedures is to remove the inflamed appendix from the body of the patient by severing the corollary tissue. In the presence of pathogenic microorganisms, fecoliths may be formed that could either obstruct the affected appendix or serve as carriers of the specific microorganisms that cause the inflammation; this latter form of activity could be enacted within the lymphoid tissue as suggested. When this occlusion transpires, the secretory products of the affected tissue culminate in a stasis, leading to a large expanse between the high osmotic pressure and subsequent edema. This would produce ischemia and gangrene inward from the pressure-inflated area (Nguyen et al., 2023).
The most efficacious cure for appendicitis is antibiotic therapy because it is a disease caused by pathogens, and the disease is prevented by manipulating them. Pathogenic bacteria are in all cases the organisms present in or attached to the appendix. Appropriate non-digestible and antibiotic therapy is marginally helpful but significant with an early dispensary admission in the situation of pitticite. As a result, the presence of pathogenic bacteria. The absence of bacteria in studies is expected to be misleading. In severely ill 12-18 year old cases, only 22 percent have appendices that are neither specifically infected nor pus-filled at the time

of normal operation. It is difficult to diagnose no-bacterial appendicitis without operating, and it can be seen undoubtedly that the elevation in neutrophils > 75*10^6 at the time of onset is a novel sign which poses the diagnostic problem. If the operation is required, both sin and mestery are likely to be 2 out of 3 of the symptoms of pitticone. Neither of the two of these two todos when used on a relatively less young sufferer. The Australian study shows that only in phlootransportism the operation was significantly different before and after the study of the operation (Becker et al., 2018).

## 7. CONCLUSION AND KEY FINDINGS

Appendicitis is characterized by inflammation of the appendix when defecation is obstructed, including bacterial invasion into the appendix tissue. However, any typical or atypical bacterium may be pathogenic bacteria representing the bacteria spectrum associated with appendicitis based on the patient's background and bias as well as the hospital environment. Therefore, the aim of this article is to summarize the association between pathogenic bacteria and appendicitis, and the susceptibility of appendicitis associated with the harboring of potential pathogens in the appendix. In fact, appendectomy to treat acute appendicitis has been scarcely revised as a standard treatment in recent decades. We suppose that such a treatment method is not wrong, assuming that appendicitis is generally an exclusion diagnosis. However, performing appendectomy due to bias against abnormal test results such as fecal occult blood, C-reactive protein, and white blood cell count may lead to unintended perforated appendicitis and overdiagnosis. This review's main findings were as follows: the absence of candidate pathogenic bacteria in appendicitis, the protective role of E. coli in appendicitis, and the differential role of E. coli in the initiation and progression of appendicitis.

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