

# Acute Appendicitis

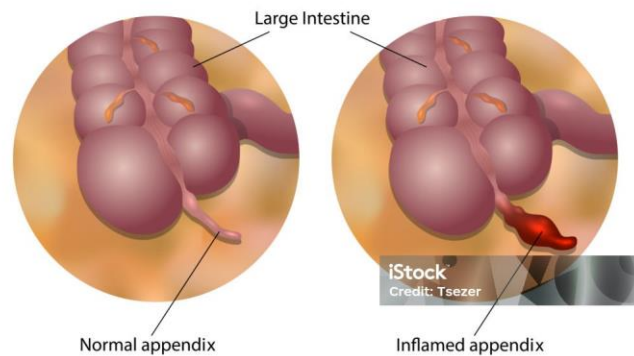
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An acute appendicitis is one of the most common surgical emergencies in the world with a lifetime risk of 8.6% in males and 6.9% in females. We were encouraged during our surgical training to treat patients suffering from an acute appendicitis, with an open appendectomy as a standard procedure. The management has changed a little nowadays with the addition of laparoscopic ablation of the appendix and the medical management of the disease. Patients with the symptoms of acute appendicitis have benefited from initial doses of antibiotic therapy followed by an open and standard procedure through a Mc Burney (mini-laparotomy) while others have only received an antibiotic therapy.

Recently, many trials have concluded that uncomplicated appendicitis may be treated non-operatively with antibiotic alone. We will review the treatment the way it is taught for children and pregnant women as well as adults once an understanding of the clinical findings and the techniques of appendectomy are well understood.

A diagnosis of "Acute Appendicitis" can be made on the symptoms without any clinical or radiological signs of perforation like an inflammatory mass or a phlegmon or an abscess. Most cases of appendicitis (80%) are not perforated at presentation. We learned in the past that appendectomy was the only therapy. It remains to be the dominant treatment thought in the world of Medicine.

Nowadays, there are mounting evidences that antibiotic therapy is not inferior to surgical treatment when a non-perforated appendicitis in a healthy patient, is diagnosed. It has been observed that a non-operative treatment, consisting in antibiotic therapy, has allowed the one suffering from an acute appendicitis or a recurrent appendicitis, to avoid a surgical treatment for the disease with a satisfactory recovery and a rapid return to work. One must accept to become a candidate for counselling and understand possibly that the disease may rebound in spite of the antibiotic therapy. The worsening the clinical picture with signs of localized or generalized peritonitis may explain a sudden perforation. Occasionally, a malignancy can be as well discovered.

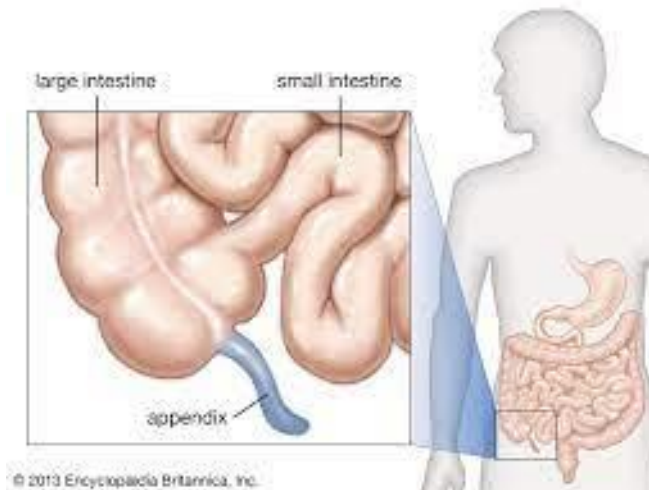


An Appendix is a small finger shaped tube that branches off the Cecum, at the first part of the large bowel, in the right lower quadrant of the abdomen and can become inflamed and infected. Rarely, it can become the site of benign and malignant tumors.

Non-operative management is now appropriated for patients who present with the clinical signs of a localized appendicitis without any physical signs of diffused peritonitis or any evidence of large abscess formation. It can be diagnosed via imaging, or presented as a phlegmon, a perforation or a tumor. Treatment may be initiated on any selected patient.

In the presence of appendicolith (calcified mass in the appendix), it has been demonstrated that the non-operative management has met a certain resistance and the failure rate appears to be higher. The presence of appendicolith presents around 25% of an increased risk in complications such as abscess. More, such patients are more susceptible to undergoing an appendectomy (CODA trial).

Antibiotic delay can also be encountered among patients older than 45-year-old especially when they present with appendicoliths and extraluminal fluid or air as well as fever or elevated inflammatory markers or symptoms observed for more than 48 hours pointing toward the presence of an appendiceal abscess. This is why such patients were excluded from the study and they were also prone to have an occult and asymptomatic appendiceal malignancy.



There are different types of Appendix cancer:

- 1- Carcinoid tumors called also “neuro-endocrine tumors” is a slow growing tumor which count for almost half of all the appendix cancers. These lesions can be present for a long period before being detected or becoming symptomatic. They receive signals from the endocrine system and release hormones.
- 2- Mucinous Cystadenoma tumors which are benign in appearance but present some lesions called mucocèles which have a precancerous potential to develop low-grade mucinous neoplasms (LAMN). They are non-cancerous tumors which form in the epithelium lining of the appendix. They will not spread in other part of the body if they remain intact but once they perforate or rupture, these neoplasms of the appendix present a rare condition called “Pseudomyxoma Peritonei” (PMP).
- 3- Mucinous Adenocarcinomas of the Appendix seems to begin on the cells lining the inside of the appendix but are generally treated as a colorectal cancer and generally present with the same symptoms. This is the second most common type of appendix cancer. They release a component of mucus called “mucin”. There is also a very rare subset which tend to be more aggressive called “Signet ring cell adenocarcinoma” because of the appearance of the cancer cells (signet) under the microscope. These “signet cells” secrete and store a large amount of mucin.
- 4- Finally, a Goblet cell adenocarcinoid or carcinoma presenting these two components of an adenocarcinoma and a carcinoid form which are more aggressive than the carcinoid types.

Upon evaluation of a patient with an acute appendicitis, it is possible that one can be asymptomatic but generally, it is more often expected to have abdominal (right lower quadrant or pelvic pain, a sensation of bloating and perhaps some ascites or ascitic fluid. A medical history can help to pinpoint the diagnosis. Changes in the bowel movements, vomiting and diarrhea and even fertility problems can be seen. The age of the patient can also help on the type of appendix cancer. Often some tests or procedures may be suggested like a Biopsy or an aspiration of the abdomen for ascitic fluid analysis, a laparoscopy etc. A CT-Scan or an MRI or even an Ultrasound may be helpful in making the diagnosis.

Contra-indications for a nonoperative management in patients suffering from an acute appendicitis, will need further trials especially when diffused peritonitis or severe sepsis is seen in immunocompromised patients or patients with inflammatory bowel diseases and even in pregnancy.

This non-operative management of a non-perforated appendicitis is not standardized and treatment protocols have shown variations from a trial study to another one. By examples, intravenous antibiotics have been used for one to three days followed by oral antibiotics up to one week to period of ten days. The choice of an antibiotic agent has not been standardized but many trials have suggested the use of a long-acting antibiotic like ceftriaxone given in combination with metronidazole. In other cases, a potential oral antibiotic in using fluoroquinolone (Cipro or Levofloxacin) in combination with metronidazole or amoxicillin-clavulanate are introduced.

In another trial (APPAC),  $\frac{3}{4}$  of the patients received 7 days of moxifloxacin while others received a two-day parenteral ertapenem followed by a five-day oral levofloxacin with metronidazole allowing them to successfully avoid an appendectomy at one year. Other experts (Up-To-Date) suggested to stay away from moxifloxacin because of the possibility of a rapid resistance to the Bacteroides type. They prefer ertapenem which is usually reserved to higher than low-risk community-acquired intra-abdominal infection, because of its broader spectrum coverage.

In another APPACK III trial, experts questioned if really antibiotics were necessary for the nonoperative management in cases of nonperforated appendicitis simply because, more than 90% of patients were treated with a placebo alone while others were treated successfully with antibiotics for 10 days. The difference was not statistically significant. In a Korean study where 245 patients were treated without any surgical treatment, a failure rate of 7% was noted with or without a four-day course of antibiotics. In both trials, all patients were hospitalized for at least 3 days. It was surprising but the two studies suggested perhaps that, uncomplicated appendicitis may be more of inflammatory

origin than infectious. It is expected that more studies will be performed prior to conclude or compare the findings of the CODA study.

Parameters like pain, fever, leukocytosis and anorexia subsided one day after the beginning of the antibiotics in the non-perforated appendicitis or in 48 hours for most of the other patients after their admission to the hospital unless deterioration of the clinical picture required a prompt rescued appendectomy. We do not know well if the period of observation should not be extended while receiving intravenous antibiotics.

In the CODA trial, the discharge of the patients from the emergency department after the 24 hours parenteral antibiotic therapy, has shown that such patients were not at greater risk of complication to necessitate an appendectomy in a hospital sitting. They did receive follow-up care through the clinic or via tele-medicine, for more than 48 hours until complete recovery and clinical improvement were noted.

As we know, many more trial studies may be needed to conclude on the different trials. 90% of patients treated with antibiotics were able to avoid surgical treatment. Antibiotics were given during the admission upon assuring a clinical diagnosis. 10 % failed to respond to conservative treatment with antibiotics and required appendectomy.

Unfortunately, there is no reliable way to predict precisely who will respond to the antibiotics unless the presence of an appendicolith may increase the risk to undergoing an appendectomy within the 30 days after the beginning of the treatment with antibiotics (21%). The majority of patients treated with antibiotics responded well clinically with a reduction of the white blood cell count, a soft abdomen with no signs of peritonitis, no diarrhea or vomiting, and an improvement of the symptoms. In brief, such treated patients have a lower pain score which required fewer doses of narcotics while missing less work days.

A small number of patients chose to undergo non-operative treatment following recurrent symptoms of appendicitis (15 patients) and they chose again a conservative treatment with a brief hospitalization and antibiotic therapy through the hospital or the emergency room. It is always better to recommend a surgical treatment, in face of recurrent symptoms especially when the patient is older than 45, given the possibility of a malignancy although another trial has shown that antibiotic alone can be offered to a younger patient.

70% of patients without appendicolith were able to avoid surgical treatment during their admission but 30% underwent appendectomy for recurrent appendicitis in the next year (6-7 months). In the different trials APPAC and CODA, a 5-year observational follow-up,

where 257 patients were treated with antibiotics only, for an uncomplicated acute appendicitis, the recurrent rate for appendicitis after one year, was 27.3% in the APPAC group but 29%, in the CODA group, increasing each year until year # 7, then a 39% of the antibiotic group finally underwent appendectomy during admission. In Sweden, there is a 25-year follow-up available because such study was initiated in 1990, and it was asserted that a cumulative risk for appendectomy for the cohort of patients who received antibiotic conservatively, was 40%.

An appendectomy is traditionally performed urgently in cases where an acute appendicitis is diagnosed to reduce the risk of perforation and peritoneum spilling. Studies have shown that the chances in having such complications following an acute appendicitis, carry a similar risk of perforation or other complications compared to those assigned to surgical treatment within 8 hours. This procedure is generally offered, once the diagnosis is ascertained within the 24 hours after the presentation at an emergency room. It can be done openly or laparoscopically.

This is a common diagnosis where large randomized trials have shown that it takes a short 24 hours-hospital stay prior to surgical or medical treatment, including work-up with labs and radiographic studies... like flat abdomen or CT scan. The risk of perforation did not increase with the delay and it is expected that a patient will receive adequate hydration and pain control medications as well as intravenous antibiotics in preparation for surgical treatment.

Prophylactic antibiotics are important in the prevention of wound infection and the formation of intra-abdominal abscess in the case where an appendectomy is necessary. The flora in the appendicular lumen is identical to the flora of the colon, notably with the presence of gram-negative aerobes and anaerobes. They conclude that patients undergoing an appendectomy should receive appropriate prophylactic antibiotic to cover gram-negative aerobes and anaerobes within 60 minutes from the surgical treatment. A broad spectrum antibiotic like Cefoxitin (2g IV) or Cefazolin or Cefotetan to which a dose of metronidazole can be added to as well. Occasionally, one can be allergic to the cephalosporin medications and medication like Ciprofloxacin, Levofloxacin or Gentamicin can be a perfect substitute for 24 hours.

We should not expect any bleeding but the patient maybe at risk for thromboembolic event. I had memory of a good friend of mine who lost his life from complications following a simple appendectomy. He was the captain of the national team of Volleyball of Haiti, in a super shape. We went to school together but we played Basketball for the country of Haiti and we just returned from a tournament in Cali, Columbia in 1972, when he passed following complications of an open appendectomy. He died of pulmonary

embolism. At that time, it was never re-enforced that precautions against pulmonary emboli with a so short surgical procedure were so critical. He died acutely, 24 hours after the operation.

The thrombotic risk needs to be assessed in any procedure which is going to ask for a general anesthesia and intubation. Pharmacokinetics of the medication can't be neglected. Aspirin, Clopidogrel (Plavix) can be given semi-urgently, in a pre-hospital setting especially for the one undergoing laparoscopic appendectomy. Be sure to use TED Stockings or compressive devices for the lower extremities. Such patient did not have any blood loss or did not require blood transfusion. Other medications like dabigatran (Pradaxa), apixaban (Eliquis) etc. may require to wait for 24 hours prior to surgical treatment. Patient on warfarin may have to receive vitamin K to reverse the profile while INR, PT, PTT will need monitoring.

In the presence of a perforated appendix. Patient may appear acutely ill with dehydration and electrolyte imbalance.

Clinically, there may be vomiting and patient may present a toxic picture, with elevation of temperature, diffused or localized abdominal pain. Free perforations can be more frequent in men than women (13%), intra-abdominal or pelvic abscess or phlegmon are looked for prior to bringing the patient in the operating theater. Bowel obstruction, bilious vomiting, jaundice, pyelophlebitis (septic portal vein thrombosis) can complicate the picture. Monitoring such patient may be difficult but necessary to assure a satisfactory outcome. An appendectomy for such patients with perforated appendix is a true surgical emergency with high risk of bleeding.

Broad spectrum antibiotic regimen to cover gram negative rods and anaerobic organisms pending culture results on the operating table. Streptococci, anaerobic organisms, Enterobacteriaceae, Pseudomonas Aeruginosa etc. can require different antibiotic therapy for a four days post op or a longer duration. I will invite you to review the protocols of different trials like STOPIT or APPIC with or without percutaneous abscess drainage or bowel resection and ileocecectomy.

One has to remember that immunocompromised patients (AIDS) are now increasingly common in surgical practice as well as patients with auto-immune diseases who may be receiving organ transplants as well as suffering from an uncomplicated vs complicated case of perforated appendix in need for surgical treatment. Symptoms of appendicitis can manifest late and often with signs of perforation. I would like not venture to deep in such fields but we will have to encourage all to review the criteria we tried to review and take them into consideration while preparing such patient for the operating room.

Finally, the children and the pregnant women may also present challenges in the diagnosis and the management of an acute appendicitis or can present with complications. I will leave you with the understanding that the treatment of an acute or recurrent, or a perforated appendix with or without signs of peritonitis, request expertise from the treating surgeon involved in the case.

The mortality may be low in cases of acute appendicitis in developed countries where the mortality rate is .09% but in resources limited countries the percentage may reach 4%. Remember well that the more an acute appendicitis is treated with days of antibiotic therapy, the more we may become unaware that although rare, a malignancy involving the appendix, may also become a surprise in the treatment of the disease.

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(Boca Raton FL (2-23-2024))

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