Appendicitis

Tara J. Loux

Key Points

- Appendicitis is one of the most common surgical illnesses of childhood. Most individual cases are easily and quickly managed, especially in countries with advanced health care. However, there is substantial combined morbidity and lost productivity on a global scale.
- Trials of non-operative management demonstrate up to 10% early failure rate and up to 60% recurrent appendicitis rate in the first 2 years after therapy. While not currently standard of care, antibiotic treatment alone can be considered in certain unique situations.
- Appendectomy can be safely delayed for 12–24 h after diagnosis of appendicitis if the patient is started immediately on broad-spectrum intravenous antibiotics. The patient should be kept *nil per os* (NPO) and given resuscitative and maintenance intravenous fluids prior to operation, with electrolyte correction as needed.
- Appendectomy is curative in cases of simple appendicitis. Complicated appendicitis presumes the spread of infection into the peritoneal cavity, which requires postoperative antibiotic therapy.

1. Epidemiology

   a. Incidence: Lifetime incidence is 7% in USA. There are 60,000 pediatric cases per year in the USA. Despite improvements in diagnosis, the rate of complicated (perforated) appendicitis in children remains between 25 and 33% of

T. J. Loux (✉)
Department of Pediatric Surgery, Geisinger Medical Center, Danville, PA, USA

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cases and has not decreased in recent years. Appendicitis is most prevalent between 5 and 25 years of age. There is seasonal variation in USA, with presentation slightly more common in summer months. Perforation is more common in the very young (<5 years), very old (>65 years) and patients with neurologic disability.

b. Mortality: Death from appendicitis is rare in pediatric patients, especially when otherwise healthy. There were 158 deaths reported in the US between 2010–2019 in the 18 and under age group. Twenty-five percent of these were in infants under one year of age, and the mortality rate for appendicitis in an infant may be as high as 25% due to its uncommon presentation, delay in diagnosis, immature immune system and concurrent pre-existing conditions such as prematurity.

c. Risk factors: Male sex (M:F ratio 1.4:1), family history of appendicitis, Caucasian, or Hispanic heritage, higher median household income, urban setting, chronic constipation, cystic fibrosis.

2. Pathophysiology:

a. Anatomy: The vermiform appendix is a small, blind-ending tubular structure that emanates from the base of the cecum. It can be intraperitoneal or retroperitoneal/retrocecal. The blood supply is from the appendiceal artery, which emanates from the ileocolic pedicle, the terminal branch of the superior mesenteric artery (Fig. 1).

b. Etiology: Appendicitis is caused by blockage of the appendiceal orifice, whether by fecalith, enlargement of lymph tissue, tumor, or other foreign body. Build-up of pressure impedes adequate blood flow, which leads to inflammation and eventually gangrene and perforation. Perforation is thought to occur 24–48 h after the initiation of symptoms, in the absence of any intervention.

c. Classification:

i. Early acute appendicitis—any non-perforated appendix with signs of acute inflammation.

ii. Perforated appendicitis—visible hole in appendix or fecalith in abdomen. Perforation can be further sub-divided into four grades:

1. Localized or contained perforation
2. Localized, well-circumscribed abscess
3. Generalized peritonitis without discrete abscess
4. Generalized peritonitis with multiple abscesses

iii. Other appendiceal pathology—includes eosinophilic appendicitis, subacute and chronic appendicitis, lymphoid hyperplasia, appendix carcinoid or other malignancy, pinworm (Enterobius vermicularis) infection, foreign body

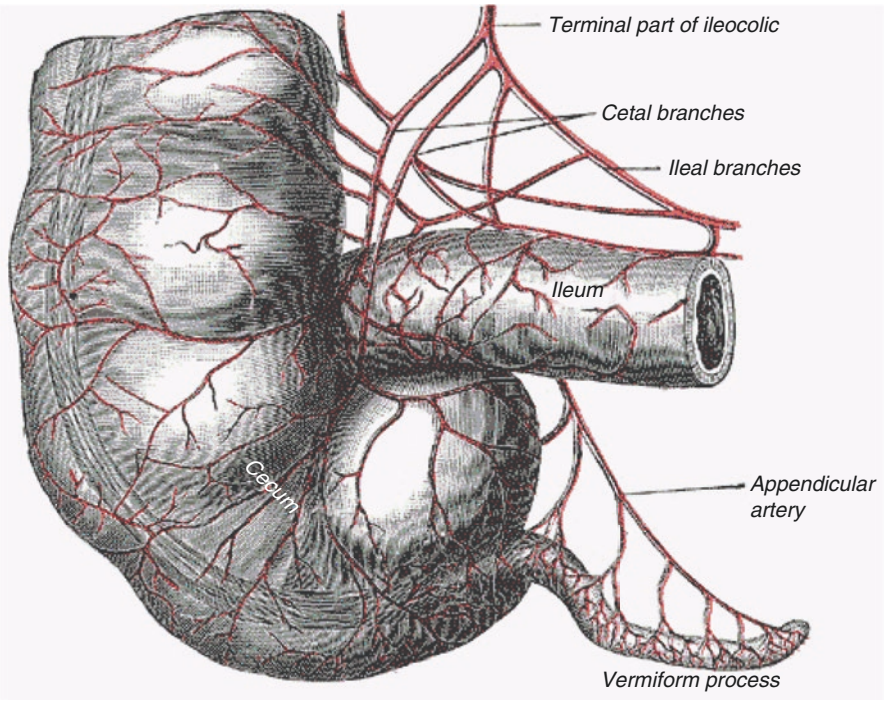

Fig. 1 Anatomy of vermiform appendix. Source: Henry Gray (1918) *Anatomy of the Human Body*. Bartleby.com: Gray's Anatomy, Plate 536

3. Clinical Features and Diagnosis

   a. Symptoms: Classically, vague abdominal pain which is persistent, worsening, and localizes to the right iliac fossa over a short duration (12–24 h) and can be accompanied by nausea, vomiting, anorexia, and low-grade fever (<100.5 F). Early onset of high fever, diarrhea, or sporadic pain is more consistent with gastroenteritis or other diagnoses. Many younger patients (<5 years old) will present with intractable vomiting, lethargy, lack of appetite and fever, as they are less likely to be cognitively able to report or describe abdominal discomfort.
   b. Examination: A complete physical examination should be performed to rule out other potential causes of abdominal pain and document levels of activity, hydration and nutrition, abdominal or other surgical scars. In particular, note should be taken of the child's spontaneous movements, temperature, pulse, and overall appearance. A full lymphatic basin exam is imperative. An external genital examination should be done in all patients to document Tanner's stage of development and rule out inguinal hernia or testicular pathology.

Abdominal examination can be difficult in younger children. Involuntary guarding is invariably present in the right lower quadrant and should be carefully ascertained. Certain signs may be present in appendicitis to aid with diagnosis:

i. McBurney sign—tenderness to palpation at McBurney point (a point 2/3 of the distance between the umbilicus and right anterior superior iliac spine)
ii. Perman sign—pain felt in right iliac fossa with palpation of the left iliac fossa (also known as Perman–Rovsing sign)
iii. Blumberg sign—rebound tenderness when releasing deep palpation in the right iliac fossa
iv. Dunphy sign—pain felt in right iliac fossa upon coughing
v. Psoas sign—pain produced by passive extension or active flexion of the right hip
vi. Obturator sign—pain produced by internal rotation of the hip

c. Laboratory Tests: A complete blood count with differential, electrolyte panel, liver function panel, lipase level and urinalysis should be sent to work up the child with abdominal pain. White blood cell count will invariably be elevated, often with leftward shift, unless the patient is neutropenic for some other reason (cytotoxic chemotherapy). C-reactive protein and procalcitonin are also usually elevated. Urinalysis should be performed to rule out urinary tract causes of abdominal pain and to perform urine pregnancy screening in postmenstrual (Postmenarchal) females. Irritation of the bladder by an inflamed appendix can cause sterile pyuria (usually <20 white blood cells/high power field), without the presence of bacteria, blood, or nitrates. Typical electrolyte abnormalities (hyponatremia, hypochloremia, metabolic acidosis or hypokalemic metabolic alkalosis) can be noted in cases where there has been prolonged vomiting or low oral fluid intake.
d. Grading Systems: Several grading systems of variable sensitivity and specificity are available for the diagnosis of appendicitis in the pediatric patient with abdominal pain (for example, the Pediatric Appendicitis Score in Fig. 2, or [1]). They use a combination of variables such as character and location of pain, associated symptoms, physical examination and laboratory values to calculate a numeric score, which classifies patients into Low, Intermediate, and High suspicion groups.

i. Low suspicion: Can safely be discharged without further workup.
ii. Intermediate suspicion: May undergo some sort of diagnostic imaging.
iii. High suspicion: Can be offered appendectomy, with or without confirmatory diagnostic imaging.

e. Radiologic Studies:

i. Ultrasound should be the first radiologic test ordered. It has a high specificity but a low sensitivity and can be operator and patient dependent. The

Pediatric Appendicitis Score	
For the presence of the following sign or symptom:	Assign the following points:
Pain in right lower quadrant on cough, hop or percussion	2
Tenderness to palpation of the right iliac fossa	2
Anorexia	1
Fever	1
Nausea/vomiting	1
Leukocytosis	1
Neutrophilia	1
Migration of pain to right iliac fossa	1
Total possible points	10
If PAS<5, appendicitis is highly unlikely. If PAS>7, appendicitis is highly likely. If PAS 5-7, likelihood is intermediate and imaging or observation may be warranted.	

Fig. 2 Pediatric Appendicitis Score. Source: Samuel M, "Pediatric Appendicitis Score." J Pediatr Surg. 2002; 37: 877–881, data from Elsevier complete source

appendix may not be visualized. An appendix over 6–7 mm in diameter is suspicious for appendicitis, especially if there is loss of compressibility, evidence of fecalith (shadowing stone), hyperemia of the appendiceal wall on Duplex and surrounding free fluid. Pelvic ultrasound should be ordered concomitantly in females to rule out ovarian pathology.

ii. Some centers use rapid magnetic resonance imaging (MRI) without contrast, which has a sensitivity and specificity similar to that of computed tomography (CT) with intravenous contrast, but is more costly and may not be available at scale in every institution [2].

iii. CT is quick, less expensive than MRI, has high sensitivity and specificity and is not operator dependent, but does involve the use of ionizing radiation and a quantifiable increase in the risk of hematologic malignancy. IV contrast should be administered, however, oral contrast is no longer given for CT when appendicitis is suspected due to poor tolerance, further delay in diagnosis and the potential need for subsequent urgent operation.

iv. Admission with serial abdominal examinations ("observation") can be an alternative to imaging, or appropriate for intermediate suspicion patients with a non-visualized appendix on ultrasound. Patients who undergo observation should be kept NPO and given appropriate intravenous analgesia, but should not be given antibiotics until the diagnosis has been confirmed.

f. Differential Diagnosis: Infectious enteritis or colitis, mesenteric adenitis, intussusception, omental infarction, Crohn's disease, typhlitis, pancreatitis, abdominal trauma (accidental or otherwise), adhesive bowel obstruction, Meckel diverticulitis, ovarian or fallopian tube pathology (ectopic pregnancy, hemorrhagic ovarian follicle or ovarian torsion), urinary tract infection or nephrolithiasis, testicular pathology (torsion of testicle or epididymal appendage, infectious or inflammatory orchiditis).
g. Occasionally, despite imaging, the diagnosis is equivocal due to a variety of factors, and diagnostic laparoscopy may be offered to clarify the diagnosis. If a normal appendix is found, it should be removed to eliminate this diagnosis in the future. However, if evidence of Crohn's disease is found on laparoscopy, the appendix should NOT be removed, as there is a high rate of appendiceal stump leak and enterocutaneous fistula. Standard therapy for Crohn's disease should be initiated. Contraindications to laparoscopy include acute abdomen with hemodynamic abnormality or history of multiple previous intraabdominal operations.
h. It is accepted that a normal appendix may be found at operation, despite a thorough preoperative workup. Prior to the availability of cross-sectional imaging, the acceptable number was as high as 25%. Currently, preoperative diagnostic sensitivity and specificity are around 96%, such that a normal appendix finding should occur in less than 4% of cases.

4. Treatment

a. Initial Measures:

i. Patient is made NPO and given 20 mL/kg 0.9% saline bolus, followed by appropriate maintenance intravenous fluids.
ii. A broad-spectrum antibiotic is started. Cefoxitin 40 mg/kg up to 2 g is appropriate unless complicated appendicitis is highly suspected or confirmed on preoperative imaging.
iii. Intravenous analgesia with morphine 0.05 mg/kg and/or acetaminophen 15 mg/kg is given for patient comfort. Analgesia should not be withheld pending surgical consultation.
iv. Patients with severe sepsis or septic shock should be stabilized medically prior to operation.

b. Subsequent Measures:

i. Operative therapy is the standard of care and should be accomplished in most cases where the patient can safely undergo general anesthesia.
ii. Operation can safely be delayed 12–24 h in patients who are receiving appropriate antibiotic therapy without risk of perforation while in hospital.
iii. In cases where the patient is not a candidate for immediate general anesthesia, intravenous antibiotic therapy should be continued until oral intake is re-established, and oral antibiotic therapy continued until the patient experiences complete resolution of symptoms. Occasionally,

symptoms continue despite antibiotic therapy and antibiotics must be continued until operation is planned.

iv. If a well-formed abscess is present, percutaneous drainage placement should be offered. Interval appendectomy may be offered 6–8 weeks thereafter.

c. Preoperative Preparation: Have patient empty bladder immediately prior to operation or perform Credé maneuver after induction of anesthesia. General anesthesia is necessary for laparoscopy, however, spinal anesthesia can be sufficient for right lower quadrant incision. Foley catheter should not be necessary in most cases. Clip abdominal hair in older patients. Tuck left arm (or both arms). Ensure antibiotic is dosed or re-dosed 15 min to 1 h prior to incision as per standard guidelines. Prep the entire abdomen with chlorhexidine or betadine solution.

d. Operative Treatment: Appendectomy can be performed open through a right lower quadrant (Rocky–Davis) or lower midline incision. However, studies have shown significantly improved short and long-term postoperative outcomes with laparoscopy, including decreased postoperative pain, quicker return to activity, fewer postoperative surgical site infections and fewer adhesive bowel obstructions. Laparoscopy can be conducted via the traditional three-port method, with SILS (single-incision multichannel laparoscopy), or with SISI (single-incision single-instrument) laparoscopy.

Regardless of how it is performed, appendectomy consists of the following steps:

i. Careful separation of omentum, adjacent bowel loops and (if applicable) adnexal structures from the inflamed appendix. This may also entail mobilization of the cecum and right colon to gain access to the appendix.

ii. Creation of a window in the mesoappendix with ligation of the appendiceal arterial pedicle.

iii. Ligation of the base of the appendix flush at its juncture with the cecum, taking care not to narrow the entrance of the terminal ileum into the cecum, nor leave behind any portion of the base that might cause stump appendicitis.

iv. Removal of all fluid, infected debris, fecalith, and purulence from the abdominal cavity.

e. Postoperative Treatment:

Patients with *uncomplicated appendicitis* can safely be discharged from the recovery room after laparoscopic surgery. No further antibiotic therapy is necessary when no perforation is found operatively. They should be allowed diet as tolerated. Pain control with oral acetaminophen and ibuprofen is sufficient. Activity, including normal bathing, should be quickly liberalized. Most patients can return to school or light duty within 3–5 days and regular activity in 2 weeks.

Perforated appendicitis presumes spread of infection within the abdominal cavity and requires postoperative antibiotic therapy. Most surgeons agree that

patients with perforative appendicitis should receive at least 5 days of antibiotic therapy. In this author's experience, antibiotics should be continued until symptoms are fully resolved, including abdominal pain, diarrhea, and fever. There is clear evidence that patients can be safely switched to oral therapy and discharged home once oral intake is tolerated (a full meal). Average hospital stay is 4–5 days. A Dutch trial comparing two days of total antibiotic therapy versus five days in patients 8 years old or greater was scheduled to finish recruiting in 2020 and will hopefully result in the near future.

Most patients with perforated appendicitis will have diarrhea initially and this does not mean they have resumed normal bowel function. A nasogastric tube should be placed to low continuous suction if they have more than one episode of vomiting postoperatively, or if they experience bilious emesis. Oral intake is the best predictor of an improving child. If oral intake has not reached or is not expected to reach normal levels by postoperative day 7, total parenteral nutrition (TPN) should be started via peripherally inserted central venous catheter (PICC). Additionally, at this time postoperative imaging should be obtained, to start with ultrasound looking for fluid collection. Waiting until day 7 to start TPN and perform imaging has shown to significantly reduce the amount of unnecessary TPN and postoperative imaging and does not increase the risk of other complications.

f. Complications: Complication rate after appendectomy for uncomplicated appendicitis should be 3% or less. Complication rate after appendectomy for ruptured appendicitis can range from 10 to 25%. Complications include bleeding, intraabdominal abscess, wound infection or dehiscence, ileus, bowel obstruction, appendiceal stump leak, enterocutaneous fistula, antibiotic-associated diarrhea or *Clostridium difficile* colitis and infertility in female patients from scarring of the fallopian tubes.

Additional Notes

Significant attention in recent years has been given to management of appendicitis with antibiotics alone, especially under the influence of the 2020 SARS-coV2 pandemic limitations on hospital, operating room and intensive care capacities. The few studies published with pediatric data are retrospective or non-randomized, and have reported an average 10% early failure rate of non-operative therapy, and 25% rate of recurrent appendicitis in the first year. Some studies show decreased number of disease-related activity limitation days in non-operative therapy groups in the short term. No study has reported follow-up in children for more than 2 years at this point. Given current antibiotic stewardship priorities, the ease and relative safety of performing appendectomy in a healthy child versus an older adult, and the much longer ensuing life span of a child, this author's opinion is that non-operative management of appendicitis in children is inferior treatment and should only be offered in select circumstances, followed by the option of outpatient interval appendectomy. Clinical trials to study this in more detail are currently ongoing [3].

Study Questions:

1) Question 1: You remove a non-perforated appendix from an otherwise healthy 8-year-old child with a one-day history of symptoms. The patient is discharged home the same day, and the pathology report resulting 5 days later notes the presence of *Enterobium vermicularis*. What should be done about this finding?

   a. No further intervention is required.
   b. Prescribe 7 days of oral amoxicillin/clavulanate.
   c. Admit to the hospital for 7 days of intravenous piperacillin/tazobactam.
   d. Prescribe oral mebendazole 100 mg, two doses separated by two weeks.

Answer to Question 1: d) Pinworm is found incident with appendicitis in up to 4% of specimens. Treatment should include members of the entire household of the patient.

2) What is the appropriate antibiotic treatment regimen in a patient with complicated appendicitis?

   a. Ceftriaxone 50 mg/kg up to 2 g and metronidazole 30 mg/kg up to 1 g intravenously every 24 h for 5 days postoperatively.
   b. Treatment regimen is dependent on patient characteristics, signs, and symptoms.
   c. Piperacillin/tazobactam 100 mg/kg up to 3.375 g, intravenously every 6 h for 7 days.
   d. Sulfamethoxazole/trimethoprim 4 mg/kg up to 160 mg trimethoprim orally twice daily for 7 days.
   e. Gentamicin 2.5 mg/kg (following peak and trough levels) and clindamycin 13 mg/kg (up to 900 mg) intravenously every 8 h for 6 days postoperatively.

Answer to Question 2: b) Patients with complicated appendicitis remain hospitalized on intravenous antibiotics until they are able to tolerate oral intake (a full meal). Options a, c, d, and e are all potential treatment regimens. The most cost-effective intravenous treatment regimen is ceftriaxone and metronidazole, given once daily. Alternatives include piperacillin/tazobactam, clindamycin + gentamicin, ciprofloxacin + metronidazole, or a carbapenem, depending on the individual patients' allergy profile. Once oral intake has stabilized, the patient can be switched to oral antibiotics and discharged home. Appropriate oral antibiotics include amoxicillin/clavulanate 22 mg/kg up to 875 mg amoxicillin every 12 h, sulfamethoxazole/trimethoprim, or ciprofloxacin 10 mg/kg up to 500 mg every 12 h + metronidazole 10 mg/kg up to 500 mg every 8 h. Most treatment protocols agree that therapy, whether oral or intravenous, should continue for a minimum of five days postoperatively, AND until full resolution of abdominal pain, diarrhea, and fever.

3) Question 3: You are called to see a 5-year-old patient with acute lymphoblastic leukemia in the oncology ward who has developed right lower quadrant pain and fever. He is currently undergoing induction therapy. The child's absolute neutrophil count (ANC) is 40 cells/uL. The pain began in the periumbilical region

before radiating to the right lower quadrant. The child has positive McBurney and Perman signs. There is no evidence of diffuse peritonitis. An ultrasound shows a blind-ending, tubular, non-compressible structure in the right lower quadrant measuring 8 mm in diameter with increased blood flow in the walls and a small amount of free fluid. What do you recommend?

a. Emergent appendectomy.
b. CT of the abdomen and pelvis with intravenous and oral contrast.
c. Broad-spectrum intravenous antibiotics, NPO, intravenous fluids, analgesia, and nutrition with the removal of the appendix when the ANC is greater than 500 cells/uL.
d. Broad-spectrum intravenous antibiotics and percutaneous drain placement.

Answer to Question 3: c). This patient is an excellent candidate for interval management of acute appendicitis. Any operation conducted in this patient with severe neutropenia will carry an extremely high risk of wound healing complications. Cases in which it would be appropriate to consider delay of operation include concomitant presentation of influenza or respiratory syncytial virus, severe neutropenia or thrombocytopenia, severe sepsis with shock or other organ failure, diabetic ketoacidosis, or other uncontrolled medical diagnoses which might increase the risk of general anesthesia or operative complications. Interval management is also best for patients who have a well-formed abscess which is amenable to percutaneous drainage. Some surgeons recommend interval management for any patient suspected of having ruptured appendicitis; while not universally accepted, it has not definitively been proven inferior. In the case of severe neutropenia, typhlitis (inflammation of the cecum and right colon) should be suspected in a child with evidence of right lower quadrant pain, hemodynamic abnormalities and peritonitis and should be confirmed by CT scan with IV contrast. Surgical intervention for typhlitis is associated with a very high mortality rate.

References

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Further Reading

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