Acute appendicitis
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Summary
Acute appendicitis is an acute inflammation of the vermiform appendix.

Typically presents as acute abdominal pain starting in the mid-abdomen and later localizing to the right lower quadrant.

Associated with fever, anorexia, nausea, vomiting, and elevation of the neutrophil count.

Diagnosis is usually made clinically. If investigation is required, computed tomography scan or ultrasonography may show dilatation of the appendix outer diameter to more than 6 mm.

Definitive treatment is surgical appendectomy. A nonoperative, antibiotic-only approach may be feasible in select patient populations.

Definition
Acute appendicitis is an acute inflammation of the vermiform appendix, most likely due to obstruction of the lumen of the appendix (by fecalith, normal stool, infective agents, or lymphoid hyperplasia).[1] [2]
Epidemiology

Acute appendicitis is one of the most common acute surgical abdominal emergencies.[4] More than 250,000 appendectomies are performed each year in the US; however, the incidence is lower in populations where a high-fiber diet is consumed.[5] [6] The overall lifetime risk of developing acute appendicitis is 8.6% for males and 6.7% for females; lifetime risk of appendectomy is around 12% in males and 23% in females.[7] [8]

Globally, the pooled incidence of appendicitis or appendectomy is around 100 per 100,000 person years.[9] Data suggest a rapid increase in incidence in newly industrialized countries.[9] Acute appendicitis most commonly occurs between the ages of 10 and 30, with the highest incidence in children and adolescence.[10] [11] There is a slight male to female predominance (1.3:1).

Etiology

Obstruction of the lumen of the appendix is the main cause of acute appendicitis. Fecalith (a hard mass of fecal matter), normal stool, or lymphoid hyperplasia are the main causes for obstruction. Retrospective appendectomy data suggest fecalith prevalence of 14% to 18% (among patients with a clinical indication/clinical syndrome of appendicitis or emergency appendectomy patients, respectively).[12] [13] In emergency appendectomy patients, fecalith prevalence was 39.4% in perforated appendicitis, but only 14.6% in nonperforated appendicitis.[12]

There is evidence suggesting a neuroimmune etiology in some cases, but this is still being investigated.[14]

Pathophysiology

The lumen distal to the appendiceal obstruction starts to fill with mucus and acts as a closed-loop obstruction. This leads to distension and an increase in intraluminal and intramural pressure. As the condition progresses, the resident bacteria in the appendix rapidly multiply. The most common bacteria in the appendix are *Bacteroides fragilis* and *Escherichia coli*.[15]

Distension of the lumen of the appendix causes reflex anorexia, nausea and vomiting, and visceral pain around the umbilicus, based on the embryonic origins of the appendix.

As the pressure of the lumen exceeds the venous pressure, the small venules and capillaries become thrombosed but arterioles remain open, which leads to engorgement and congestion of the appendix. The inflammatory process soon involves the serosa of the appendix, hence the parietal peritoneum in the region, which causes classical right lower quadrant pain at McBurney point.

Once the small arterioles are thrombosed, the area at the antimesenteric border becomes ischemic, and infarction and perforation ensue. Bacteria leak out through the walls and pus forms (suppuration) within and around the appendix. Perforations are usually seen just beyond the obstruction rather than at the tip of the appendix.[16]
Case history

Case history #1

A 22-year-old male presents to the emergency room with abdominal pain, anorexia, nausea, and low-grade fever. Pain started in the mid-abdominal region 6 hours ago and is now in the right lower quadrant of the abdomen. The pain is steady in nature and aggravated by coughing. Physical examination reveals a low-grade fever (100.5°F [38°C]), pain on palpation at right lower quadrant (McBurney sign), and leukocytosis (12,000/microliter) with 85% neutrophils.

Case history #2

A 12-year-old girl presents with sudden-onset severe generalized abdominal pain associated with nausea, vomiting, and diarrhea. On exam she appears ill and has a temperature of 104°F (40°C). Her abdomen is tense with generalized tenderness and guarding. No bowel sounds are present.

Other presentations

Atypical appendiceal anatomy, such as retrocecal or long appendix, may present with back, hip, or left-sided abdominal pain that is confused with an alternate intra-abdominal diagnosis. Older patients are less likely to have classical symptoms and may present with nonspecific abdominal pain without associated features, or confusion. The delay in presentation or diagnosis in this group results in increased risk of morbidity and mortality. The diagnosis of acute appendicitis during pregnancy is often delayed, as the location of the pain is affected by displacement of the appendix by the uterus, and symptoms such as nausea and vomiting are frequently associated with pregnancy itself.[3]
Acute appendicitis

Approach

History and physical examination form the initial approach in the evaluation of a patient with possible appendicitis. It is routine practice in the US to request a computed tomography (CT) scan for patients presenting to the emergency room with features of acute appendicitis. Validated clinical decision tools such as the Alvarado score demonstrate high sensitivities and are useful for excluding appendicitis, but lack specificity.

Ultrasound or magnetic resonance imaging (MRI) of the abdomen are recommended if the patient is pregnant. Women of childbearing age should have a pelvic examination to rule out other pelvic pathology.

History

Abdominal pain is the main presenting complaint. Pain typically starts at the mid-abdominal region and later (1 to 12 hours) shifts to the right lower quadrant. Pain is usually constant in nature and with intermittent abdominal cramps and is usually worse on movement and coughing.

Location of the pain may vary depending upon the position of the appendix:

- Retrocecal appendix may cause flank or back pain
- Retroileal appendix may cause testicular pain due to irritation of the spermatic artery or ureter
- Pelvic appendix may cause suprapubic pain
- A long appendix with tip inflammation in the left lower quadrant may cause pain to that region.

Anorexia is another important symptom almost always associated with acute appendicitis. Without anorexia the diagnosis of acute appendicitis is in question. Nausea and vomiting are also present in 75% of patients. Absolute constipation is a late feature.

The sequence of presentation in 95% of patients with acute appendicitis usually starts with anorexia, followed by abdominal pain and then vomiting. However, in pregnant patients, the only features shown to be significantly associated with a diagnosis of appendicitis are nausea, vomiting, and local peritonitis.

Complicated appendicitis (perforation or intra-abdominal abscess) is more likely the greater the duration of symptoms and in older patients (>50 years).

Physical exam

Usually, there are no significant changes in vital signs. Patients may have a low-grade fever. In patients presenting with a high-grade fever, another diagnosis should be considered. Tachycardia may also be present.

A classic sign is right lower quadrant abdominal tenderness (McBurney sign) and localized rebound tenderness, if appendix is anterior. There may also be pain in the right lower quadrant after compressing the left lower quadrant (Rovsing sign).

Pain may be elicited in the right lower quadrant with the patient lying on their left side and slowly extending the right thigh to cause a stretch in the iliopsoas muscle (psoas sign) or by internal rotation of the flexed right thigh (obturator sign).
Acute appendicitis

Bowel sounds may be reduced, particularly on the right side compared with on the left.

Classic abdominal findings may not be present if the appendix is in an atypical position.

Patients with perforation may present acutely ill with hypotension, tachycardia, and a tense, distended abdomen with generalized guarding and absent bowel sounds.

A palpable mass may be felt with appendiceal perforation that has been contained by the omentum, resulting in a periappendiceal abscess.

In children, pain with coughing and hopping can support the diagnosis.[38] Analgesia may be useful to facilitate abdominal exam if pain limits the examination. Analgesia does not lead to missed diagnoses in children.[39] [40]

Investigation

All patients with abdominal discomfort should have a complete blood count taken. Mild leukocytosis (10,000 to 18,000/microliter) with increased neutrophils is usually present. In children, CRP level on admission ≥10 mg/L and leukocytosis ≥16,000/microliter are strong predictive factors for appendicitis.[10]

Some form of imaging is usually warranted. Most nonpregnant patients presenting to the emergency room with abdominal pain suggestive of appendicitis will have a CT scan of the abdomen and pelvis.[30] [10] Preoperative imaging with a CT scan of the abdomen (ultrasound or MRI for pregnant women) now forms the usual standard of care. Women and children, in particular, may benefit from preoperative imaging.[26] [41] [38]

Choice of imaging modality

Although CT scan has greater sensitivity and specificity than ultrasound in diagnosing appendicitis, the latter is readily available, rapid, and able to be performed at the bedside.[42] [43] [44] In children, ultrasound may be preferred over CT scan in order to limit radiation exposure. There is evidence to suggest enhanced sensitivity and specificity of ultrasound in children compared with adults.[41] [45] [46] If, on ultrasound, a normal appendix is visualized in its full length, then acute appendicitis can be excluded. However, this is rarely the case, and the greatest utility for ultrasound is to detect an alternative cause of abdominal pain that excludes appendicitis.[47]

Appendiceal CT scan is increasingly used as the initial diagnostic test for acute appendicitis, and it is routine practice in the US to request a CT for patients presenting to the emergency room with features of acute appendicitis.[26] A CT is also indicated in atypical presentations.[30] [48] However, delayed surgery subsequent to CT scan for presumed appendicitis is associated with an increased rate of appendiceal perforation.[49] Intravenous contrast-enhanced CT scan with or without oral contrast has up to 100% sensitivity compared with 92% sensitivity in nonintravenous contrast-enhanced CT scan.[50] [51]
In pregnant women presenting with features of appendicitis, an abdominal sonogram should be performed to identify the appendix. If the sonogram examination is inconclusive, an abdominal MRI (particularly in early pregnancy) may be appropriate.[31][30] However, a negative or inconclusive MRI does not exclude appendicitis and surgery should still be considered if clinical suspicion is high.[10]

In children, point-of-care ultrasound is the most appropriate first-line diagnostic tool, if an imaging investigation is indicated based on clinical assessment. In children with inconclusive ultrasound results, a second-line imaging technique (CT or MRI) can be chosen based on local availability and expertise.[10] Low-dose CT is preferred in young people if they have a negative ultrasound.[10]

**Tests to exclude other causes**

A urinalysis should be performed to exclude possible urinary tract infection or renal colic. Sexually active women of childbearing age should have a urinary pregnancy test.

**History and exam**

**Key diagnostic factors**

**abdominal pain (common)**

- Constant mid-abdominal pain which later (1 to 12 hours) shifts to right lower quadrant. Usually worse on movement and coughing.

**anorexia (common)**
• An important symptom almost always associated with acute appendicitis.[32] Without anorexia the diagnosis of acute appendicitis is in question.

right lower quadrant tenderness (common)
• A classic sign is right lower quadrant abdominal tenderness (McBurney sign). There may be localized rebound tenderness, especially if the appendix is anterior. Compressing the left lower quadrant may also elicit pain in the right lower quadrant (Rovsing sign). Pain may also be elicited with the patient lying on their left side and slowly extending the right thigh to cause a stretch in the iliopsoas muscle (psoas sign) or by internal rotation of the flexed right thigh (obturator sign).

Other diagnostic factors

age of occurrence (common)
• Most commonly occurs between the ages of 10 and 30, with the highest incidence in children and adolescence.[10] [11]

nausea (common)
• Nausea and vomiting are present in 75% of patients.[32]

fever (common)
• Low-grade, usually 1.8°F (1°C) increase in body temperature.

diminished bowel sounds (common)
• Bowel sounds may be reduced, particularly on the right side compared with the left.

tachycardia (common)
• Tachycardia may be present, particularly in patients with perforation.[37]

vomiting (uncommon)
• Nausea and vomiting are present in 75% of patients.[32]

Rovsing sign (uncommon)
• Pressing the left side of the abdominal cavity elicits pain in right lower quadrant.

psoas sign (uncommon)
• Extending the right thigh on left lateral position elicits pain in right lower quadrant.

obturator sign (uncommon)
• Pain is elicited in the right lower quadrant of abdomen by internal rotation of the flexed right thigh.

Risk factors

Weak
**<6 months of breastfeeding**

- Affects immunologic responses to certain microbial organisms. Children who received <6 months of breastfeeding had a higher incidence of acute appendicitis compared with those who received >6 months of breastfeeding.[17] [18]

**low dietary fiber**

- Known to cause constipation. Children with appendectomies have low fiber in their diet compared with controls.[6] [19] However, this theory is controversial.[20]

**improved personal hygiene**

- A higher incidence of acute appendicitis in Western society may be related to the living conditions and improved personal hygiene.[21]
- A balance of gastrointestinal microbial flora is important for prevention of infection, for digestion, and providing important nutrients.[22] Frequent use of antibiotics and improved hygienic conditions lead to decreased exposure and/or imbalance of gastrointestinal microbial flora that may eventually lead to a modified response to viral infection and thereby trigger appendicitis.[23]

**smoking**

- Children exposed to passive smoking have significantly increased incidence of acute appendicitis.[24] There is also an increased incidence of acute appendicitis in adult patients who smoke compared with adults who never smoked.[24] [25]
# Investigations

## 1st test to order

<table>
<thead>
<tr>
<th>Test</th>
<th>Result</th>
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<tbody>
<tr>
<td><strong>CBC</strong></td>
<td>mild leukocytosis (10,000 to 18,000/microliter)</td>
</tr>
<tr>
<td>• Increased polymorphonuclear leukocytes (&gt;75%). High discriminatory power when combined with history.[52]</td>
<td></td>
</tr>
<tr>
<td>• Leukocytosis ≥16,000/microliter and CRP level on admission ≥10 mg/L are strong predictive factors for appendicitis in children.[10]</td>
<td></td>
</tr>
<tr>
<td><strong>CRP</strong></td>
<td>there is no clear cut-off value for a raised CRP in children, CRP likely to be elevated</td>
</tr>
<tr>
<td>• C-reactive protein is likely to be elevated.[38]</td>
<td></td>
</tr>
<tr>
<td>• CRP level on admission ≥10 mg/L and leukocytosis ≥16,000/microliter are strong predictive factors for appendicitis in children</td>
<td></td>
</tr>
<tr>
<td><strong>abdominal and pelvic CT scan</strong></td>
<td>abnormal appendix (diameter &gt;6 mm) identified or calcified appendicolith seen in association with periappendiceal inflammation, fat stranding</td>
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<tr>
<td>• Wall thickening, wall enhancement, and inflammatory changes in the surrounding tissues are additional findings seen in a CT scan of abdomen and pelvis.[53]</td>
<td></td>
</tr>
<tr>
<td><img src="CT_abdomen.png" alt="CT abdomen - thickened appendix" /></td>
<td></td>
</tr>
<tr>
<td>• Appendiceal CT scan is increasingly used as the initial diagnostic test for acute appendicitis, and it is routine practice in the US to request a CT for patients presenting to the emergency room with features of acute appendicitis.[26]</td>
<td>A CT is also indicated in atypical presentations.[30] [48]</td>
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<td>• Intravenous contrast-enhanced CT scan with or without oral contrast has up to 100% sensitivity compared with 92% sensitivity in nonintravenous, contrast-enhanced CT scan.[50] [51]</td>
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<tr>
<td>• In pregnant women presenting with features of appendicitis, an abdominal sonogram should be performed to identify the appendix. If the sonogram examination is inconclusive, abdominal MRI (particularly in early pregnancy) may be appropriate.[30] [48]</td>
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<tr>
<td><strong>urinary pregnancy test</strong></td>
<td>negative</td>
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<tr>
<td>• If positive, the possibility of ectopic pregnancy should be considered.</td>
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### Other tests to consider

<table>
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<tr>
<th>Test</th>
<th>Result</th>
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<tr>
<td><strong>abdominal ultrasound</strong></td>
<td>aperistaltic or noncompressible structure with outer diameter &gt;6 mm, fluid collection if perforated, fat stranding, appendicolith</td>
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</table>
| • In children, point-of-care ultrasound is the most appropriate first-line diagnostic tool, if an imaging investigation is indicated based on clinical assessment.  
• Sensitivity and specificity of ultrasound may be higher in children compared with adults.[43] [45] [46]  
• In children with inconclusive ultrasound results, a second-line imaging technique (CT or MRI) can be chosen based on local availability and expertise.[10] |
| **urinalysis**                | negative                                                               |
| • If positive for red cells, white cells, or nitrates, an alternative diagnosis such as renal colic or urinary tract infection should be considered. |
| **abdominal and pelvic MRI in pregnancy** | abnormal appendix (diameter >6 mm) identified and evidence of periappendiceal inflammatory changes, appendicolith, fat stranding |
| • In pregnant women presenting with features of appendicitis, an abdominal sonogram should be performed to identify the appendix. If the sonogram examination is inconclusive, abdominal MRI (particularly in early pregnancy) may be appropriate.[30] [48]  
• A negative or inconclusive MRI does not exclude appendicitis and surgery should still be considered if clinical suspicion is high.[10] |
### Differentials

<table>
<thead>
<tr>
<th>Condition</th>
<th>Differentiating signs / symptoms</th>
<th>Differentiating tests</th>
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| **Acute mesenteric adenitis** | • Usually presents in children with a recent history of upper respiratory infection.  
• Pain in the abdomen is usually diffuse with tenderness not localized to the right lower quadrant.  
• Guarding may be present, but rigidity is usually absent.  
• Generalized lymphadenopathy may be noted. | • There is no specific test to confirm the diagnosis.  
• Relative lymphocytosis in WBC differential counts is suggestive.  
• Negative ultrasound or CT findings help exclude other diagnoses. |
| **Viral gastroenteritis**   | • Common in children; caused by viruses, bacteria, or toxin.  
• Characterized by profuse watery diarrhea, nausea, and vomiting.  
• Crampy abdominal pain often precedes the diarrhea, and no localizing signs are present.  
• If caused by typhoid fever, intestinal perforation may cause localized abdominal pain and/or generalized and rebound tenderness. In this scenario, associated maculopapular rash, inappropriate bradycardia, and leukopenia will differentiate from appendicitis. | • No specific test unless due to typhoid ( *Salmonella typhi* from stool or blood will confirm the diagnosis). |
| **Meckel diverticulitis**   | • Usually asymptomatic.  
• Clinical presentation of diverticulitis is similar to acute appendicitis. | • Technetium pertechnetate scan may show the enhancement of diverticulum if gastric mucosa is present. |
| **Intussusception**         | • Occurs in young children (age <2 years).  
• Sudden onset of colicky pain; between episodes of pain the child is calm.  
• A sausage-shaped mass may be palpable in the right lower quadrant. | • Barium enema may demonstrate the intussusception with a coil-spring sign at the point of bowel invagination. |
| **Crohn disease**           | • Young adult with fever, nausea, vomiting, diarrhea, right lower quadrant pain, and localized tenderness. | • CT scan may show intra-abdominal abscess.  
• Contrast study of the small bowel and colon may show |

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### Condition | Differentiating signs / symptoms | Differentiating tests
--- | --- | ---
**Acute appendicitis** | stricture or a series of ulcers and fissures (cobblestone appearance) of mucosa. | 
**Peptic ulcer disease** | • May or may not have a history of peptic ulcer disease.  
• Pain is abrupt, severe in intensity, and may be localized to right lower quadrant. | • Erect chest x-ray and abdominal x-ray may show free air under the diaphragm | 
**Right-sided ureteric stone** | • Pain is usually colicky in nature and severe in intensity. May be referred to the labia, scrotum, or penis and associated with hematuria.  
• Fever usually absent. | • Urinalysis positive for blood.  
• Leukocytosis usually absent.  
• Abdominal x-rays or tomogram may show calcified stone.  
• Pyelography and CT scan without oral and intravenous contrast confirm the diagnosis. | 
**Cholecystitis** | • Pain and tenderness are usually in the right upper quadrant. In one third of patients the gallbladder can be palpable.[54] | • Abdominal ultrasound shows thick wall with pericholecystic collection, and tenderness is present over gallbladder area (Murphy sign).  
• Hepatobiliary iminodiacetic acid scan will show nonvisualization of gallbladder at >4 hours. | 
**Urinary tract infection** | • Pain and tenderness is usually in suprapubic area associated with burning micturition.  
• Acute right-sided pyelonephritis may present with fever, chills, and tenderness at the right costovertebral angle. | • Urine microscopy and culture confirm presence of bacteria. | 
**Primary peritonitis** | • Most patients present with abrupt abdominal pain, fever, distension, and rebound tenderness.  
• History of advanced cirrhosis or nephrosis. | • CT scan may show fluid in the abdomen.  
• Peritoneal fluid shows >500/microliter count and >25% polymorphonuclear leukocytosis. | 
**Pelvic inflammatory disease** | • Occurs in females usually aged between 20 and 40 years.  
• Presents with bilateral lower quadrant tenderness, usually within 5 days of the last menstrual period. | • Endocervical swab may confirm the pelvic inflammatory disease due to *Chlamydia trachomatis*. [55] |
### Criteria

There are multiple validated decision tools utilized in the diagnosis of appendicitis. These include the Adult Appendicitis Score (AAS), Alvarado, Appendicitis Inflammatory Response (AIR), and RIPASA scoring systems. These scoring systems involve a combination of history, examination findings, and investigation results.

The Alvarado score is commonly used and has undergone the most validation studies. The AIR score performed well in one systematic review of clinical prediction rules. It showed high sensitivity (92%) and specificity (63%) in predicting acute appendicitis. The RIPASA score was more sensitive than the Alvarado score, with improved diagnostic odds ratio, but lower specificity.

The Alvarado score can be used to rule out appendicitis but should not be used to confirm a diagnosis of appendicitis.

The AIR score and the AAS seem currently to be the best performing clinical prediction scores and have the highest discriminating power in adults with suspected acute appendicitis. The AIR and AAS scores decrease negative appendectomy rates in low-risk groups and reduce the need for imaging studies and hospital admissions in both low- and intermediate-risk groups.

Scoring systems can be used to determine the likelihood or rule out the diagnosis of appendicitis in order to guide further investigations and management.

- The AIR score or the AAS can be used to determine whether a patient is at high, intermediate or low risk of having appendicitis.

<table>
<thead>
<tr>
<th>Condition</th>
<th>Differentiating signs / symptoms</th>
<th>Differentiating tests</th>
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| Ruptured Graafian follicle (mittelschmerz) | • Midmenstrual cycle, brief period of lower abdominal pain not usually associated with nausea and vomiting and fever.  
• Tenderness is usually diffuse, not localized. | • Clinical diagnosis. No investigation indicated.                                         |
| Ectopic pregnancy             | • Female within childbearing age presents with missed menstrual period, right lower quadrant pain, or pelvic pain with some degree of vaginal bleeding or spotting.  
Cervical motion tenderness may be present on pelvic examination. | • Human chorionic gonadotropin hormone level is high in serum and in urine.  
• Ultrasound reveals presence of mass in fallopian tubes. |
| Ovarian torsion               | • Female with right lower quadrant pain. Occasionally presents with mass in the right lower quadrant. | • Ultrasonography shows ovarian cyst and decreased blood flow.                         |
• High-risk patients who are aged <40 years, and have strong symptoms and signs of appendicitis, may go straight to surgery without imaging. However, local protocols should be checked as this varies in practice.
• Intermediate-risk patients may undergo further imaging and observation.
• Low-risk patients may be safely discharged without diagnostic imaging, as long as they have appropriate safety-netting.

Adult Appendicitis Score (AAS)[56]
The higher the score, the greater the chance of having acute appendicitis. This scoring system reliably reduces the need for imaging studies and hospital admissions in both low- and intermediate-risk groups.[10][57]

Pain in right lower quadrant = 2 points.
Pain relocation = 2 points.

Right lower quadrant tenderness
• Women, aged 16-49 years = 1 point.
• All other patients = 3 points.

Guarding
• Mild = 2 points.
• Moderate or severe = 4 points.

Blood leukocytes (∗10⁹/L)
• ≥7.2 and <10.9 = 1 point.
• ≥10.9 and <14.0 = 2 points.
• ≥14.0 = 3 points.

Proportion of neutrophils %
• ≥62 and <75 = 2 points.
• ≥75 and <83 = 3 points.
• ≥83 = 4 points.

CRP (mg/L), symptoms <24 hours
• ≥4 and <11 = 2 points.
• ≥11 and <25 = 3 points.
• ≥25 and <83 = 5 points.
• #83 = 1 point.

CRP (mg/L), symptoms >24 hours
• ≥12 and <53 = 2 points.
• ≥53 and <152 = 2 points.
• ≥152 = 1 point.
Acute appendicitis

Sum ≥16 = high risk.

Sum 11 to 15 = intermediate risk.

Sum 0 to 10 = low risk (further investigation not needed).[10]

Alvarado (MANTRELS) score[27]

Score is based on clinical characteristics of the patients. The higher the score out of a possible total of 10, the greater the chance of having acute appendicitis.

M: Migration of pain to right lower quadrant = 1 point.

A: Anorexia = 1 point.

N: Nausea and vomiting = 1 point.

T: Tenderness in right lower quadrant = 2 points.

R: Rebound tenderness = 1 point.

E: Elevated temperature = 1 point.

L: Leukocytosis = 2 points.

S: Shift of WBC count to left = 1 point.

Appendicitis Inflammatory Response (AIR) score[58]

Vomiting = 1 point.

Pain in right inferior fossa = 1 point.

Rebound tenderness: light = 1 point; medium = 2 points; strong = 3 points.

Body temperature ≥38.5 = 1 point.

Polymorphonuclear leukocytes: 70% to 84% = 1 point; ≥85% = 2 points.

WBC count: 10.0 to 14.9 ×10⁹/L = 1 point; ≥15.0 ×10⁹/L = 2 points.

CRP concentration: 10 mg/L to 49 mg/L = 1 point; ≥50 = 2 points.

(Maximum 12 points.)

Sum 0 to 4 = low probability. Outpatient follow-up if unaltered general condition.

Sum 5 to 8 = indeterminate group. In-hospital active observation with rescoring/imaging or diagnostic laparoscopy according to local traditions.

Sum 9 to 12 = high probability. Surgical exploration is proposed.

RIPASA Score for Acute Appendicitis[59]
The higher the score out of a possible total of 16, the greater the chance of having acute appendicitis. The scoring system was developed for Asian populations.

Female = 0.5 points.

Male = 1 point.

Age <39.9 years = 1 point.

Age >40 years = 0.5 points.

Right iliac fossa (RIF) pain = 0.5 points.

Migration of pain to RIF = 0.5 points.

Anorexia = 1 point.

Nausea and vomiting = 1 point.

Duration of symptoms <48 hours = 1 point.

Duration of symptoms >48 hours = 0.5 points.

RIF tenderness = 1 point.

Guarding = 2 points.

Rebound tenderness = 1 point.

Rovsing sign = 2 points.

Fever = 1 point.

Raised WBC = 1 point.

Negative urine analysis = 1 point.

(Maximum 16 points.)

**Acute Physiology and Chronic Health Evaluation II (APACHE II) score[60]**

The APACHE score is commonly used to establish illness severity in the intensive care unit (ICU) and predict the risk of death. There is a high risk of death if the score is 25 or above.

There are several other models that have been developed for use in the ICU, including APACHE III, Mortality in Emergency Department Sepsis score, Simplified Acute Physiology Score, Sepsis-related Organ Failure Assessment, and Mortality Probability Model II.[61] [62] [63]

Early diagnosis remains challenging in children due to atypical clinical features and the difficulty of obtaining a reliable history and physical examination. In children with suspected acute appendicitis, scoring tools such as the Alvarado score and Samuel's Pediatric Appendicitis Score (PAS) are useful to exclude appendicitis.[10] The PAS includes similar clinical findings to the Alvarado score in addition to a sign more relevant in children: right lower quadrant pain with coughing, hopping, or percussion. However, diagnosis should not be based on clinical scores alone.[10]
**Approach**

The usual standard of care for the management of uncomplicated appendicitis in adults continues to be operative.

There is emerging evidence to suggest that a nonoperative, antibiotic-only approach may be feasible in select patient populations. The evidence supporting nonoperative management of appendicitis continues to be conflicting, and further research is warranted. There is more evidence to support a nonoperative approach in children than in adults.\[10\] \[66\] \[67\] \[68\] \[69\] \[70\] \[71\] \[72\] \[73\]

**Uncomplicated presentation**

Once the diagnosis of acute appendicitis is made, patients should be given nothing by mouth.

Intravenous fluids, such as lactated Ringer solution, should be started.

**Adults**

Prompt appendectomy remains the treatment of choice in international guidelines and should be recommended in most cases. A single preoperative dose of broad-spectrum antibiotic such as cefoxitin should be given to patients with uncomplicated appendicitis undergoing appendectomy. Postoperative antibiotics are not indicated.\[10\]

An antibiotic-only approach may be reasonable for select groups with uncomplicated appendicitis (suspected or confirmed on computed tomographic scan), where patients understand the risk of recurrent appendicitis.\[10\] \[73\] \[71\]

An antibiotic-only approach is not recommended if an appendicolith is present since nonoperative management carries a significant failure rate.\[10\] \[74\] A conservative approach should be avoided in pregnant patients.\[10\]

**Children**

Guidance from the World Society of Emergency Surgery supports nonoperative management as feasible, safe, and effective as initial treatment unless an appendicolith is present.\[10\] However, in the US the usual standard of care for the management of uncomplicated appendicitis in children continues to be operative. Postoperative antibiotics are not indicated in children with uncomplicated acute appendicitis since there is no evidence they decrease the rate of surgical infection.\[10\]

Appendicectomy should not be delayed for children with uncomplicated acute appendicitis needing surgery beyond 24 hours from admission. Surgery performed within this time is not associated with increased risk of adverse outcomes such as perforation, complications, or operating time in children who receive timely administration of antibiotics and undergo appendectomy less than 24 hours after diagnosis.\[10\]

As for adults, surgery is not recommended in children with appendicoliths since the failure rate of nonoperative management increases in these cases.\[10\]

**Complicated presentation**

**Adults**
Complications of acute appendicitis occur in 4% to 6% of patients and include gangrene with subsequent perforation or intra-abdominal abscess.\[16\]

Initial management includes keeping the patient nothing by mouth and starting intravenous fluids. Patients who are in shock should be given a bolus of intravenous fluid, such as lactated Ringer solution, in order to maintain a stable pulse rate and BP.\[75\] \[76\]

Intravenous antibiotics (e.g., cefoxitin or piperacillin/tazobactam) should be started immediately and continued until the patient becomes afebrile and the leukocytosis is corrected. For more severe infections, a carbapenem antibiotic may be used as a single agent. Combination antibiotic regimens may also be used based on local sensitivities and protocols.\[16\]

In patients with acute peritonitis, appendectomy should be performed without delay. Patients presenting with right lower quadrant abscess should be managed with intravenous antibiotics and drainage either by interventional radiology (computed tomography-guided drainage) or by operative drainage. If there is clinical improvement and the signs and symptoms are completely resolved, interval appendectomy may be unnecessary.\[10\] \[77\] \[78\] \[79\] \[80\]

Interval appendectomy is associated with a non-negligible rate of morbidity.\[79\]

Interval appendectomy is performed after 6 weeks if the symptoms are not completely resolved.\[10\] \[11\]

Adoption of a wait-and-see approach, reserving appendectomy for patients with recurrent symptoms, is the most cost-effective strategy compared with routine interval appendectomy.\[10\]

The incidence of appendicular neoplasms is high (3% to 17%) in patients ≥40 years old with complicated appendicitis. Any patient ages ≥40 years who has conservative management without interval appendicectomy should also undergo screening with colonoscopy and interval full-dose contrast-enhanced CT scan.\[10\]

The optimal management for appendicitis with phlegmon or abscess remains subject to debate.\[10\]

Latest evidence suggests that laparoscopic appendectomy is associated with fewer readmissions and fewer additional interventions than conservative management, provided advanced laparoscopic expertise is available.\[10\]

However, nonoperative management with antibiotics and, if available, percutaneous image-guided drainage is a reasonable alternative if the patient is stable and laparoscopic appendectomy is unavailable, although there is a lack of evidence for its use on a routine basis.\[10\]

Children

As with adults, initial management includes keeping the patient nothing by mouth and starting intravenous fluids and intravenous antibiotics. Early appendectomy within 8 hours should be performed in case of complicated appendicitis.\[10\]

Laparoscopic appendectomy is preferred over open appendectomy in children where laparoscopic equipment and expertise are available.\[10\]

Postoperative antibiotics for less than seven days seems to be safe and is not associated with an increased risk of complications. These can be switched from intravenous to oral form after 48 hours in children with complicated appendicitis with an overall length of therapy shorter than seven days.\[10\]

As per management of adults with phlegmon or abscess, nonoperative management (antibiotics and, if available, percutaneous image-guided drainage) is a reasonable alternative if the patient is stable and laparoscopic appendectomy is unavailable. Nonoperative management has been associated with better
Acute appendicitis

Management

MANAGEMENT results in terms of complication rate and readmission rate in children but evidence does not support its routine use.[81]

Surgical options

There are 2 operative options for appendectomy: open and laparoscopic. Most procedures are now undertaken laparoscopically.

In adults, the choice of appendectomy generally depends upon the experience of the surgeon. Studies have shown laparoscopic appendectomy to have better cosmetic results, shorter length of hospital stay, reduced postoperative pain, and reduced risk of wound infection, compared with open appendectomy.[82] Laparoscopic appendectomy is recommended for uncomplicated appendicitis, as well as complicated and perforated appendicitis.[83] [84] It is also considered the safest approach in obese patients.[10] [85]

In children, laparoscopic appendectomy decreases the incidence of overall postoperative complications, including wound infection and duration of total hospital stay.[86] [87] [82] [88] [89]

In pregnant patients, laparoscopic appendectomy should be preferred to open appendectomy when surgery is indicated and where expertise of laparoscopy is available. It is safe in terms of risk of fetal loss and preterm delivery. Compared to open surgery during pregnancy, laparoscopic appendectomy is associated with shorter length of hospital stay and lower incidence of surgical site infection. Laparoscopy is technically safe and feasible during pregnancy.[10] [91]

Antibiotic-only therapy

Antibiotics alone for the treatment of uncomplicated appendicitis can be successful in selected patients who wish to avoid surgery, and who accept the risk of up to 39% recurrence. In such cases, it is recommended that the diagnosis of uncomplicated appendicitis is confirmed by imaging, and that patient expectations are managed via a shared decision-making process.[10] [92] [71] [73] An antibiotic-only approach is not recommended in pregnant patients or if an appendicolith is present.[10] [74]

Outpatient laparoscopic appendectomy

Some patients may be discharged safely after laparoscopic appendectomy without hospitalization. This outpatient approach is suitable for patients with uncomplicated appendicitis, provided that an ambulatory pathway with well-defined ERAS (Enhanced Recovery After Surgery) protocols and patient information/consent are locally established.[10] ERAS implementation after laparoscopic appendectomy carries similar rates of morbidity and readmissions compared with conventional care.[93] Its potential benefits include earlier recovery after surgery and lower hospital and social costs.[10]

Treatment algorithm overview

Please note that formulations/routes and doses may differ between drug names and brands, drug formularies, or locations. Treatment recommendations are specific to patient groups: see disclaimer.
<table>
<thead>
<tr>
<th>Acute</th>
<th>( summary )</th>
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</thead>
<tbody>
<tr>
<td>uncomplicated acute appendicitis</td>
<td></td>
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<tr>
<td>1st</td>
<td>appendectomy + supportive care</td>
</tr>
<tr>
<td>adjunct</td>
<td>intravenous antibiotic therapy</td>
</tr>
<tr>
<td>2nd</td>
<td>antibiotic-only therapy</td>
</tr>
<tr>
<td>ill with perforation or abscess</td>
<td></td>
</tr>
<tr>
<td>1st</td>
<td>intravenous antibiotic therapy + supportive care</td>
</tr>
<tr>
<td>perforation</td>
<td>plus appendectomy</td>
</tr>
<tr>
<td>abscess</td>
<td>plus drainage ± interval appendectomy</td>
</tr>
</tbody>
</table>
Treatment algorithm

Please note that formulations/routes and doses may differ between drug names and brands, drug formularies, or locations. Treatment recommendations are specific to patient groups: see disclaimer.
Acute appendicitis

Management

Acute uncomplicated acute appendicitis

1st appendectomy + supportive care

» Once the diagnosis of acute appendicitis is made, patients should be given nothing by mouth.

» Intravenous fluids, such as lactated Ringer solution, should be started.

» Appendectomy should be performed without delay, as early appendectomy reduces the chances of perforation and intra-abdominal abscess.

» There are 2 operative options for appendectomy: open and laparoscopic. In adults, the choice of appendectomy generally depends upon the experience of the surgeon.

» Studies have shown laparoscopic appendectomy to have better cosmetic results, shorter length of hospital stay, reduced postoperative pain, and reduced risk of wound infection, when compared with open appendectomy. [82]

» Laparoscopic appendectomy is recommended for uncomplicated appendicitis.[83] It is also considered the safest approach in obese patients.[85]

» In pregnant patients, laparoscopic appendectomy should be preferred to open appendectomy when surgery is indicated and where expertise of laparoscopy is available. It is safe in terms of risk of fetal loss and preterm delivery. Compared to open surgery during pregnancy, laparoscopic appendectomy is associated with shorter length of hospital stay.
Acute appendicitis

Management

Acute and lower incidence of surgical site infection. Laparoscopy is technically safe and feasible during pregnancy.[10] [91]

» In children, nonoperative management is feasible, safe, and effective as initial treatment unless an appendicolith is present.[10] However, in the US the usual standard of care for the management of uncomplicated appendicitis in children continues to be operative.

» Laparoscopic appendectomy decreases the incidence of overall postoperative complications, including wound infection and duration of total hospital stay.[86] [87] [82] [88] [89] [94]

» Some patients with uncomplicated appendicitis may be discharged safely after laparoscopic appendectomy without hospitalization, provided that an ambulatory pathway with well-defined ERAS (Enhanced Recovery After Surgery) protocols and patient information/consent are locally established.[10] ERAS implementation after laparoscopic appendectomy carries similar rates of morbidity and readmissions compared with conventional care.[93] Its potential benefits include earlier recovery after surgery and lower hospital and social costs.[10]

» Patients with higher APACHE (Acute Physiology and Chronic Health Evaluation) scores seem to be at higher risk of development of postoperative complications.

adjunct intravenous antibiotic therapy

Treatment recommended for SOME patients in selected patient group

Primary options

» ceftoxitin: 2 g intravenously as a single dose 30-60 minutes before surgery

» A single preoperative dose of broad-spectrum antibiotic such as ceftoxitin should be given to patients with uncomplicated appendicitis undergoing appendectomy. Postoperative antibiotics are not indicated for these patients.[10]

2nd antibiotic-only therapy

» Antibiotics alone for the treatment of uncomplicated appendicitis can be successful in selected patients who wish to avoid surgery, and who accept the risk of up to 39% recurrence. In such cases, it is recommended that the diagnosis of uncomplicated appendicitis be confirmed by imaging, and that patient
Acute appendicitis

Management

Acute expectations be managed via a shared decision-making process.\cite{95} \cite{92} \cite{71} \cite{73}

» An antibiotic-only approach is not recommended if an appendicolith is present since nonoperative management carries a significant failure rate.\cite{10} \cite{74}

» A conservative approach should be avoided in pregnant patients.\cite{10}

Ill with perforation or abscess

ill with perforation or abscess

1st intravenous antibiotic therapy + supportive care

Primary options

» cefoxitin: 1-2 g intravenously every 8 hours

OR

» piperacillin/tazobactam: 3.375 g intravenously every 6 hours
  Dose consists of 3 g piperacillin plus 0.375 g tazobactam.

OR

» meropenem: 1 g intravenously every 8 hours

» These patients have evidence of perforation, mass, or abscess.

» Initial management includes keeping the patient nothing by mouth and starting intravenous fluids. Patients who are in shock should be given a bolus of intravenous fluid, such as lactated Ringer solution, in order to maintain a stable pulse rate and blood pressure.\cite{75} \cite{76} Following on, maintenance intravenous fluids should be given until the condition of the patient improves and an oral diet can be tolerated.

» Intravenous antibiotics (e.g., cefoxitin or piperacillin/tazobactam) should be started immediately. For more severe infections, a carbapenem antibiotic may be used as a single agent. Combination antibiotic regimens may also be used based on local sensitivities and protocols.\cite{16}

» Antibiotics should be continued until the patient becomes afebrile and leukocytosis is corrected.

» Patients with higher APACHE (Acute Physiology and Chronic Health Evaluation)
### Acute appendicitis

**Management**

<table>
<thead>
<tr>
<th>Acute</th>
<th>plus</th>
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</thead>
<tbody>
<tr>
<td>perforation</td>
<td>appendectomy</td>
</tr>
<tr>
<td>scores seem to be at higher risk of development of postoperative complication.</td>
<td></td>
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<tr>
<td>Treatment recommended for ALL patients in selected patient group</td>
<td></td>
</tr>
<tr>
<td>» There are 2 operative options for appendectomy: open and laparoscopic. In adults, the choice of appendectomy generally depends upon the experience of the surgeon.</td>
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</tr>
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<td>» Laparoscopic appendectomy is recommended for complicated and perforated appendicitis. [84] It is also considered the safest approach in obese patients. [85] In pregnant patients, laparoscopic appendectomy should be preferred to open appendectomy when surgery is indicated and where expertise of laparoscopy is available. It is technically feasible and is safe in terms of risk of fetal loss and preterm delivery. Compared to open surgery during pregnancy, laparoscopic appendectomy is associated with shorter length of hospital stay and lower incidence of surgical site infection. [10] [91]</td>
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<td></td>
</tr>
<tr>
<td>abscess</td>
<td>drainage ± interval appendectomy</td>
</tr>
<tr>
<td>Treatment recommended for ALL patients in selected patient group</td>
<td></td>
</tr>
<tr>
<td>» Abscess usually occurs as a progression of the disease process, particularly after perforation.</td>
<td></td>
</tr>
<tr>
<td>» Presents with tender right lower quadrant mass, swinging fever, and leukocytosis. Ultrasonography or computed tomography (CT) scan will show the abscess.</td>
<td></td>
</tr>
<tr>
<td>» Initial treatment includes intravenous antibiotics and CT-guided or operative drainage of the abscess.</td>
<td></td>
</tr>
<tr>
<td>» If there is clinical improvement and the signs and symptoms are completely resolved, interval appendectomy may be unnecessary. [10] [77] [78] [79] [80] Interval appendectomy</td>
<td></td>
</tr>
</tbody>
</table>
Acute appendicitis is associated with a non-negligible rate of morbidity. Any patient ages ≥40 years who has conservative management without interval appendectomy should also undergo screening with colonoscopy and interval full-dose contrast-enhanced CT scan since the incidence of appendicular neoplasms is high.

» Interval appendectomy is performed after 6 weeks if the symptoms are not completely resolved. Adoption of a wait-and-see approach, reserving appendectomy for patients with recurrent symptoms, is the most cost-effective strategy compared with routine interval appendectomy.

» For patients with phlegmon or abscess, management remains subject to debate. Latest evidence suggests that laparoscopic appendectomy is associated with fewer readmissions and fewer additional interventions than conservative management, provided advanced laparoscopic expertise is available. However, nonoperative management with antibiotics and, if available, percutaneous image-guided drainage is a reasonable alternative if the patient is stable and laparoscopic appendectomy is unavailable, although there is a lack of evidence for its use on a routine basis.
Emerging

Eravacycline

Eravacycline is a novel antibiotic of the tetracycline class. One clinical trial indicated that it is at least as effective as ertapenem in treating complicated intra-abdominal infections (cIAIs).[97] Eravacycline may have a role in the treatment of complicated appendicitis. The Food and Drug Administration (FDA) and the European Medicines Agency have approved eravacycline (Xerava, Tetraphase Pharmaceuticals) for the treatment of cIAIs in adults.

Meropenem/vaborbactam

Meropenem/vaborbactam is a carbapenem beta-lactamase inhibitor combination that has demonstrated higher clinical cure rates, versus best available therapy, for the treatment of carbapenem-resistant Enterobacteriaceae, among other infections.[98] The Committee for Medicinal Products for Human Use of the European Medicines Agency has recommended granting authorisation for meropenem/vaborbactam for the treatment of several types of infection, including cIAIs. Meropenem/vaborbactam is approved by the FDA for the treatment of complicated urinary tract infections in adults.

Imipenem/cilastatin/relebactam

Imipenem/cilastatin/relebactam is a three-drug combination containing imipenem-cilastatin, a previously FDA-approved antibiotic, and relebactam, a new beta-lactamase inhibitor. The FDA has approved this combination to treat adults with complicated urinary tract infections and cIAIs.

Patient discussions

Patients can be started on a clear liquid diet on the same day as the operation if there is no nausea or vomiting and can start a regular diet the next day. Patients are usually given at least 1 week off work or school. Future level of activity, driving, or return to work should be determined at the follow-up appointment.
Monitoring

Patients are usually discharged from hospital 1 day after surgery for uncomplicated appendicitis. Complicated appendicitis may require a longer hospital stay depending on the response to treatment. In some countries, patients are followed up postoperatively regardless of complicated or uncomplicated appendicitis; for example, 1 week after discharge, with further follow-up visits arranged as needed.
## Complications

<table>
<thead>
<tr>
<th>Complications</th>
<th>Timeframe</th>
<th>Likelihood</th>
</tr>
</thead>
<tbody>
<tr>
<td>perforation</td>
<td>short term</td>
<td>low</td>
</tr>
</tbody>
</table>

May occur after >12 hours of progressive appendiceal inflammation.

Usually a consequence of a delay in seeking medical treatment.

Presents with more severe abdominal pain, high fever (>101°F [38.3°C]), localized tenderness, and decreased bowel sounds.

Appendectomy should be performed in all cases. Procedure can be open or laparoscopic.

| generalized peritonitis    | short term  | low        |

Large perforation of acutely inflamed appendix results in generalized peritonitis.

Presents with an acute abdomen (high fever, diffuse abdominal pain, generalized tenderness, and absent bowel sounds).

If the diagnosis is suspected as acute appendicitis, appendectomy can be performed. If diagnosis is in doubt, exploratory laparotomy should be performed through midline incision, and the appendix, if inflamed, should be removed.

| appendicular mass          | short term  | low        |

Usually due to delay in medical treatment.

Presents with tender right lower quadrant mass. Ultrasonography or computed tomography scan will show a mass.

If the patient appears otherwise well, the initial management is conservative treatment with intravenous fluids and broad-spectrum antibiotics. If there is clinical improvement and the signs and symptoms are completely resolved, then there is no need for interval appendectomy.[77] [78] [79] Interval appendectomy is performed after 6 weeks if the symptoms are not completely resolved.[10]

In older patients, carcinoma should be excluded.

| appendicular abscess       | short term  | low        |

Usually occurs as a progression of the disease process, particularly after perforation.

Presents with tender right lower quadrant mass, swinging fever, and leukocytosis.

Ultrasonography or computed tomography (CT) scan will show the abscess.

Initial treatment includes intravenous antibiotics and CT-guided drainage of abscess.

The optimal management for appendicitis with phlegmon or abscess remains subject to debate. Latest evidence suggests that laparoscopic appendectomy is associated with fewer readmissions and fewer additional interventions than conservative management, provided advanced laparoscopic expertise is available. However, nonoperative management with antibiotics and, if available, percutaneous image-
**Complications** | **Timeframe** | **Likelihood**
--- | --- | ---
guided drainage is a reasonable alternative if the patient is stable and laparoscopic appendectomy is unavailable, although there is a lack of evidence for its use on a routine basis.[10]

**surgical wound infection** | short term | low

Decreased incidence if laparoscopic approach and prophylactic antibiotic used.[99]

---

**Prognosis**

If patients are treated in a timely fashion, the prognosis is good. Wound infection and intra-abdominal abscess are potential complications associated with appendectomy. Laparoscopic appendectomy has been shown to decrease the incidence of overall complications.[83]
## Diagnostic guidelines

### International

  
  **Published by:** American College of Radiology  
  **Last published:** 2018

  
  **Published by:** American College of Radiology  
  **Last published:** 2018

- **ACR Appropriateness Criteria: fever without source or unknown origin - child** ([http://www.acr.org/Quality-Safety/Appropriateness-Criteria](http://www.acr.org/Quality-Safety/Appropriateness-Criteria)) [64]
  
  **Published by:** American College of Radiology  
  **Last published:** 2015

- **Critical issues: evaluation and management of emergency department patients with suspected appendicitis** ([https://www.acep.org/patient-care/clinical-policies](https://www.acep.org/patient-care/clinical-policies)) [65]
  
  **Published by:** American College of Emergency Physicians  
  **Last published:** 2010

- **WSES Jerusalem guidelines for diagnosis and treatment of acute appendicitis** ([https://www.wses.org.uk/guidelines](https://www.wses.org.uk/guidelines)) [10]
  
  **Published by:** World Society of Emergency Surgery  
  **Last published:** 2020

## Treatment guidelines

### International

- **WSES Jerusalem guidelines for diagnosis and treatment of acute appendicitis** ([https://www.wses.org.uk/guidelines](https://www.wses.org.uk/guidelines)) [10]
  
  **Published by:** World Society of Emergency Surgery  
  **Last published:** 2020

  
  **Published by:** World Society of Emergency Surgery  
  **Last published:** 2017
### Key articles


### References


### References


Acute appendicitis

References


Figure 1: Acute appendicitis - intraoperative specimen.

Nasim Ahmed, MBBS, FACS; used with permission
Figure 2: CT abdomen - thickened appendix.

Nasim Ahmed, MBBS, FACS; used with permission
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Regardless of the language in which the content is displayed, numerals are displayed according to the original English-language numerical separator standard. For example 4 digit numbers shall not include a comma nor a decimal point; numbers of 5 or more digits shall include commas; and numbers stated to be less than 1 shall be depicted using decimal points. See Figure 1 below for an explanatory table.

BMJ accepts no responsibility for misinterpretation of numbers which comply with this stated numerical separator standard.

This approach is in line with the guidance of the International Bureau of Weights and Measures Service.

Figure 1 – BMJ Best Practice Numeral Style
Contributors:

// Authors:

Peter Szasz, MD, PhD, FRCSC
General and Minimally Invasive Surgeon
Toronto, Ontario, Canada
DISCLOSURES: PS declares that he has no competing interests.

// Acknowledgements:

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// Peer Reviewers:

John M. Davis, MD
General Surgery
Jersey Shore Medical Center, Neptune, NJ
DISCLOSURES: JMD declares that he has no competing interests.