

Review of the Appendix and Appendicitis

Part 1

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Jacopo Berengario da Carpi (1460 – 1530), Italian physician, first described the human appendix in his publication *Isagoge breves* (1522 – English translation *A short introduction to anatomy*).¹ He was considered the most important anatomist before Andreas Vesalius. Reginald H. Fitz, American physician, provided the first detailed description of acute appendicitis in 1886 providing a clear concept of the course of the disease and is credited with giving the disease its name (Figure 1).²

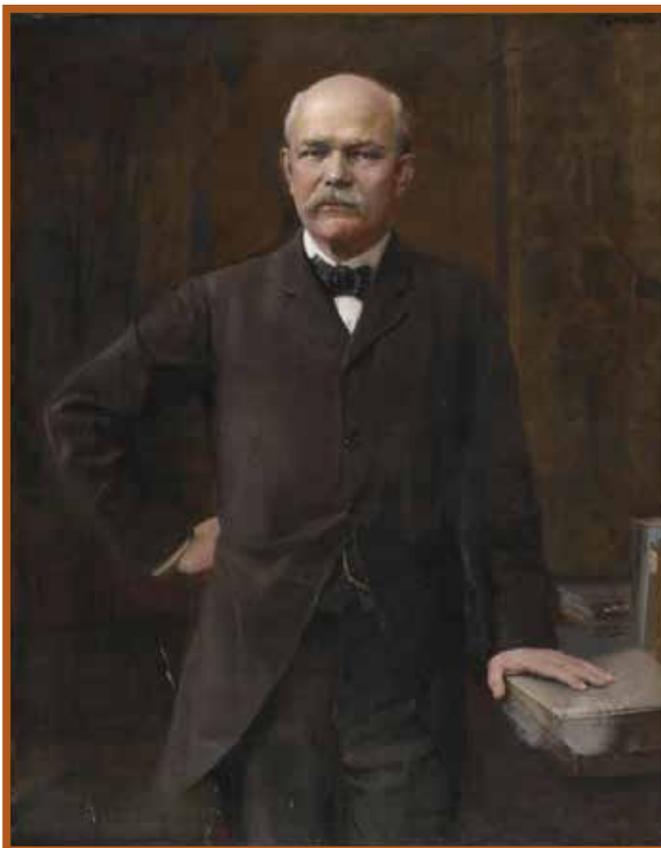


Figure 1 Reginald H. Fitz

LEARNING OBJECTIVES

- ▲ Describe the anatomy of the appendix
- ▲ Understand the histology of the appendix
- ▲ Discuss the pathophysiology of appendicitis
- ▲ Review the details of the various types of risk scores

KEYWORDS

acute appendicitis, complicated appendicitis, left shift, McBurney's point, uncomplicated appendicitis

DEFINITIONS

Acute appendicitis: The general term referring to sudden appendicitis that includes uncomplicated and complicated appendicitis.

Acute uncomplicated appendicitis: Usually referred to as uncomplicated appendicitis. A phlegmonous inflamed appendix without signs of necrosis or rupture.

Complicated appendicitis: Occurs when focal or transmural necrosis is present that can lead to perforation. Also characterized by the presence of an abscess, phlegmon, and appendiceal rupture that can result in peritonitis.

Guarding: A finding during an examination of the abdomen. It is an involuntary reflex of the patient during palpation of a tender abdomen. The patient tenses the abdominal wall muscles in an attempt to "guard" the area during palpation.

Leukocytosis: Increase in the number of leukocytes in the circulating bloodstream. It can be a sign that the body is fighting an infection (bacterial or viral), inflammation, injury, or stress, but can be a sign of other serious conditions such as bone marrow disorders and leukemia. It can also temporarily occur because of intense exercise, pregnancy, and ingesting specific medications such as corticosteroids.

Periappendiceal fat stranding: Inflammation of the fat layer that surrounds the appendix. The fatty layer is normally dark in color but appears white and streaky on CT scan when the patient has appendicitis. During appendicitis, inflammatory substances are released that cause fluid and immune cells to leak into the fat layer causing the small vessels and lymphatics in the fat to swell. It's an important sign of acute appendicitis and can correlate with the severity of the condition.

Phlegmon: Inflamed mass.

The incidence of appendicitis in North America is approximately one occurrence per 1,000 people per year.³ In the United States (U.S.) the incidence rate ranges from 100 to 233 new cases per 100,000 individuals per year.^{4,5} In the U.S., approximately 300,000 hospital visits are reported annually because of appendicitis.⁶ Appendicitis remains one of the most common surgical emergencies in pediatric patients.^{1,2} It is the fifth most common reason for hospitalization among children in the U.S.⁷ The peak incidence in children and adolescents is 10 to 19 years of age.^{2,3} Hospitalization related to appendicitis costs approximately \$3 billion per year within the U.S.⁷⁻⁹

Although acute appendicitis can occur at any age, it most commonly occurs between the ages of 5 to 45, signifying that the highest incidence of appendicitis occurs during childhood, adolescence, and early adulthood.¹⁰ The lifetime incidence of acute appendicitis is slightly higher in males occurring 8.6% as compared to 6.7% in females.¹¹

Combined with immature immunity and weakness of the appendix wall, perforation is more common in children with appendicitis, which is one of the most serious health-related problems worldwide. When the diagnosis of appendicitis is made in less than 24 hours in children 5 – 12 years of age the perforation rate is approximately 7%, if between 24 – 48 hours it increases to 38%, and if more than 48 hours is as high as 98%.¹²

ANATOMY AND PHYSIOLOGY OF THE APPENDIX

Simply put, the appendix is a narrow, elongated, blind-ended tube that is attached to the posteromedial end of the cecum. It is suspended from the terminal ileum by the mesoappendix, a fold of mesentery (Figure 2). In adults, the appendix is typically 6 – 10 cm in length and 3 – 8 mm in diameter with a 1 – 3 mm lumen (Figure 3).^{1,2} In the neonatal, the appendix averages 4.5 centimeters (cm) in length.

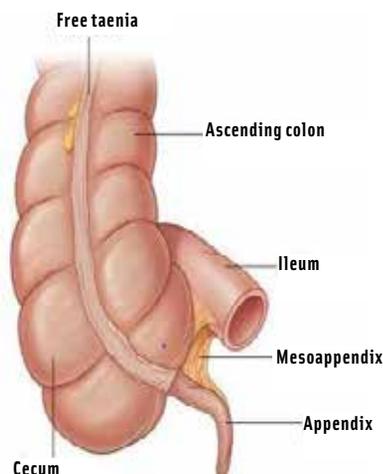


Figure 2
Appendix anatomy

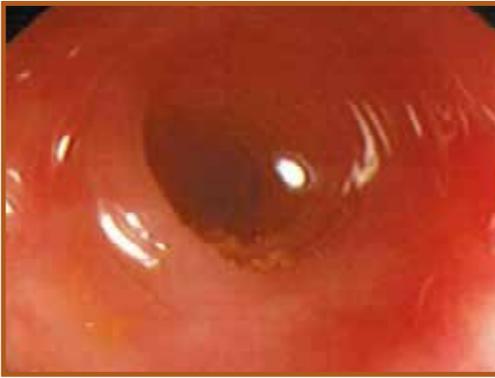


Figure 3
Colonoscopy view of the lumen of the appendix

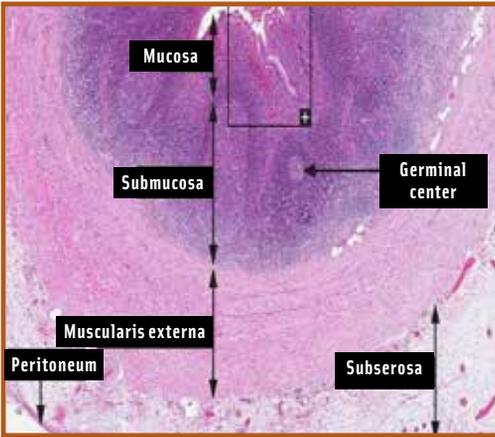


Figure 4
Histology of appendix

The appendix forms in the midgut of the fetus. At week 6 the cecal diverticulum has formed and is the origin for the development of the cecum and appendix.¹³ The appendix is visible by the 8th week of pregnancy.² As the colon develops and elongates, the cecum and appendix medially rotate along with the rest of the midgut and descend into the right lower quadrant (RLQ). During the 14th and 15th weeks of pregnancy, the mucosa within the appendix develops lymphoid tissue, contributing to the suggestions made in recent multiple studies that the appendix has a function in immunity.¹³ (This will be discussed in the Part 2 article.) By the age of 2 – 3 years, the appendix has matured.²

The layers are the same as the colon – mucosa, submucosa, muscularis propria, and serosa (Figure 4). However, the appendix differs from the other sections of the colon in that it contains a large concentration of lymphoid tissue, particularly in younger children. The significance of the presence of the lymphoid tissue and its relation to appendicitis in young patients is discussed later in the article.

The position of the appendix can vary and is categorized into five locations depending on the positional relationship to the cecum, ileum, and pelvis (Figure 5).¹ The positions can be remembered by applying clock positions:

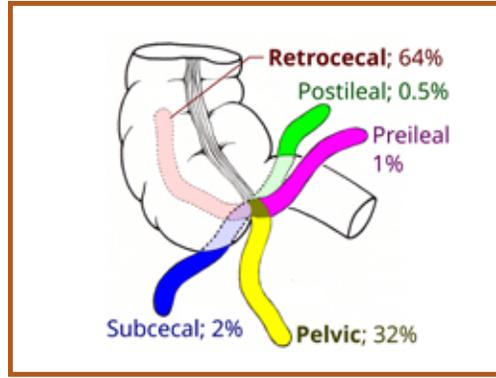


Figure 5
Various positions where the appendix can be located

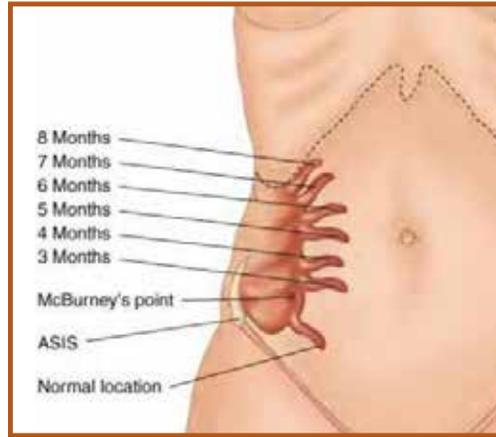


Figure 6
Location of appendix during pregnancy

- Retrocecal – The most common position, behind the cecum at the 11:00 position.
- Post-ileal – Posterior to the terminal ileum at the 1:00 or 2:00 position.
- Pre-ileal - Anterior to the terminal ileum at the 1:00 or 2:00 clock position.
- Pelvic – Descending over the pelvic brim at the 5:00 position.
- Subcecal – Below the cecum at the 6:00 position.

The appendix also changes position in pregnant women depending on the month of pregnancy (Figure 6). (In the figure, ASIS refers to the anterior superior iliac spine).

Vascular Supply

The arterial supply is from the appendicular artery, a branch of the ileocolic artery which is a branch of the superior mesenteric artery.¹ The venous drainage occurs through the appendicular vein to the ileocolic vein, which is a branch of the superior mesenteric vein that drains through the liver via the hepatic portal vein.¹ The appendicular artery and vein are contained in the mesoappendix (Figure 7).

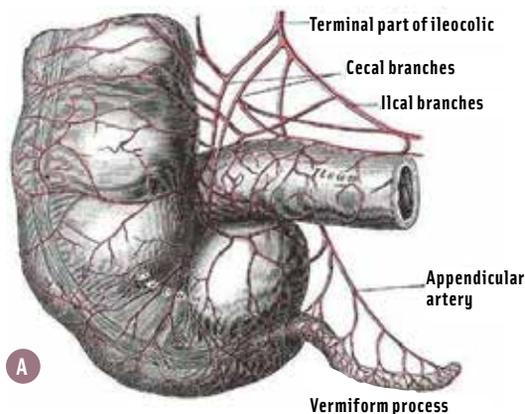


Figure 7 Arterial supply: (A) Diagram of blood supply, (B) Mesoappendix displayed demonstrating the appendicular artery

Nerve Supply

Sympathetic and parasympathetic branches of the autonomic nervous system innervate the appendix. The parasympathetic innervation arises from the fibers of the vagus nerve (CN X) and the sympathetic fibers arise from the lateral horns of the inferior thoracic spinal cord.¹ A clinically important note to remember is that the afferent nerve fibers of the appendix travel along the sympathetic pathway in reverse and attach to the spinal cord at the T10 level accounting for why the patient initially feels visceral pain in the central area of the abdomen during the early stages of appendicitis.¹

Lymphatic Drainage

The lymphatic drainage follows the arterial course in reverse from a single node contained within the mesoappendix to the ileocolic lymph nodes that surround the ileocolic artery and drainage proceeds into the superior mesenteric lymph nodes.^{1,13}

ETIOLOGY AND PATHOPHYSIOLOGY OF APPENDICITIS

Appendicitis is caused by the obstruction of the appendiceal lumen leading to inflammation. There are various causes of the obstruction such as appendiceal tumors, fecaliths, and hyperplasia of the lymphoid tissue, resulting in acute appendicitis. It is important to understand that the causes of the obstruction vary with age groups, emphasizing the need to take under consideration the specific factors that affect each age group when evaluating and diagnosing appendicitis.

In children and adolescents, the appendix contains a great quantity of lymphoid tissue that makes the young-

er patient prone to appendicitis because of lymphoid hyperplasia leading to inflammation and ischemia.¹¹ The inflammation increases the risk for perforation, the formation of an abscess, and proceeding peritonitis. Infancy through early middle childhood, the omentum is continuing to develop. It is during this period of time that it is not able to contain the purulent material that escapes when an appendiceal perforation occurs.¹² Therefore, the reason for peritonitis following perforation more likely happens in children.

In adults, acute appendicitis is commonly caused by fecaliths, infections, or tumors.¹⁰ Appendiceal neoplasms occur in 1.2 cases per 100,000 in the U.S. Gastroenteropancreatic neuroendocrine tumors (GEP-NETs), also called carcinoid tumors, are one of the common types of appendiceal malignancies.¹⁴ The neoplasm usually forms a 2 cm to 3 cm mass at the distal tip.¹³ Fortunately, they rarely metastasize and if that occurs the primary metastatic sites are the liver and lymph nodes, thus prompting clinical evaluations of the liver and lymph nodes in patients suspected for GEP-NET. Because the tumor forms in the distal tip, they rarely cause an obstruction and can remain asymptomatic.¹³ However, 10% of the tumors form at the base of the appendix and can cause appendicitis. An appendectomy that demonstrates negative margins is the only procedure that needs to be performed when the tumor is less than 1 cm in size.¹⁰ However, a right hemicolectomy will be performed for tumors that are more than 2 cm in size, as well as if there are enlarged lymph nodes or mesenteric invasion.¹¹

Irrespective of the cause, the obstruction of the lumen causes an increase in both the intraluminal and intramu-

ral pressures. The pressure produces the inability for lymph fluid to properly flow, occludes small vessels and causes thrombosis.¹⁰ The appendix becomes distended because of the accumulation of mucus and the lack of lymphatic and vascular circulation that causes the wall of the appendix to necrose. Additionally, bacteria accumulate inside the appendix, beginning with aerobic microorganisms in the early stages of appendicitis followed by a mixture of aerobic and anaerobic microorganisms such as *Bacteroides*, *Escherichia coli*, and *Pseudomonas*.¹⁰ The appendix is prone to perforation when it has become grossly inflamed and swollen and advanced necrosis has occurred.

DIAGNOSING APPENDICITIS

Physical Signs and Symptoms and Examination

Achieving an accurate diagnosis is obviously paramount to being able to properly treat the patient because there are multiple other pathologies that mimic the symptoms of appendicitis. For example, gastroenteritis is one of the most common misdiagnoses, with a history of diarrhea a common presentation.¹² To achieve an accurate clinical diagnosis, physicians rely on the physical signs and symptoms presented by the patient, laboratory results, and possibly imaging results. Most patients seek treatment when they are affected by the classic group of symptoms – diarrhea, fever, malaise, nausea and vomiting, and RLQ. The patient may not exhibit all the symptoms with fever and RLQ pain occurring most often. Approximately 40% of patients with acute appendicitis have a fever.¹⁰

Appendicitis remains one of most common surgical emergencies in pediatric patients.

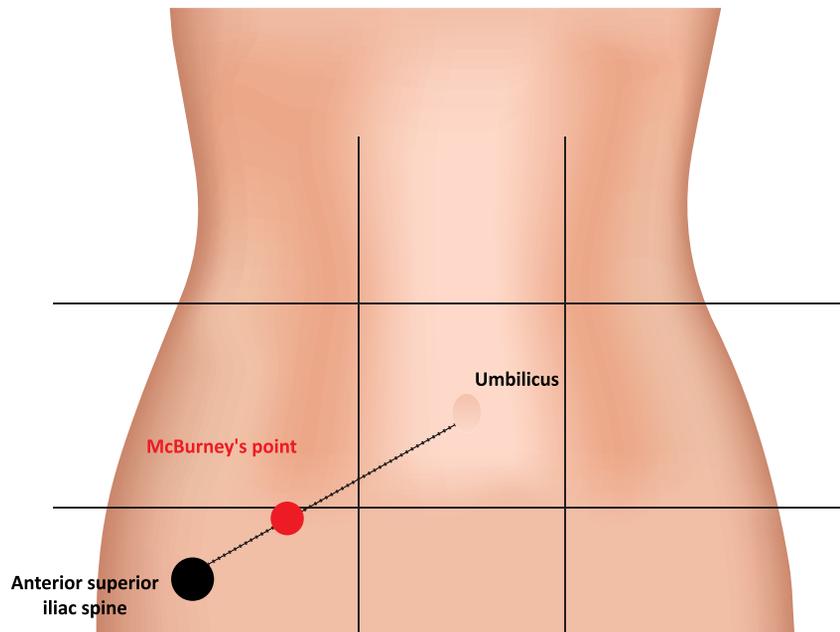


Figure 8 McBurney's Point

Initially, the primary symptom of acute appendicitis is diffuse or periumbilical pain caused by stimulation of the visceral afferent fibers that travel along the sympathetic innervation and enter the spinal cord at the T10 level.¹¹ As the appendix becomes more inflamed, it irritates the parietal peritoneum causing the classic sign of pain in the RLQ. The abdomen is most tender at McBurney's point located one-third the distance from the right anterior superior iliac spine to the umbilicus (Figure 8).¹³

There are three signs that can be encountered during the physical examination in patients with suspected appendicitis, but it must be emphasized that these signs are not diagnostic. The Dunphy sign, described by the physician John Dunphy (1908 – 1981) in his book *Physical Examination of the Surgical Patient* (1975), is when the patient experiences increased abdominal pain when coughing.^{10,15} The Rovsing sign, established by the Danish surgeon Niels Rovsing (1862 – 1927), is RLQ pain that is prompted by palpation of the left lower quadrant.^{10,16} If the surgeon has the patient extend their right leg it can elicit RLQ pain indicating a positive psoas sign.¹⁰ The pain occurs because of irritation to the psoas muscle by the inflamed appendix, accounting for the reason why some patients flex the hip to shorten the muscle and relieve the pain.

The timeline for symptoms in acute appendicitis varies; however, symptoms may continue for 12 to 24 hours and possibly beyond 48 hours.¹⁰ Approximately 75% of patients with acute appendicitis will present within the 24 hours of the onset of symptoms.¹⁰ The risk of rupture also varies, with approximately 2% of cases rupturing within 36 hours after the onset of symptoms and the risk increases every 12 hours that passes.¹⁰ However, the younger the patient the earlier the perforation has been shown to occur. Approximately 70% of patients less than three years of age experience perforation within 48 hours of the onset of symptoms.¹²

Scoring Systems for Diagnosing Young Patients

To assist physicians in diagnosing infants, young children, and adolescents three scoring systems have been used for several years that are based on signs, symptoms, and laboratory values – Alvarado Score, Pediatric Appendicitis Risk Calculator, and Pediatric Appendicitis Score. However, before going into detail about the scoring systems, it will help to review the normal laboratory values for neutrophils and gain an understanding of the term “left shift”.

Leukocytes make up approximately 1% of the total blood volume in healthy adults (see Table 1).^{17,18} The five types of leukocytes in order from highest percentage to lowest are neutrophils, basophils, lymphocytes, monocytes, and eosinophils. Neutrophils make up approximately 55% - 70% of leukocytes with an average blood count of 2,400 – 7,000 cells per microliter (these numbers are averages and can vary according to the research article consulted).^{17,18} Of patients with appendicitis, approximately 80% - 85% will have a leukocyte count above normal.¹⁹ About 78% of adults with appendicitis have a neutrophil count that is over 75% of their leukocytes, referred to as neutrophilia.¹⁹ Among children, 93% will exhibit neutrophilia.¹⁹

TABLE 1: NORMAL LEUKOCYTE COUNTS ACCORDING TO AGE GROUP¹⁷

Age Group	Leukocyte Count Per Microliter of Blood
0 – 2 weeks	9,000 to 30,000/mm ³
2 – 8 weeks	5,000 to 21,000/mm ³
2 months to 6 years	5,000 to 19,000/mm ³
6 – 18 years	4,800 to 10,800/mm ³
19+	4,500 to 10,500/mm ³

The term “left shift” has been a laboratory term used for many years to refer to the abnormal increase in the proportion of immature neutrophils in the circulating blood.^{3,20} It is used to indicate that the bone marrow has increased the production of neutrophils that are released into the bloodstream prematurely in response to an infection or inflammation. Historically, when hematologists or laboratory technicians were viewing leukocytes through the microscope there would be a diagram of the line of neutrophils from the most immature on the left to fully mature on the right. Even though modern day microscopes no longer have the old style key for counting leukocytes to include neutrophils, the term has stuck throughout history and is still in use.

The modified Alvarado Score for Acute Appendicitis has seven diagnostic categories in which a point system is used of either 1 or 2 points. Two points are given for RLQ tenderness and leukocytosis.³ One point is given for fever, rebound tenderness in the RLQ, migration of pain to the RLQ, anorexia, and nausea or vomiting.¹⁰ The highest score a patient can be assigned is 9 points. A score of 7 points or higher is a good indicator for acute appendicitis.

The Pediatric Appendicitis Score (PAS) also uses a point system based on eight signs, symptoms, and laboratory values. Two points are given for RLQ tenderness when coughing or palpation and tenderness over the right iliac fossa.³ One point is given for anorexia, fever of more than or equal to 38.0 degrees C, nausea or vomiting, leukocytosis of more than 10,000, neutrophilia of more than 7,500, and migration of pain to the RLQ.³ Less than 4 points is a low risk PAS and other causes of the

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acute abdominal pain should be considered. A score of 4 to 6 is an indicator that imaging, such as abdominal computed tomography (CT) scan, magnetic imaging resonance (MRI) or ultrasound (US), can be helpful in arriving at a definitive diagnosis. A score of more than 6 is a high risk PAS and a surgical consult should be arranged.

The Pediatric Appendicitis Risk Calculator (pARC) is also based on eight categories but does not use a scoring system. Rather, the physician indicates what are the signs, symptoms, and laboratory values to arrive at a diagnosis. The pARC is intended for use in children more than or equal to 5 years of age with a duration of acute abdominal pain less than 96 hours. Multiple studies have shown that the pARC is possibly better than the PAS as it more accurately quantifies risk, improving imaging decisions by the physician and leading to fewer false positives.^{21,22} It provides a continuous score rather than a point system cutoff to assist physicians in ruling patients in or out. The clinical signs and symptoms that are recorded include duration of pain in hours, white blood cell count, percentage of neutrophils, presence of maximum RLQ tenderness, presence of guarding, and history of migration of RLQ pain.²³

Imaging Modalities

Acute appendicitis is primarily diagnosed based on clinical evaluation and history and physical examination of the patient. However, imaging such as CT scan, MRI, or US may be used as an adjunct in arriving at a diagnosis. CT scan with intravenous contrast has diagnostic accuracy and excellent visualization of the appendix.¹¹ It is particularly useful to evaluate complications associated with acute appendicitis including presence of an

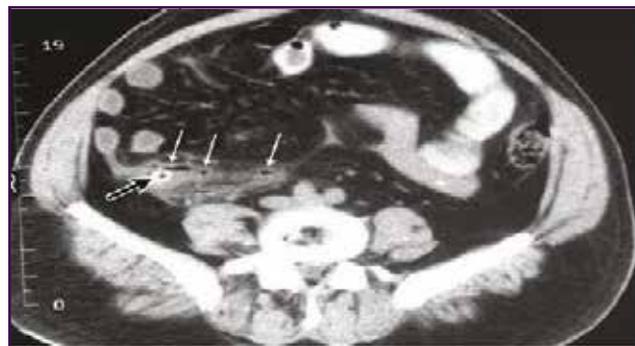


Figure 9 Abdominal contrast enhanced computed tomography scan showing a fecalith (black arrow) at the base of a distended (>6 mm) appendix with intramural gas (white arrow).

abscess, fistula formation, and perforation. The criteria for diagnosing appendicitis when CT scan is used include an appendix with an outer diameter of more than 6 mm to 9 mm, a thick appendiceal wall that measures more than 2 mm to 3 mm, periappendiceal fat stranding, inflamed tissue at the appendiceal base, and the presence of a fecalith.¹¹ A fecalith can be easily detected with CT scan (Figure 9). However, the main disadvantages are exposing young patients to ionizing radiation when their tissues are more radiosensitive and the higher cost.^{4,20}

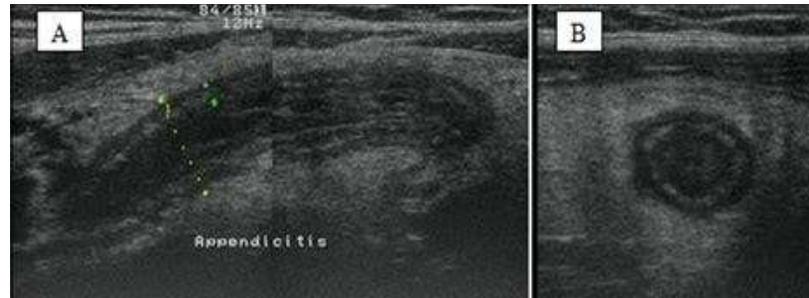


Figure 10 Ultrasound of acute appendicitis

Ultrasound is the preferred imaging modality for children and pregnant women because of the lack of ionizing radiation and contrast media (Figure 10).^{10,20} It is more convenient because it can be performed at the bedside and is less expensive. However, the disadvantage is that it has a lower diagnostic accuracy when compared to CT scans, with reports of 50% to 80% of normal appendices not visualized on US.¹⁰ A primary limitation is its use in patients with an unhealthy weight. The increase in the adipose tissue makes it challenging to visualize the appendix and assess for signs of appendicitis.¹⁰

Abdominopelvic MRI is also useful when US results are inconclusive. It is equal to CT scans in accuracy and visualization of the appendix, without the risk of ionizing radiation. However, it has several limitations including high cost, the need for a specialized interpreter who has the skills for interpreting the images and longer scan times. Because of the increased scan time, younger children may require sedation. Additionally, intravenous gadolinium contrast should not be used in pregnant women because of placental diffusion.¹¹

Conditions That Can Mimic Acute Appendicitis in Infants and Sexually Active Adolescents

There is a wide range of conditions that can cause abdominal pain that may mimic acute appendicitis. Thorough

clinical evaluation that includes history and physical examination and laboratory and imaging studies are essential to rule appendicitis in or out. The following are examples of those conditions.

- Ectopic pregnancy – Should be ruled out in sexually active adolescent females. It can present with lower abdominal pain, amenorrhea, and possibly vaginal bleeding.¹¹
- Gastroenteritis – As previously stated, gastroenteritis is a common misdiagnosis. It causes symptoms like appendicitis including abdominal pain, diarrhea, nausea and vomiting.
- Intussusception – The condition may be initially missed when the patient is being evaluated because it mimics the pain symptoms of appendicitis. It presents with intermittent, severe abdominal pain and an abdominal mass that can be felt upon palpation.
- Pelvic inflammatory disease – This condition should be considered in sexually active adolescent women who present with lower abdominal or pelvic pain.¹¹

Part 2 will include a broad discussion of the various facets of an appendectomy and focus on the recent information regarding antibiotic non-operative treatment.

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Review of the Appendix and Appendicitis *Part 1*

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1. **What percentage of patients with acute appendicitis have a fever?**
 - a. 40%
 - b. 35%
 - c. 30%
 - d. 25%
2. **What histologically differentiates the appendix from the rest of the colon?**
 - a. Tissue layers are thinner
 - b. There are only three layers
 - c. Contains lymphoid tissue
 - d. Is not attached by mesentery
3. **Which white blood cell's count increases during appendicitis?**
 - a. Lymphocytes
 - b. Eosinophils
 - c. Monocytes
 - d. Neutrophils
4. **Where is the abdomen most tender when the pain has localized?**
 - a. Periumbilicus
 - b. Left lower quadrant
 - c. McBurney's point
 - d. Pubic tubercle
5. **The appendicular artery is a branch of the:**
 - a. ileocolic artery.
 - b. anterior cecal artery.
 - c. right colic artery.
 - d. inferior mesenteric artery.
6. **Which of the following is a common misdiagnosis of appendicitis?**
 - a. Esophagitis
 - b. Mesenteric ischemia
 - c. Peptic ulcer
 - d. Gastroenteritis
7. **Which of the following refers to the patient experiencing pain upon flexing the hip?**
 - a. Rovsing sign
 - b. Psoas sign
 - c. Obturator sign
 - d. Dunphy sign
8. **What is the reason for patients initially feeling pain from appendicitis in the middle of the abdomen?**
 - a. Afferent nerve fibers attached at T10 level of spine.
 - b. Vagus nerve is irritated by the inflammation.
 - c. Appendicitis causes inflammation of surrounding tissues.
 - d. Fluid buildup places pressure on the peritoneal layer.
9. **What is the most common anatomic position of the appendix?**
 - a. Subcecal
 - b. Pelvic
 - c. Post-ileal
 - d. Retrocecal
10. **What should the CST be ready for the surgeon to perform if a GEP-NET is larger than 2 cm?**
 - a. Ileectomy
 - b. Right hemicolectomy
 - c. Appendectomy
 - d. Total colectomy

REVIEW OF THE APPENDIX AND APPENDICITIS *PART 1*

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2	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
3	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
4	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
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7	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
8	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
9	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
10	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>

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