REVIEW ARTICLE: MANAGEMENT OF ACUTE APPENDICITIS: A REVIEW

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ABSTRACT
The diagnosis and treatment of acute appendicitis is a rapidly changing landscape.
This review article takes a panoramic look at the appendix and appendicitis along with the various treatment approaches which have been utilized. Non operative management is discussed and the challenges and pitfalls inherent in this approach in a resource challenged environment are examined. Appendicitis in special populations is highlighted and newer surgical options for appendectomy are outlined.

Key Words: *Modern, Management, Appendicitis, Adults, Children.*

Introduction

Acute appendicitis remains the most common acute abdominal condition which a medical practitioner will encounter in his career[6]. While management follows an ever evolving set of principles, proper diagnosis is the sheet anchor and *sine qua non* of treatment. Management options for appendicitis have evolved and multiplied in recent times resulting in a more complex clinical, diagnostic and therapeutic landscape. [20]

Historical Perspective

Leonardo da Vinci first depicted the appendix in anatomic drawings in 1492 [3] while Berengaria da Carpi was the first to describe the appendix in 1521.[4] Philippe Verheyen coined the term appendix vermiformis in 1710[45] while Giovanni Morgagni provided the first detailed anatomic description of the appendix in 1719 [3, 4.] Claudius Amyand in 1736 successfully removed an inflamed appendix from a hernia sac from a 14-year-old boy[3,4,6]. Lawson Tait in 1880 performed the first deliberate appendectomy for appendicitis.[3] Reginald Fitz in 1886 correctly identified the appendix as the primary cause of right lower quadrant inflammation. He coined the term appendicitis and recommended early surgical treatment [3,4.]

Chester McBurney in 1889 described characteristic migratory pain and localization of the pain along an oblique line from the anterior superior iliac spine to the umbilicus.[4]. Later in 1894 he described a right lower quadrant muscle splitting incision for removal of the appendix [3, 4] while R.H. Dawbarn in 1895 advocated invagination of the appendiceal stump to prevent fistula [3,4].
A.J Ochsner in 1902 advocated non-operative treatment to localize spreading peritonitis [4,5].
H.A. Kelly in 1905 advocated against "ligating, amputating and burying the little stump" [3,4].
The introduction of broad-spectrum antibiotics in the 1940's improved the

mortality rate from appendicitis. De Kok in 1977 carried out laparoscope aided appendectomy with a minilaparotomy before Kurt Semm in 1982 carried out the first full laparoscopic appendectomy. [4] This has since become the surgical modality of choice in most practice environments.

Anatomy

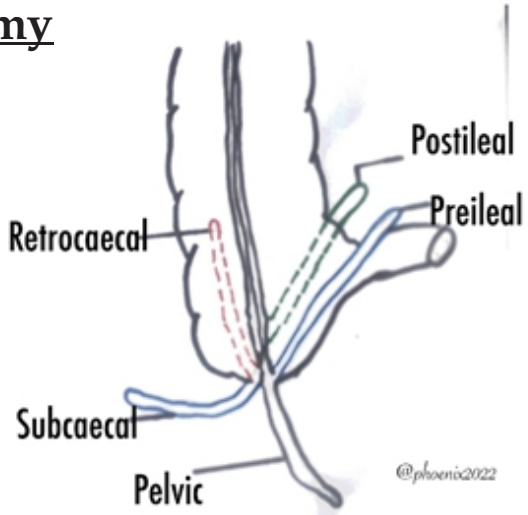

Figure 1-Common positions of the Appendix.

The appendix arises from the posteromedial aspect of the caecum about 2.5cm from the ileocaecal valve. It varies in length from 12mm to 25cm and varies in position, most commonly being retrocaecal.

The appendicular artery, a branch of the ileocolic artery, represents the entire vascular supply of the appendix. It runs first in the edge of the mesoappendix and then distally along the wall of the appendix. An accessory appendicular artery can arise from the posterior caecal artery and may be damaged during appendectomy causing significant bleeding. It should be searched for and ligated once the main appendicular artery has been controlled [1].The appendicular vein drains blood from the appendix. It is located in the mesoappendix and accompanies the appendicular artery. It drains into the ileocolic vein [1].

Lymphatic drainage of the appendix is into lymph nodes in the mesoappendix and from there into the ileocolic lymph nodes running along the ileocolic artery and via coeliac nodes into the cisterna chyli [1].The appendix is innervated by sympathetic and parasympathetic nerves from the superior mesenteric plexus. Afferent fibres for pain accompany the sympathetic nerves and enter the spinal cord at the level of the 10^{th} thoracic segment [1].

Embryology.
The appendix arises from the midgut. The caecal diverticulum appears at the sixth week of life and is the precursor of the caecum and appendix [1].The appendix is histologically visible by the eighth week of life.

Histology.

The inner lining facing the lumen is covered by a glandular epithelium with intestinal mucus glands that extend into the deeper layers of the mucosa. The glands are lined with epithelial cells (simple columnar epithelium) and a high number of mucus producing goblet cells. The lamina propria usually contains lymphocytes that partly obscure the muscularis mucosa which separates the mucosa from the submucosa. The submucosa is largely occupied by lymphoid tissue arranged in primary and secondary lymphoid follicles.

An inner circular muscular layer and a thin external longitudinal muscle layer make up the muscularis externa which encircles the appendix. Outside the muscularis externa is a serosa containing blood vessels and nerves [2,6].

Functions of the Appendix.

- The Safe House Theory: The appendix protects a collection of beneficial gut bacteria when diarrhoea and other diseases wipe them out elsewhere in the gut. Once the immune system has addressed the infection, the bacteria emerge from the appendix biofilm and recolonize the gut [7].

- Immune Function: The appendix has a distinct abundance of natural killer (NK) lymphocytes that produce cytokines and chemokines rapidly following activation [7].

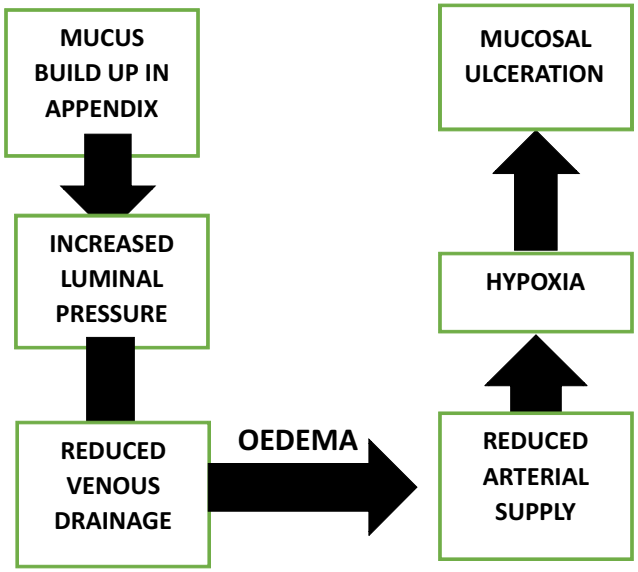

Figure 2- Pathophysiology of Acute Appendicitis[3,4,6,8].

Clinical Features.

History.

- Pain: Initial periumbilical, epigastric or generalized abdominal pain which is due to hyperperistalsis of the appendix to overcome obstruction. It is visceral in origin. After some hours the pain shifts and becomes localized in the right lower quadrant with tenderness on palpation. This pain is somatic in origin.

The position of the appendix may affect the manifestation of pain with a retrocaecal appendix causing minimal or no symptoms. A pelvic appendix may cause suprapubic pain, urinary symptoms or even pain on defecation [3, 4].Other features include

Anorexia

Nausea and vomiting: This is due to bowel wall distension.

Constipation: This is usual but diarrhea may also occur

Fever

Frequency and dysuria: This may be due to an inflamed pelvic appendix.

Physical Examination.

- Fever: This may be absent in the early stages or modified by intake of analgesics, antipyretics and antibiotics especially in our environment where self-medication is the norm.
- Tachycardia: This is due to fever and sympathetic response to pain.
- Hypotension: This may be due to sepsis following perforation.
- Tenderness in the right lower quadrant at McBurney's point
- Rebound tenderness **(**Blumberg's sign).
- Rovsing's sign: Palpation in the left lower quadrant causes pain in the right lower quadrant.
- Obturator sign: Internal rotation of the right hip results in pain.
- Dunphy's sign: Increased pain in the right lower quadrant on coughing, hopping or shaking the bed.
- Iliopsoas sign: Extending the right hip causes pain along the posterolateral back and hip and may indicate retrocaecal appendicitis.
- Rosenstein (Sitkovskiy) sign: Increased pain in the right lower quadrant when the patient lies on the left side [3,4,5,6].

Investigations.

- Full Blood Count: This may be normal in the early stages or may show a polymorphonuclear leukocytosis. It may be modified by medication [3,4,5].
- Urinalysis.
- C - reactive protein (CRP) **-** This may be elevated.
- Bilirubin**-** This may be elevated.
- Fibrinogen- This may be elevated.
- Lactoferrin**,** Calprotectin and Serum Amyloid A**-** Significantly elevated in acute appendicitis [16,18].
- Pregnancy Test in females of child bearing age.
- Electrolytes, Urea and Creatinine
- Plain Abdominal radiograph: This is rarely helpful but a faecolith may be visualized in the right lower quadrant. Other findings may include loss of the psoas shadow and deformity of the caecal outline. Free air under the diaphragm may be seen in perforated appendicitis [3,4,5].
- Ultrasound: This is operator dependent and might affect diagnostic accuracy. There is however zero radiation exposure. Typical findings consistent with acute appendicitis

include [4]:
Distended appendix of 7mm or more in anteroposterior diameter.

A thick walled non-compressible luminal structure seen in cross section (Target sign).
Increased wall vascular flow on colour enhancement (Ring of fire sign).

Presence of a faecolith.

- Computed Tomography: Contrast enhanced low dose tomography is the investigation of choice. It provides less radiation exposure and diagnostic yield is equivalent to conventional CT. Classic findings include [4]:

  Distended appendix of 7mm or more in anteroposterior diameter.

  Circumferential wall thickening and enhancement (Target or Halo sign).

  Peripheral fat stranding as the disease progresses.

  Oedema, peritoneal fluid or a periappendiceal abscess.

  Presence of a faecolith.

CT scan is not a routine investigation in all cases of acute appendicitis and is of greatest value in older patients in whom the differential diagnosis is complex, clinical findings are equivocal and surgery carries more risk [18].
Magnetic Resonance Imaging: Findings are similar to those found on computed tomography. It is of greatest value in diagnosis of acute abdominal pain in pregnant women [3,4]
Scoring systems in acute appendicitis.
In an attempt to improve diagnosis and reduce the negative appendectomy rate, several scoring systems have been proposed. The first of these was the Alvarado scoring system which was introduced in 1986 by Alfredo Alvarado, an American general surgeon [35, 36]. This has since been further refined into the Modified Alvarado Score [36]

The Alvarado score is not reliable in differentiating complicated from uncomplicated appendicitis in elderly patients and is less sensitive in patients with HIV. [4]

Table 1-Modified Alvarado Score.

Parameters	**Points**
Migratory Right iliac fossa pain	1.0
Anorexia	1.0
Nausea and Vomiting	1.0
Tenderness Right Iliac fossa	2.0
Rebound Tenderness Right Iliac fossa	1.0
Fever	1.0
Leucocytosis	2-0
Total Score	**9.0**

<3-Low likelihood 4-6-Consider further imaging >7-High likelihood

Appendicitis Inflammatory Response (AIR) Score.

This resembles the Alvarado Score but uses more graded variables and includes C-reactive protein estimation [3,4]. Studies have shown it to perform better than the Alvarado score in predicting acute appendicitis.[3,4].

Parameters		**Points**
Vomiting		1.0
Pain in the Right iliac fossa		1.0
Rebound Tenderness		
	Light	1.0
	Medium	2.0
	Strong	3.0
Body Temperature>38.5^{o}C		1.0
Polymorphonuclear Leucocytosis		
	70-84%	1.0
	≥85%	2.0
White Blood Cell Count		
	10.0-14.9 x10^{9}/l	1.0
	≥15.0 x10^{9}/l	2.0
C-Reactive Protein concentration		
	10-49g/l	1.0
	>50g/l	2.0

0-4: Low Probability 5-8: Indeterminate Group 9-12: High Probability

The AIR score along with the Adult Appendicitis Score (AAS) are currently the best performing clinical prediction scores and have the highest discriminating power in adults with suspected appendicitis[18].

Parameters		**Scores**
Pain in Right Lower Quadrant		2.0
Pain Relocation		2.0
Right Lower Quadrant Tenderness		3/1*
Guarding		
	Mild	2.0
	Moderate or Severe	4.0
White Blood Cell Count		
	>7.2 and < 10.9 x10^{9}/l	1.0
	>10.9 and < 14.0 x10^{9}/l	2.0
	>14.0 x10^{9}/l	3.0
Proportion of Neutrophils		
	>62 and <75%	2.0
	>75 and <83%	3.0
	>83%	4.0
CRP (mg/l), Symptoms< 24hours		
	>4 and <11mg/l	2.0
	>11 and <25mg/l	3.0
	>25 and <83mg/l	5.0
	>83mg/l	1.0
CRP (mg/l), Symptoms >24hours		
	>12 and <53	2.0
	>53 and <152	2.0
	>152	1.0

*Men and Women aged 50^{+}/Women aged 16-49
Table 3-Adult Appendicitis Score (AAS).
In children the Paediatric Appendicitis Score is the most helpful scoring system [18].

Parameters	**Scores**
Right Lower Quadrant pain with cough, percussion or hopping.	2.0
Right Lower Quadrant tenderness on light palpation.	2.0
Migration of pain to the Right Lower Quadrant.	1.0
Anorexia.	1.0
Nausea or Vomiting	1.0
Fever >38^{o}C.	1.0
Leucocytosis (>10 x10^{9}/l).	1.0
Shift to the Left (>75% Neutrophilia).	1.0
	10.0

1-3: Low Risk 4-7: Intermediate Risk 7-10: High Risk
Table 4-Paediatric Appendicitis Score (PAS)
RIPASA Score.
The Raja Isteri Penigran Anak Saleha Appendicitis (RIPASA) score was developed in 2008 at the hospital of the same name in Brunei Darussalam. The score has 18 parameters with a high sensitivity, specificity and diagnostic accuracy especially in Asian and Middle Eastern populations [11, 18].

Appendicitis in special populations.

Children.
Diagnosis may be difficult in this age group since they cannot explain their symptoms properly. Perforation is thus a very common sequel. Lethargy, irritability and anorexia may be present in the early stages with fever, vomiting and abdominal pain manifesting as the disease progresses.
In equivocal cases ultrasound is useful in differential diagnosis. Appendicitis tends to be more florid in children because of the relatively large size of the appendix and the underdeveloped omentum which is unable to localize infection [3,4,5,10,15,21,30,31].

The Elderly.
Diagnosis may be difficult in this age group because the history is usually atypical. The pain may be vague and diffuse, localizing in the right lower quadrant only after several days. Tenderness may also not be very marked. Diagnosis is thus usually delayed and given the atrophic nature of the omentum, perforation and other complications are relatively frequent [3,4,5].

Pregnancy.
Appendicitis is more common in the first two trimesters and diagnosis is relatively straightforward[20,39]. In the third trimester there may be a diagnostic challenge due to upward displacement of the caecum and appendix by the enlarging uterus with the pain thus manifesting in the right hypochondrium [20,39].

Immunocompromised patients.
The incidence of appendicitis is increased in HIV positive patients [4]. Clinical presentation is similar to that of uninfected patients but it is important to note that most HIV positive

patients will not present with leukocytosis [4]. The incidence of perforation is also higher and this may be related to a low CD4 count. In the differential diagnosis of right lower quadrant pain in HIV positive patients the differential diagnostic window should be widened to include opportunistic infections.

Differential Diagnosis of Acute Appendicitis.

The differential diagnosis of appendicitis includes a wide range of surgical, gynaecological and medical diseases which the clinician needs to be aware in order to enable proper patient management.

a. Intra-abdominal diseases [3,4,5,6].

- Typhoid perforation.
- Perforated peptic ulcer.
- Acute cholecystitis.
- Acute intestinal obstruction.
- Amoebic perforation of large bowel.
- Acute diverticulitis.
- Non-specific mesenteric adenitis in children.
- Intussusception.
- Acute Crohn's disease.
- Meckel's diverticulitis
- Non-specific abdominal pain.
- Leaking aortic aneurysm.
- Mesenteric infarction
- Colonic carcinoma
- Torsion of the appendices epiploicae.

b. Gynaecological diseases [3,4,5,6].

- Salpingitis.
- Ruptured ectopic gestation.
- Twisted ovarian cyst.
- Ruptured Graafian follicle (Mittelschmerz).
- Endometriosis.

c. Urological diseases [3,4,5,6].

- Right ureteric colic.
- Right pyelonephritis.
- Right acute epididymo-orchitis

d. Medical conditions [3,4,5,6].

- Gastroenteritis.
- Diabetic ketoacidosis
- Herpes zoster.
- Sickle cell crisis.
- Right lobar pneumonia.
- Malaria.
- Tonsillitis.
- Pancreatitis.
- Henoch-Schonlein purpura.
- Acute intermittent porphyria

Treatment of Acute Appendicitis.

The conventional treatment for appendicitis is appendectomy.

Recent studies [wewtn] have however revealed the benefits of non-operative management (NOM) in patients with uncomplicated, non-obstructive appendicitis. Uncomplicated appendicitis is defined as appendicitis without perforation, abscess or mass formation.

NOM consists of:

- Nil per oral regime.
- Intravenous fluids.
- Intravenous antibiotics.

There is resolution in 80-90% of cases but 15-20% will recur within one year [6].

NOM is contraindicated in:

- Complicated appendicitis (perforation, abscess, mass).
- Appendicitis with faecolith obstruction.
- Patients with severe co-morbidities (diabetes, hypertension, COPD).
- Elderly patients.
- Immunosuppressed patients.

It should however be stated without

equivocation that NOM is a proposition fraught with risk in resource challenged environments of the tropics and subtropics. Most of those patients do not present early and usually have complicated appendicitis on hospital review.

In addition to this a large number of them have already commenced antibiotics obtained from various sources. Proper case selection is necessary in implementing NOM and the surgeon must be ready to change his treatment approach if the patient no longer satisfies the above inclusion criteria.

Appendectomy.

Open Appendectomy.

This is done via a gridiron or Lanz incision, the latter being preferred because exposure is better, extension is easier and cosmesis is superior. The incision is carried down through the layers of the anterior abdominal wall and the peritoneal cavity is entered. The caecum is identified by the presence of taeniae coli and the appendix delivered. The appendicular vessels are clamped and ligated in the mesoappendix and the base of the appendix is crushed, clamped and ligated. Purse string inversion of the appendix stump does not offer any additional advantages in outcome [9,17, 18,19].

Laparoscopic Appendectomy.

This is the current gold standard in the operation of appendectomy, offering less morbidity and reduced hospital stay, reduced wound infection, less post-operative complications and a faster return to work [6,8,9,17,18, 43].

Contraindications to laparoscopic appendectomy.

- Lack of surgical expertise and necessary equipment.
- Severe pulmonary disorders (COPD, interstitial lung disease)
- Bleeding diatheses
- Severe heart failure.
- Portal hypertension.
- Intolerance of Trendelenburg positioning.
- Severe adhesions from previous abdominal surgery.
- First trimester of pregnancy.
- Radiation therapy.
- Immunosuppressive therapy.

Single incision laparoscopic surgery (SILS).

This technique uses one incision to enter the peritoneal cavity and to deploy various operative ports and instruments as needed. The primary reason for this surgery is cosmesis but it also results in a longer procedure and is more expensive [8, 9].Post-operative pain is also more significant than in mainstream laparoscopic appendectomy.

Natural Orifice Transluminal Surgery (NOTES).

This is a procedure where the peritoneal cavity is accessed via a natural orifice such as the mouth, vagina or rectum. Once the peritoneum is accessed in this fashion the appendectomy is performed. Hybrid NOTES is a procedure where in addition to entry via a natural orifice additional abdominal trocars are deployed.Advantages include decreased risk of wound infections, trocar hernias and neuropathic scar pain [8,9,44].

Endoluminal Appendectomy.

A modified colonoscope is passed via the rectum or a colostomy until the appendicular orifice is visualized and cannulated with a shark tooth grasping forceps. The appendix is then inverted into the bowel lumen, an endoloop placed at the base and the appendix

transected with a snare loop. Haemostatic clips are used to reinforce the closure of the appendicular lumen [9,44].

Appendectomy and special situations.

Appendix not found: The caecum is mobilized and the taeniae coli are traced to their point of convergence on the caecum. Only if the appendix cannot be located after this maneuver is the diagnosis of absent appendix made [6].

Appendicular Tumour**:** Small tumours (<2cm) can be treated by appendectomy. Larger tumours will require a right hemicolectomy [6].

Appendix Abscess: If found by imaging percutaneous drainage and intravenous antibiotics are the modalities of choice. If found at operation the abscess is drained and intravenous antibiotic therapy commenced. In the face of a frankly necrotic appendix or caecum a right hemicolectomy may be required. An appendix abscess presenting during management of an appendix mass will usually not resolve via percutaneous drainage and will need a laparotomy for proper resolution [6].

Appendix Mass**:** If the patient's condition is satisfactory the Ochsner-Sherren regime is instituted.[6] This consists of:

- 4 hourly measurement of pulse and temperature.
- Intravenous fluids with maintenance of proper fluid balance.
- Intravenous antibiotics.
- Daily monitoring of the size of the mass by marking the limits with a skin pencil.

Clinical improvement is usually apparent within 48 hours. Using this regime >90% of cases will resolve and it is no longer mandatory to carry out an interval appendectomy after 6-8 weeks.

Appendectomy should however still be considered in vulnerable populations like very young children and the elderly who are likely to present with perforation and will tolerate a new episode of appendicitis poorly. Patients over the age of 40 years should have colonoscopy and follow up imaging to ensure resolution since about 5% may have an underlying appendicular or colonic malignancy [6].

There are specific indications for abandoning this regime [6]:

- A rising pulse rate.
- Increasing or spreading abdominal pain.
- Increasing size of the mass.

Appendicitis in Pregnancy

Appendicitis is the most common non-obstetric emergency in pregnancy, occurring in 1 in 500 pregnancies[39]. Diagnosis may pose a challenge because the history and physical examination may be equivocal, some laboratory parameters like leucocytosis are normal in this state and imaging modalities like CT scan are contraindicated [12,16,17].Ultrasound and MRI of the abdomen without contrast are the imaging modalities of choice [20].

Rapid diagnosis of acute appendicitis in pregnancy is very necessary because of the adverse effects of complications. It is important to note that there is no room for non-operative management of appendicitis in pregnancy [39].

Appendectomy in pregnancy may be by the open or laparoscopic route even though concerns have been raised about the possible effects of pneumoperitoneum on the pregnancy. [39]

Conclusion

Appendicitis remains the most common abdominal emergency.

Prompt and accurate diagnosis is key in treatment.

Management has undergone a seismic change in recent years with nonoperative management gaining currency. This however requires proper case selection to ensure that the patient meets the laid down criteria and will indeed benefit from it.

NOM remains a challenge in the tropics, subtropics and other low income practice environments. This is because most patients will only present to orthodox care after exhausting other options. Most will show definite and florid features of appendicitis, thus narrowing the treatment options to surgery. In summary therefore, widespread use of NOM in our environment will have to await improved patient awareness, education, and improvement in imaging and other diagnostic services
History and physical examination are very important in diagnosis and will remain so for the foreseeable future.

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