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REVIEW

Acute appendicitis and its treatment: a historical overview

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Abstract

Purpose Acute appendicitis (AA) is the leading cause of acute abdomen worldwide, with an incidence of 90–100 cases per 100,000 individuals annually and a lifetime risk of 7–12%. Despite its prevalence, historical accounts of AA are limited, particularly when compared to conditions like haemorrhoids, likely due to the appendix's internal location. This article traces the historical evolution of AA treatment from ancient times to the present, highlighting key contributions.

Methods A review of common research databases and relevant literature on AA was conducted.

Results Evidence from ancient Egypt suggests early recognition of the appendix, referring to it as the "worm of the bowel." However, detailed anatomical descriptions and treatment approaches for AA did not emerge until the Renaissance, particularly with contributions from Leonardo da Vinci and Berengario da Carpi. The article traces the progression of AA management, including the first autopsies and surgeries, the development of surgical techniques predating anaesthesia and antisepsis, and advancements achieved from the nineteenth to the twenty-first century. The shift from conservative to surgical approaches is discussed, alongside innovations such as laparoscopic appendicectomy, single-incision laparoscopic surgery (SILS), natural orifice transluminal endoscopic surgery (NOTES), and endoscopic retrograde appendicitis therapy (ERAT). The impact of the COVID-19 pandemic on AA treatment, including adaptations in medical practices, is also explored.

Conclusions This review highlights the significant historical developments in AA treatment and its pivotal role in advancing abdominal surgery.

Keywords Acute appendicitis · History · Historical overview · Appendicectomy · Appendectomy · Laparoscopy · ERAT · Laparoscopic · History of medicine

Background

Acute appendicitis (AA) is globally recognised as the leading cause of acute abdomen, with an incidence of approximately 90–100 new cases per 100,000 individuals annually [1, 2]. The lifetime risk of experiencing an episode is estimated to be between 7 and 12% [3, 4]. Despite its prevalence, historical records of this condition are sparse, in contrast to those for conditions such as haemorrhoids and rectal prolapse [5]. This discrepancy may stem from the internal and 'invisible' anatomical location of the appendix, in contrast to external conditions such as haemorrhoids. Furthermore, the appendix itself lacked a clear anatomical description until the Renaissance.

Consequently, no specific treatment strategies were proposed until the mid-nineteenth century. Given its high frequency and the relative simplicity of surgical management, the history of AA surgery is not only intriguing on its own

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but also serves as a remarkable metaphor for the evolution of abdominal surgery.

The aim of this article is to provide a comprehensive overview of the historical progression of AA treatment, highlighting the most significant contributions from ancient times to the present.

Ancient history

It is plausible that the ancient Egyptians were aware of the appendix's existence due to their practice of preserving organs in canopic jars during mummification. Notably, some jars bearing inscriptions referencing the 'worm of the bowel' have been discovered. Furthermore, Herodotus in V century B.C., during a visit to Egypt, reported the presence of physicians specialised in bowel diseases [6].

In ancient times, some cases of right iliac fossa pain associated with pus discharge have been described, but it is impossible to make a differential diagnosis with other abdominal pathologies.

This is exemplified by ***Aretaeus of Cappadocia***, who drained an abscess in the right lower quadrant around 50 A.D., and ***Soranus of Ephesus***, who managed a similar case around 100 A.D. [7]. There is no evidence to suggest an understanding of the appendix or its inflammation during the Middle Ages.

Renaissance

The first known drawing of the vermiform appendix (Fig. 1) belongs to Leonardo da Vinci and is dated to approximately 1508 [8]; however, the earlier structured description of the organ is ascribable to ***Berengario da Carpi*** (also known as Jacopo Barigazzi) (Fig. 2) [9], an Italian anatomist who lived between 1466 and 1530, spending most of his career in Bologna [10]. The description was reported on "Isagogae Breves" in the section "De Sacco Intestino" in 1522 (Fig. 3): "*it is found […] attached to the colon and to the ileum and is, as it were, a sort of addition. Its form appears compactly pressed together. Inside, it is hollow and is less than a little finger in breadth; it is three inches, or nearly that, in length.*'' [11].

Twenty-one years later, in 1543, ***Andreas Vesalius*** (1514–1564) (Fig. 4) published his masterwork "De Humani Corporis Fabrica," which, in "Libri Septem," reported the first detailed illustration of the appendix. Vesalius referred to the appendix as "*the blind intestine*" and described it as ''*vermis in modo convolutus*'' (curled in the manner of a worm) [12] (Fig. 5).

In 1554, ***Johannes Fernelius*** reported an autoptic observation likely indicative of AA (Fig. 6). He described a perforation of the caecum in a seven-year-old girl who died following an episode of abdominal pain, although his account does not specifically mention the appendix [13].

Contemporaneous and subsequent authors, including ***Guido Guidi*** (1544), ***Johann Eichmann*** (1557), ***Realdo Colombo*** (1559), ***Gabriele Falloppio*** (1561), and ***Gaspard Bauhin*** (1605), consistently used the term 'caecum' (blind intestine) to refer to both the appendix and the caecum, often described as 'caput coli' (head of the colon).

Bartolomeo Eustachio (circa 1510–1574), an anatomist contemporary to the period, initially employed the term ''*vermiformis*'' to describe the appendix. However, the widespread adoption of the term *appendix vermiformis* emerged only two centuries later, following the posthumous publication of his works by ***Bernhard Siegfried Albinus*** (commonly referred to as Albinus) in 1744 [12]. Notably, no significant advancements in this field were made for approximately two centuries thereafter.

Eighteen century

New attention to the appendix was given by the Italian ***Giovanni Battista Morgagni*** (1682–1771) (Fig. 7), "*father of pathologic anatomy and pioneer of modern medicine*" [14], who published a very detailed drawing associated with the description of the organ's lumen and its continuity with the caecum in 1719 [15] (Fig. 8).

Johann Nathanael Lieberkühn (1711–1756), a German physician, further contributed to this field in 1739 with a pivotal essay on the appendix, marking the first description of the eponymous mucosal crypts [6].

The earliest documented autopsy clearly indicating an acute appendicitis was performed by ***Lorenz Heister*** (1683–1758) (Fig. 9), who described a perforated appendix accompanied by an abscess in 1711. This case, however, was not published until 1753.

Claudius Amyand (1880–1740) (Fig. 10), born circa 1680 in Saintonge (France) but naturalised British in 1698 and was compelled to flee to the United Kingdom following the revocation of the Edict of Nantes as Huguenot, performed a landmark surgery in 1735. He operated on Hanvil Anderson, an 11-year-old boy who had developed perforated appendicitis due to a previously swallowed pin. This surgery, which was conducted at St. George's Hospital in London, is recognised as the world's first successful appendicectomy [16]. This case was exceptional because the appendix was situated in the sac of an inguinal hernia, a condition currently referred to as Amyand's hernia [17].

However, the first successful appendicectomy may have occurred earlier, in 1731, by ***William Cookesley***, albeit unrecognised during the procedure. Cookesley, a general practitioner surgeon in Crediton (England), excised a section of "*necrotic ileum*" during an operation for a strangulated inguinal hernia on Abraham Pike, a 30-year-old chimney

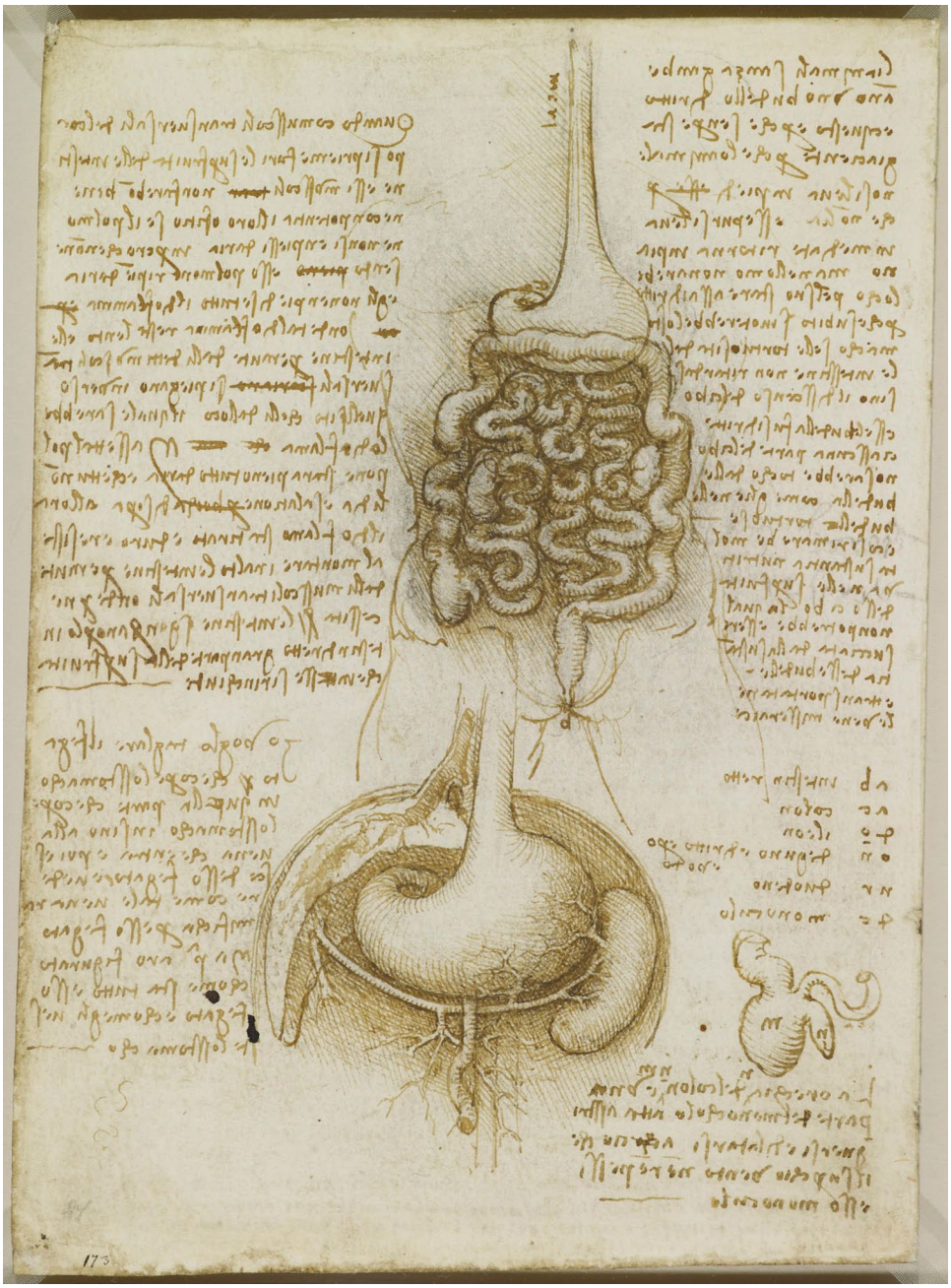

Fig. 1 Leonardo Da Vinci (1452–1519), "The gastrointestinal tract, the stomach, liver and spleen" c. 1508 (Royal Collection) https://www.rct.uk/collection/. Public domain

sweep, who had lived with a reducible inguino-scrotal hernia for several years [18]. Thirty-one years after the operation, the patient died of unrelated causes, and an autopsy by John Symons revealed a missing appendix. William Hunter corroborated the theory of an "*accidental appendicectomy*" leading to the classification of this case as an unrecognised Amyand's hernia [19]. This episode was documented [20], and the specimen is located at the Hunterian Museum in Glasgow (Fig. 11).

Before the introduction of general anaesthesia in 1846, such excruciating operations necessitated multiple assistants to restrain patients, making these procedures quite dramatic. The anguish experienced in these conditions is vividly depicted in Gaspare Traversi's paintings "*la visita medica*" (Fig. 12) and "*l'intervento chirurgico*" (Fig. 13), created around 1750 by the Neapolitan artist.

First half of the nineteenth century

For many years, the notion that inflammation of the appendix could lead to acute peritonitis was not recognised, and there were no specific treatments available for this condition. However, the findings of various authors have gradually revealed that the appendix could be the initial site of

Fig. 2 Portrait of Berengario da Carpi (1460–1530), 1495 (Museum of Palazzo dei Pio, at Carpi, Italy). Public domain

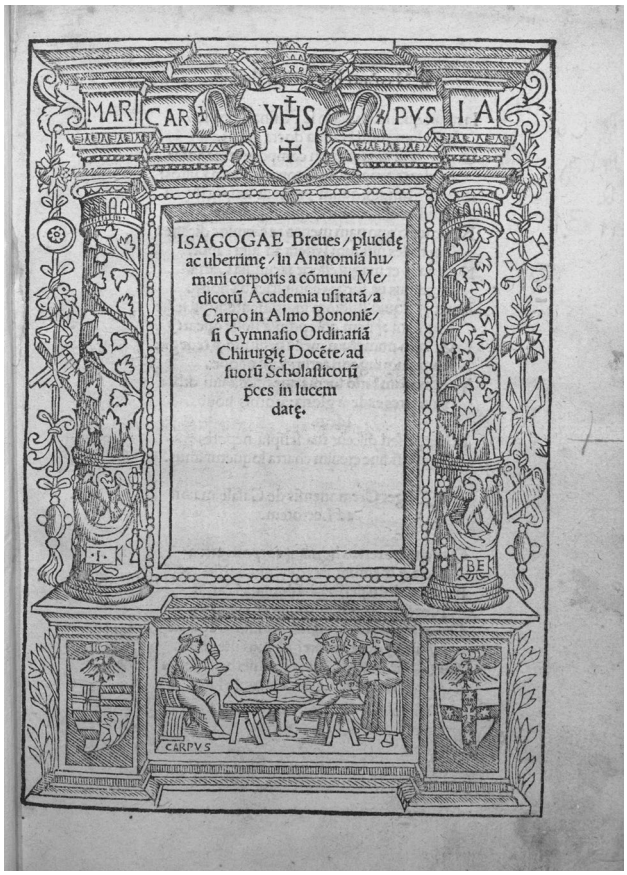

Fig. 3 Frontispiece of "Isagogae Breves 1522" (Wikipedia) https://upload.wikimedia.org/wikipedia/commons/4/41/Isagogae_breves_in_anatomiam_humani_V00114_00000010.tif Public domain

abdominal inflammation, laying the groundwork for specific treatments.

Key figures in this development included ***James Parkinson*** (London, 1755–1824), more famously known for his description of "*paralysis agitans*" (Parkinson's disease). In 1812, he treated a 5-year-old boy. Unfortunately, the patient developed early perforation, leading to an inevitable fatal outcome with the treatments available at that time. Nonetheless, this tragic case was not without value, as Parkinson meticulously documented the progression from the initial symptoms to the autopsy, offering a comprehensive account of the natural history of the disease and contributing to greater awareness of this relatively unknown condition [21].

Another significant contributor was ***Thomas Hodgkin*** (Fig. 14), who later became famous for identifying Hodgkin lymphoma. In his 1836 work, "Lectures on the Morbid Anatomy of the Serous and Mucous Membranes" [22], he described the case of a young medical student who died of peritonitis. Hodgkin proposed that appendicitis could be the origin of the disease and hypothesised that the initial trigger for AA might be the obstruction of the appendiceal lumen by fecaliths.

Despite the contributions of these early pioneers, the concept that inflammation of the appendix could cause peritonitis was not widely accepted during the first half of the nineteenth century. A notable instance of opposition to these emerging ideas came from ***Guillaume Dupuytren*** (1777–1835), a prominent surgeon in Paris.

Dupuytren firmly believed that inflammation on the right side of the abdomen originated from the caecum rather than the appendix [23]. His position significantly shaped the medical community's understanding of the issue, overshadowing the contributions of ***Francois Melier***, who, in 1827, published six autopsy cases of acute appendicitis, proposing appendicectomy to treat the disease [23].

In 1840, ***Richard Bright*** and ***Thomas Addison***, in their "*Elements of the Practice of Medicine*" [24], described multiple post-mortem dissections that revealed abscesses in the right iliac region, attributing their origin to diseases of the appendix. They postulated that the appendix is prone to inflammation, ulceration, and even gangrene, noting that the caecum could also become inflamed and ulcerated. The pathophysiological theory they proposed was that an obstruction in the lumen of the appendix could lead to its painful enlargement due to the accumulation of its own secretions.

Fig. 4 Portrait of Andrea Vesalio (1514–1564) "De humani corporis fabrica 1543" (Wikipedia) https://images.app.goo.gl/eC7KdyKmsXJUDMsY9. Public domain

They hypothesised that this obstruction could be caused by faecal matter or foreign objects, such as a cherry stone, or more specifically, a distinct type of concretion composed of layers of earthy phosphates (fecalith). Following these insights, the concept of "appendicitis" gained widespread acceptance, and knowledge about it began to disseminate globally.

The first documented autopsy descriptions of AA in America were published in 1837 by Wolcott Richards in Cincinnati and Edward Hallowell in Philadelphia. In 1847, German anatomist ***Joseph Von Gerlach*** provided the first description of a variable structure at the origin of the appendix, which he termed "valvula processus vermiformis," later known as the "Gerlach valve" [6].

Despite advancements in understanding and classifying the disease, treatment for AA during this period remained limited to the Hippocratic adage "*Ubi pus ibi evacua*." Surgical intervention primarily involved draining abscesses when fluctuation was detected. Medical therapy centred on bowel evacuation using water and soap enemas supplemented with large doses of opium for pain management [25].

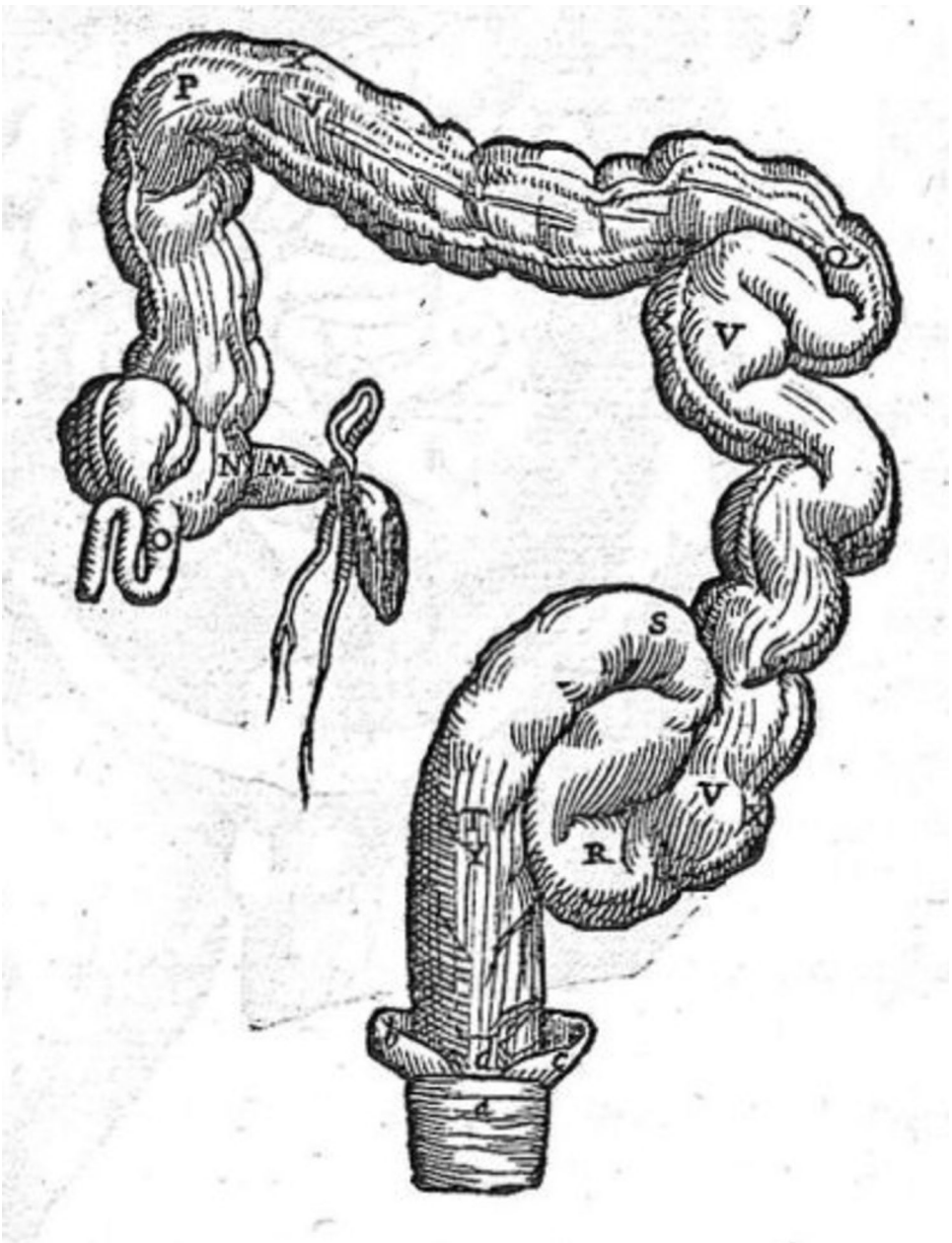

Fig. 5 Anatomical drawing of the large bowel by Andrea Vesalio (The National Library of Medicine). Public domain

Second half of the nineteenth century

The first significant advancement in acute appendicitis treatment occurred in 1848 when ***Henry Hancock***, President of the Medical Society of London, published in The Lancet the first case of an operation for suspected AA prior to the onset of fluctuation [26]. Hancock examined a patient on April 15, 1848, who presented with pain in the right iliac fossa but no swelling or lump. Suspecting AA, he administered enemas, calomel, and opium, but these measures failed to provide relief. After 17 days of worsening symptoms without fluctuation, Hancock, aware that patients often did not survive until this sign appeared, decided to operate. He made an incision starting at the right anterior superior iliac spine, extending medially in line with the Poupart's ligament. A substantial amount of pus was drained immediately, and two days later, elements identified as fecalith were expelled through the wound. The wound healed by secondary intention over several weeks, leading to the patient's full recovery [27]. No appendicectomy was performed.

Hancock advocated for early surgical intervention before fluctuation, believing it could save many lives, but surgery struggled to gain widespread acceptance for years. In 1867, in the "*New York Medical Record,*" ***Willard Parker*** published his experience with four cases of AA operated on before fluctuation using a technique similar to that used by

Fig. 6 Portrait of Johannes Fernelius (1497–1558) c. 1550 (The National Library of Medicine) http://resource.nlm.nih.gov/101414339?_gl=1*4lacai*_ga*NjU2OTcxMjE2LjE3MTIwNDA4NTk.*_ga_7147EPK006*MTcxMjIyNjcwNS4xLjAuMTcxMjIyNjcwOC4wLjAuMA..*_ga_P1FPTH9PL4*MTcxMjIyNjcwNS4xLjAuMTcxMjIyNjcwOS4wLjAuMA. Public domain

Hancock [28]. Parker, focusing on AA pathophysiology, suggested that the ideal timing for incision was between the fifth and twelfth day after symptom onset. He also argued that an incision made before pus formation, even if "*incorrect*" would have not worsen the condition. Parker's experience showed that early surgery saved 75% of cases compared to nearly 50% mortality without surgery. A personal connection, as narrated by Dr. Daniel Stimson, may have fuelled Parker's interest in AA; he was deeply affected by the death of a friend's daughter from the condition: Parker performed the autopsy himself, regretting not operating on her sooner [7–29].

Parker's publication generated many discussions, and the use of abdominal incisions for the treatment of AA began to be known as the "Parker operation" in the USA. In 1903, Howard A. Kelly noted that although both Parker and Hancock proposed similar approaches, Parker was more successful because Hancock was ahead of his time [7].

Surgery remained a last resort due to associated risks and pain until the introduction of anaesthesia by William

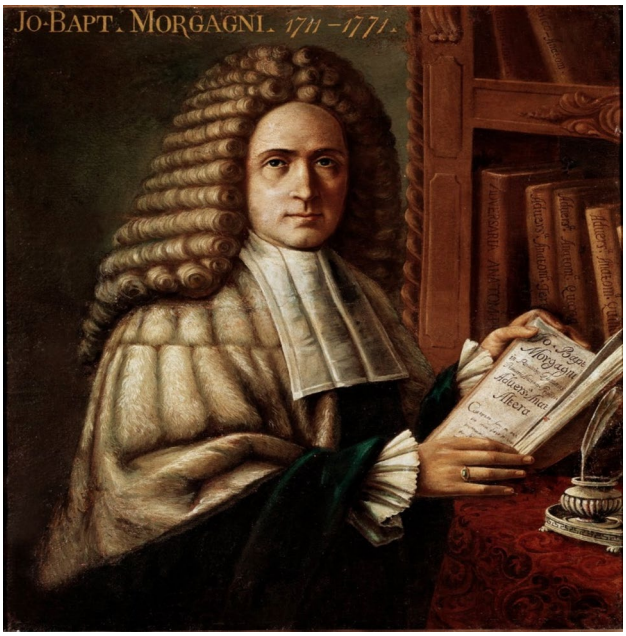

Fig. 7 Portrait of Giovanni Battista Morgagni (1682–1771) (University of Padua, Italy). Public domain

T.G. Morton in 1846 in Massachusetts, using ether [30], and antisepsis in 1868 in Glasgow by Joseph Lister, applying phenol [31]. The widespread adoption of anaesthesia and antisepsis, which took decades and varied across hospitals, became more common after 1880.

The second significant development in AA treatment was the removal of the appendix through an abdominal incision. The first such cases were reported in the 1880s in Europe and the USA. The earliest attributed case was performed by ***Robert Lawson Tait*** (1845–1899) (Fig. 15), a gynaecologist from Edinburgh who, in 1880, operated on a 17-year-old woman with a three-month history of recurrent abdominal pain and suspected peritonitis. He made a midline incision finding a gangrenous appendicitis and removing the appendix, suturing the caecum with stitches. The patient recovered within a month [32]. Tait, a firm believer in antisepsis but a critic of Lister's methods, was one of the pioneers of modern surgery [33].

The first case of appendicectomy for AA (operated within three days of symptom onset) is attributed to ***Rudolf Ulrich Krönlein*** in 1884 (published in 1886). Krönlein, a professor of surgery in Zurich, removed the appendix of a 17-year-old man through a midline incision, although the patient unfortunately died two days later [34, 35]. ***Thomas George Morton*** (Fig. 16), a professor of surgery in Philadelphia, successfully performed an early appendicectomy for AA on a 26-year-old man in 1887, publishing the case in 1888 [36].

A key moment in the history of appendicitis treatment was in 1886, when ***Reginald Herber Fitz*** (1843–1913), a pathologist and internist at Harvard University, published "Perforating Inflammation of the Vermiform Appendix; With Special Reference to Its Early Diagnosis and Treatment" [37]. Fitz, a Professor of Pathological Anatomy at his University, analysed autopsies of patients who died of peritonitis and found more than 250 cases secondary to appendiceal disease. He asserted that AA was the most common cause of peritonitis originating in the right iliac fossa, underpinning the role of appendix famously described by other authors as "*the unstable explosive carelessly left by Nature hidden away in the body of man*" [38]. Fitz also coined the term "*appendicitis*" replacing the outdated terms "*typhilitis*" and "*perytiphilitis*." His suggestion to treat AA through appendicectomy was groundbreaking, although most of the significance of his article lay in its timing, aligning with when surgery was ready to embrace and disseminate these teachings globally.

Before Fitz, the prevalent approach to treating AA involved bed rest, fasting, and opiates, with surgery reserved for abscesses and peritonitis. After Fitz, early appendicectomy for suspected AA began to gain acceptance, albeit not yet standardised, and various experiences with the operation were published.

In 1889, in the *Boston Medical and Surgical Journal,* ***Eduard R. Culter*** reported a series of 11 patients who underwent appendicectomy over a 2.5-year period [39].

Charles McBurney (1845–1913) (Fig. 17), a prominent figure of this era, born in 1845 in Massachusetts, educated at Harvard University, and Chief of Surgery at Roosevelt Hospital in New York, was an innovator in multiple surgical fields and an early adopter of surgical gloves, following the advice of William Halsted. McBurney's contributions to the diagnosis and treatment of AA, particularly the "McBurney point" and the "McBurney incision" remain well known. In his paper "Experiences with early operative interference in cases of disease of the vermiform appendix," he described the point of maximum tenderness in AA (McBurney's point) and emphasised the need for early surgical intervention to prevent complications such as perforation or abscess formation [40]. He also introduced the gridiron, muscle-splitting incision (McBurney's incision), which reduced perioperative morbidity and mortality, while minimising the risk of incisional hernia [41].

In 1894, ***George Ryerson Fowler*** published the first book on AA, sharing his experience with 200 appendicectomies and asserting that AA was the most common disease of the abdominal lower quadrant [21]. Most surgeons initially performed a simple ligation-section of the appendix at its origin. However, to reduce complications such as enteric fistulae, Fowler suggested burying the appendiceal stump within the caecal wall [42]. In 1895, ***Robert H.M. Dawbarn*** first recommended using a purse-string suture at the caecum's base and closing it after inverting the appendiceal

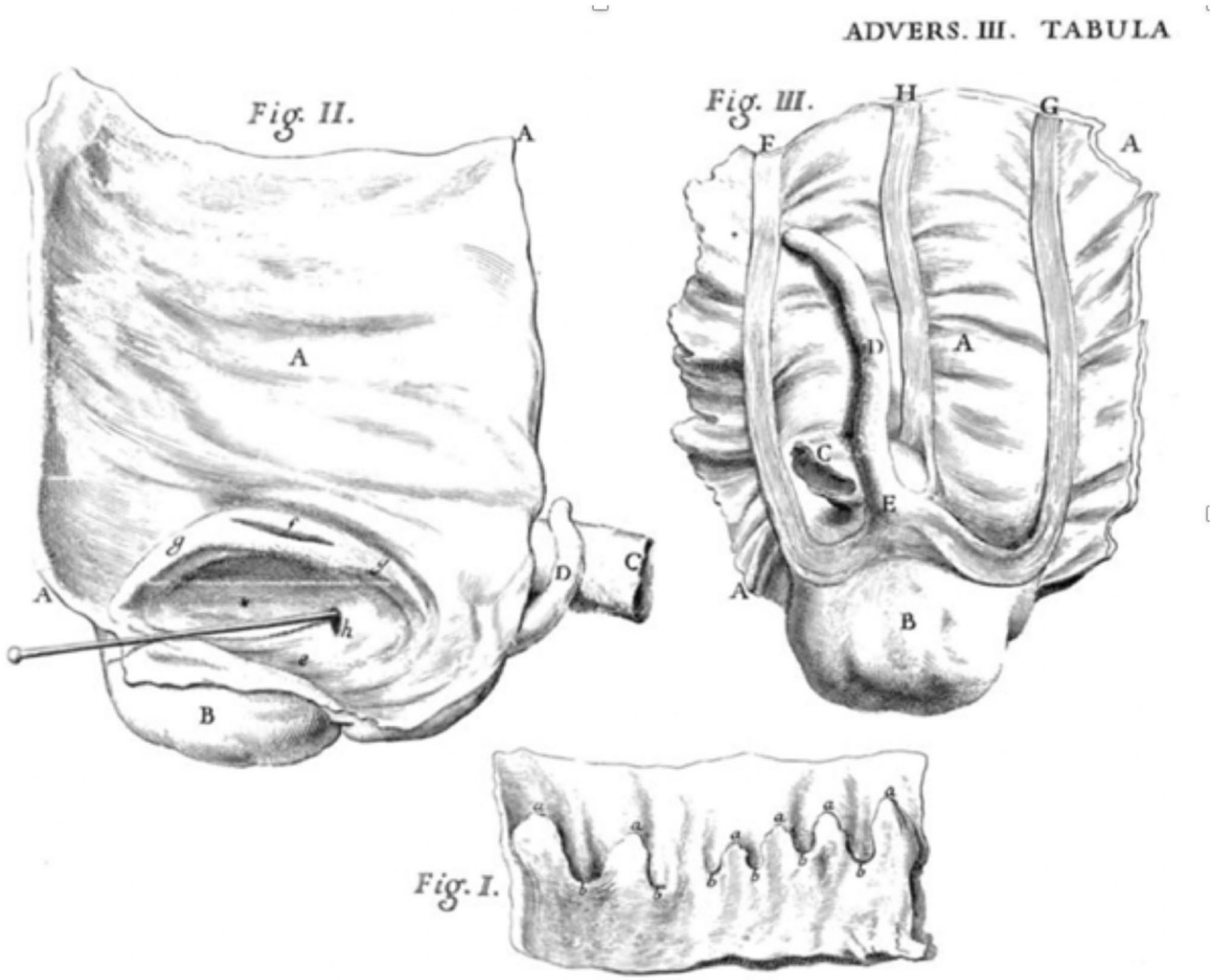

Fig. 8 Anatomical drawing of the caecum by Giovanni Battista Morgagni from "*De sedibus et causis morborum per anatomen indagati*", Nicolás León Library of the Department of History and Philosophy of Medicine, UNAM. Public domain

stump to prevent abscess formation between the caecum and the appendiceal stump [43]. In 1898, ***Augustus Bernays*** reported a series of 71 consecutive successful appendicectomies [44].

First half of the twentieth century

In 1902, ***Albert John Ochsner*** (1858–1925), in his work "A Handbook of Appendicitis," advocated for delayed surgical intervention in cases where a skilled surgical team was unavailable at the onset of symptoms or if the patient's condition was too critical. Notably, this approach was proposed during the preantibiotic era, when medical therapy primarily consisted of gut rest [45].

That same year, ***Robert Fulton Weir*** (1838–1927) pioneered the therapeutic use of the "useless" appendix by performing an appendicostomy to treat ulcerative colitis. This procedure involved irrigating the colon with potassium permanganate through the appendix [46]. This innovative procedure laid the groundwork for utilising the appendix as a flap in various reconstructive surgeries, owing to its small tubular shape and consistent vascular supply [47].

Niels Thorkild Rovsing (1862–1927), a Danish physician renowned for his contributions to multiple surgical fields, is best known for the eponymous semiological sign associated with the diagnosis of acute appendicitis (AA) [48]. In 1907, he published a paper stating that pressure applied to the descending colon could elicit pain in the right iliac fossa in patients with AA. This pain was attributed to an increase in intraluminal pressure caused by the induced movement of bowel content. This technique proved useful for differential diagnosis from other pathologies that cause pain upon

Fig. 9 Portrait of Lorenz Heister (1683–1758) 1750 (Wikipedia) https://commons.wikimedia.org/wiki/File:Lorenz_Heister.jpg. Public domain

direct pressure on the right iliac fossa, such as ureteral stones and salpingitis [49]. An abstract subsequently published in JAMA reported that in a series of 100 patients with pain at McBurney's point, none were positive for Rovsing's sign unless there was an appendix pathology [50]. This finding highlighted the diagnostic value of the manoeuvre in differential diagnosis. Interestingly, Rovsing did not name the sign himself; it was the German physician Carl Lauenstein who

Fig. 10 Portrait of Claudius Amyand (1680–1740), portrait by Thomas Gainsborough. Public domain

introduced the eponym in a critical review [51]. In response to Lauenstein's misunderstanding of the technique, Rovsing remarked, "*It seems to me that my method has accomplished something unexpectedly beautiful: it not only didn't elicit pain at McBurney's point, and therefore spoke against appendicitis but also directed Dr. Lauenstein toward the suffering area of the gallbladder! May my little method always be so well preserved!*" Further addressing critiques, Rovsing elaborated on the correct application of his method, emphasising the importance of isolating the descending colon in the left iliac fossa and applying pressure to increase intracolonic pressure effectively [52].

In 1904, the Swedish surgeon ***Emil Samuel Perman*** published his five-year experience with 268 appendicectomies for AA, revealing pathological findings in 171 cases (64%) [53]. Perman introduced a diagnostic technique involving sudden cessation of pressure in the left quadrant, leading to a rapid decrease in bowel lumen pressure and right iliac fossa pain, as an alternative to Rovsing's sign for diagnosing AA. This method was later referred to as the "Perman-Rovsing sign," although it was often reported as Rovsing's sign.

John Benjamin Murphy (1857–1916), born in Wisconsin in 1857 to Irish immigrant parents, graduated from Rush Medical College in 1879. He later worked closely with Theodor Billroth in Vienna in 1882 [54]. Murphy became a distinguished professor of surgery and lent his name to multiple medical tests, signs, and devices (Murphy's Percussion Test, Murphy's Punch Test, Murphy's sequence, Murphy Button, Murphy-Lane bone skid, and Murphy's Drip). However, he is most famously associated with Murphy's sign of acute cholecystitis.

Fig. 11 Drawing of the anatomical specimen with missing appendix by Jan van Rymsdyk (1767). Credit: Wellcome Library, London. Public domain

In 1889, Murphy presented a paper to the Chicago Medical Society advocating for early appendicectomy in cases of AA to prevent complications [55]. Despite initial skepticism, he unwaveringly upheld the principle: "*in cases of acute appendicitis, of opening the abdomen as quickly as possible and closing it more quickly*" [6]. In 1895, he presented a paper titled "Appendicitis: with original report and analysis of one hundred and forty-one histories and laparotomies for that disease under personal observation: read before the Pan-American Medical Congress" [56]. Over the years, Murphy meticulously documented his appendicectomy cases, culminating in a report of 2000 appendicectomies presented in 1904 [57]. Through his work, Murphy significantly contributed to establishing early appendicectomy as the primary treatment for AA. He was lauded by William James Mayo as "*the surgical genius of his generation*" [58].

In September 1897, while still a surgical resident, ***Harvey Williams Cushing*** (1869–1939) operated on a patient with a perforated appendix who died ten days later. Two weeks following this event, Cushing began experiencing abdominal pain and self-diagnosed an episode of AA. Fearing for his life, he convinced William Halsted to perform an early appendicectomy on him. Although Cushing's recovery was fraught with complications, he ultimately healed completely [59].

James Sherren, in 1903, described the "Sherren triangle." A suspicion of AA was considered if there was cutaneous hyperalgesia in the area "*bounded below by Poupart's ligament, above by a line drawn out from the umbilicus, and to the inner side by a vertical line just to the right of the midline, its apex is at the anterior superior spine*" [60]. Sherren analysed 51 consecutive cases of AA, focusing on the distinction between deep and cutaneous signs. He asserted that the abrupt disappearance of a well-defined zone of tension,

Fig. 12 Painting by Gaspare Traversi "la visita medica", 1752 (Gallerie dell'Accademia, Venezia, Italy). Public domain

Fig. 13 Painting by Gaspare Traversi "l'intervento chirurgico" (Wikipedia) https://commons.wikimedia.org/wiki/File:1753_Traversi_Operation_anagoria.JPG. Public domain

without overall improvement, indicated appendix perforation and mandatory urgent surgery [61].

In 1901, upon Queen Victoria's death, her legitimate successor, ***Edward***, ***Prince of Wales***, fell gravely ill just few days before his coronation. His physician, Sir Francis Laking, sought the expertise of eminent surgeons, including Sir Joseph Lister and Sir Frederick Treves. Although both agreed on a diagnosis of an appendiceal abscess, their treatment recommendations diverged. Lister opposed surgery, whereas Treves advocated for it. Initially reluctant, the King, whose condition was deteriorating, eventually consented to surgery. Under immense pressure, Treves performed an abscess drainage without appendicectomy at Buckingham Palace, leading to the King's full recovery [62]. This incident significantly increased public awareness of AA and popularised appendicectomy. Notably, Treves himself remained opposed to early appendicectomy, and tragically, years later, his daughter died from AA.

In 1908, ***Otto Lanz*** (1865–1935), a renowned Swiss surgeon for his appendicectomy techniques, identified the eponymous Lanz point (at the right extremity of the first third of the bisiliac line) and proposed a modification to McBurney's incision. Lanz advocated for an oblique incision (employing a muscle-splitting technique) in the same region as McBurney's incision, arguing that it offered better cosmetic results [63]. This incision, known as the "Lanz incision" or "Rockey-Davis incision," can be extended both medially and laterally using a muscle-cutting technique if intraoperative needs arose.

In 1925, ***Arthur Rendle Short*** from Bristol proposed that AA was a disease predominantly found in Western civilisations based on his geographical study. He linked this occurrence to the low-fibre diet prevalent in Western countries [64]. This hypothesis was later supported by ***Denis Burkitt***, who suggested that a low-fibre diet may lead to slower faecal transit times and alterations in the microbiome, potentially increasing the risk of AA and colonic diverticulitis. He also observed a decrease in AA cases in England during wartime, attributing this to changes in dietary habits [65].

In his 1926 publication, ***Le Grand Guerry*** (1873–1947) cited 2959 personal cases of appendicectomies, reporting 16 deaths (0.54%), all of which were associated with complex cases [66]. This significant reduction in mortality, compared to the overall rate of 26% in 1890 [67], was attributed to several factors. The most impactful were the enhanced understanding of pathophysiology, the refinement and standardisation of surgical techniques, the widespread adoption of antisepsis, advancements in anaesthesia, and the emphasis on fluid resuscitation.

No substantial improvements in mortality rates were noted until the advent of the antibiotic era in the 1940s.

In 1930, ***Hamilton Bailey*** proposed the "Ochsner-Sherren" treatment for AA. While some authors, such as Ochsner [45] and Sherren [60], had already advocated for a non-surgical approach to AA, the prevailing practice among surgeons at the time was to perform early appendicectomies indiscriminately. In response, Bailey developed a protocol named after these two authors [68]. According to Bailey, patients without generalised peritonitis and presenting

Fig. 14 Photo of Thomas Hodgkin (1798–1866) (Wellcome images) https://wellcomeimages.org/indexplus/image/L0008709.html. No changes were made

symptoms for more than 48 h should be medically managed with bed rest, gut rest, and no morphine. Surgical intervention was suggested at a later stage to reduce the risk of recurrence [68].

In 1946, **Karl A. Meyer**, in a paper titled "Progress in the Treatment of Acute Appendicitis" [69], summarised contemporary treatment approaches, detailing both medical therapy and surgical techniques (Fig. 18). He highlighted recent

Fig. 15 Photo of Robert Lawson Tait (1845–1899) (The National Library of Medicine) http://ihm.nlm.nih.gov/images/B24811. Public domain

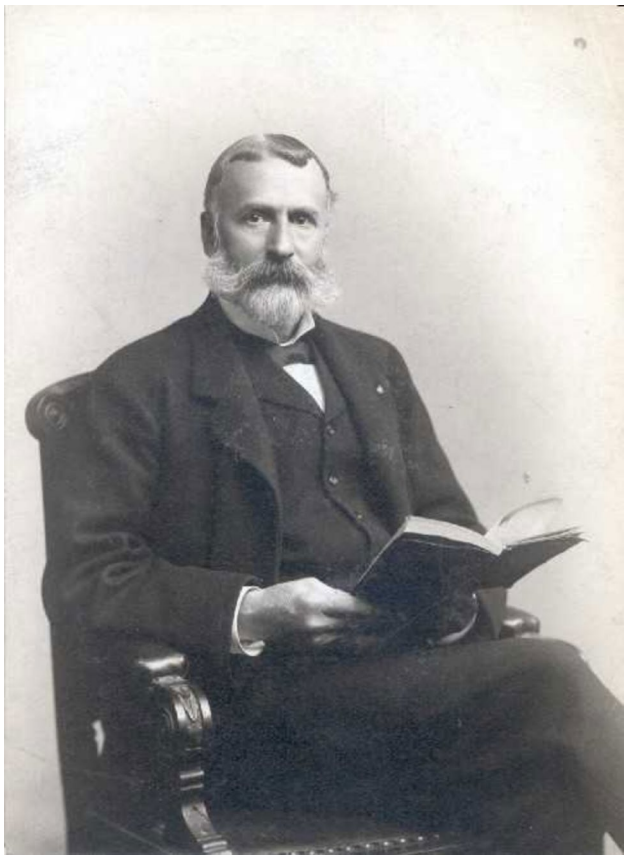

Fig. 16 Photo of Thomas George Morton (1835–1903) (University of Pennsylvania image gallery)

innovations such as antibiotic administration, widespread use of Levin's tube, intravenous vitamin therapy, etc. Meyer also discouraged the practice of intraperitoneal drainage.

Second half of the twentieth century

During this period, there was a notable decrease in mortality rates, primarily attributed to advancements in peritonitis treatment and the introduction of antibiotics [70]. Therefore, in the 1950s, some authors started to propose an initial conservative approach involving antibiotics with the selective use of surgery [71].

However, the excision of a proportion of normal appendices (15–30%) was deemed acceptable, as the majority of severe complications were linked to appendiceal perforation. Consequently, the risks associated with a superfluous appendicectomy were considered lower than those associated with neglecting a potentially life-threating disease [72].

A significant breakthrough in AA management occurred in 1980 with the advent of the first laparoscopic appendicectomy. Initially termed "peritoneoscopy," laparoscopy began as a diagnostic tool in the early twentieth century.

Fig. 17 Photo of Charles McBurney (Wellcome images) https://wellcomeimages.org/indexplus/image/L0017167.html. No changes were made

The first attempt to inspect the abdominal cavity's contents without a major incision was conducted by Ott in Russia in 1901, employing a speculum and head mirror [73]. Over the following decades, enhancements were made through the introduction of pneumoperitoneum, the development of specialised instruments, and the capability for biopsy extraction. Despite these advancements, the technique was predominantly used for diagnostic purposes for approximately 80 years.

Kurt Semm (1927–2003), a German gynaecologist (Fig. 19), performed the first laparoscopic appendicectomy on a patient diagnosed with endometriosis affecting the appendix on May 30, 1980. He first shared his findings at the Pan American Conference in Puerto Rico in 1982. Despite initial resistance from the scientific community due to the incorporation of surgical manoeuvres into laparoscopy, Semm persisted. His attempts to publish a German-language manuscript detailing the laparoscopic appendicectomy were initially met with scepticism, with one scientific journal commenting that accepting such a proposal would have been "*ridiculous*" [74]. However, the paper, finally published in 1983 [75], included comprehensive details of the surgical procedure and the necessary equipment, recommending laparoscopic appendicectomy only for non-acute cases.

The resistance Kurt Semm faced was so pronounced that the President of the German Surgical Society penned a letter to the Board of Directors of the German Gynaecological Society, urging the suspension of this "*impertinent*" colleague's medical license. Furthermore, as Semm recounted in his autobiography, "*once during a slide presentation on ovarian cyst enucleation by laparoscopy, the projector was abruptly unplugged by a colleague with the argument that such unethical surgery should not be presented at a scientific meeting*." Despite these adversities, Semm continued to refine laparoscopic surgery and received numerous honours, ultimately earning recognition as the "*father of laparoscopy*" [76, 77].

Despite the prevailing scepticism, the adoption of laparoscopic surgery was sluggish throughout the 1980s, with the technique primarily serving diagnostic purposes. Nevertheless, an increasing body of work on minimally invasive appendicectomies began to emerge [78, 79].

Alfredo Alvarado, with the objective of reducing the frequency of "uninflamed appendectomies" (which still constituted 15–30% in the 1980s) without elevating the risk of preoperative perforation, introduced the "Alvarado score" in 1986 [80]. This score was derived from the sum of values assigned to each of the following factors: localised right lower quadrant abdominal tenderness, onset of leucocytosis, migration of pain, shift to the left, fever, nausea/vomiting, anorexia, and direct rebound pain. The score obtained facilitated the stratification of AA risk.

Subsequently, numerous trials have been conducted to validate the efficacy of the Alvarado score, and although other scores have been proposed, the Alvarado score remains one of the most globally adopted and is still utilised today with the inclusion of ultrasound, referred to as the "modified Alvarado score" [81, 82].

In the early 1990s, the first prospective trials comparing laparoscopic to open surgery for AA were published, yielding inconclusive results [83, 84].

Open appendicectomy continued to be the benchmark procedure, yet there was no unanimous consensus regarding which cases should undergo surgery or might benefit from a conservative treatment approach.

In 1995, ***Staffan Eriksson*** performed the first randomised controlled trial comparing appendicectomy to antibiotic therapy for AA, revealing that conservative management was equally effective as surgery for uncomplicated AA, albeit with an increased risk of subsequent appendicitis episodes in this group [85]. These findings were then underscored by other authors [86, 87].

Towards the end of the 1990s, a shift in perspective occurred with the publication of high-quality studies demonstrating that laparoscopy was superior to open surgery in terms of diagnostic accuracy, postoperative hospitalisation duration, and both early and late complications [88, 89].

With the endorsement of laparoscopic appendicectomy, numerous modifications to Semm's initially described technique were adopted, such as the use of only three trocars and the introduction of various devices for managing the appendiceal stump, including endoclips (both metallic and polymeric), linear staplers, and radiofrequencies [90].

Twenty-first century

The twenty-first century has been marked by two main elements: on the one hand, an enhanced understanding of the pathogenesis and pathophysiology of AA, which has allowed a tailored approach to the disease; on the other hand, the establishment of laparoscopic surgery as the gold standard in clinical practice.

In 2007, ***Roland E. Andersson*** (Fig. 20), a Swedish surgeon, suggested [91] a re-evaluation of the principles of acute appendicitis (AA) management based on a better understanding of the natural history of the disease: an increasing body of evidence suggested, in fact, that acute appendicitis was not necessarily a progressively worsening condition and that many cases resolved without progressing to perforation. An approach of watchful waiting would, therefore, reduce the number of negative appendectomies, with only an apparent increase in cases of perforated appendicitis, as most cases of uncomplicated appendicitis resolved spontaneously and did not require surgery. In 2008, Andersson's group proposed the **Appendicitis Inflammatory**

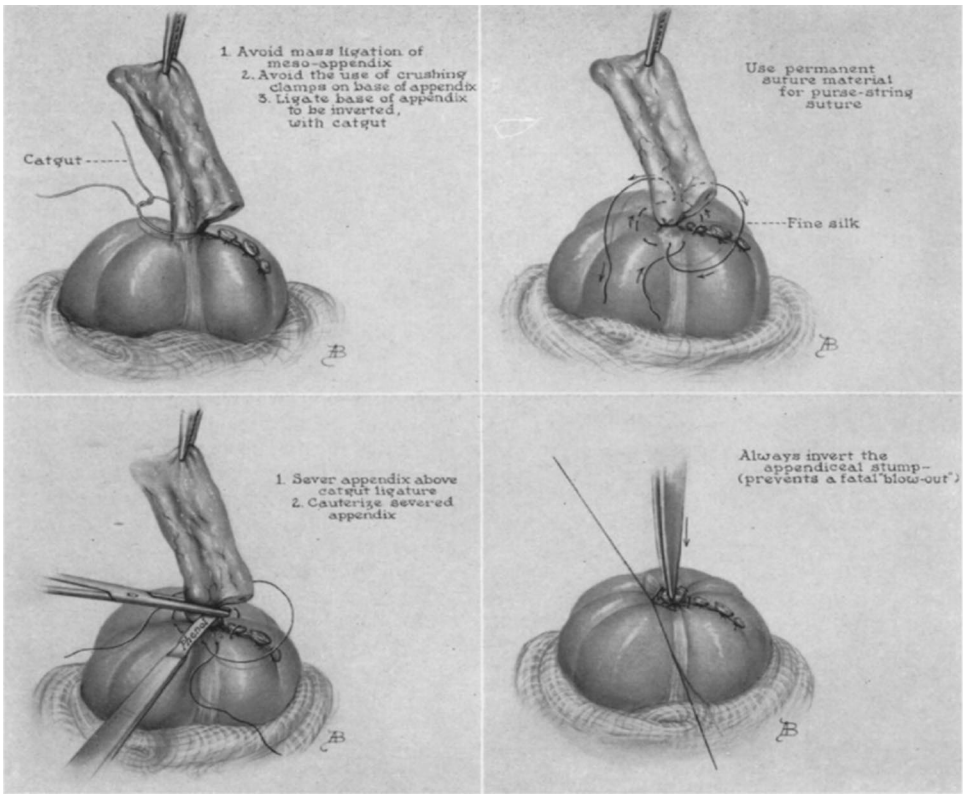

Fig. 18 MEYER KA et al. Progress in the treatment of acute appendicitis. Elsevier Licence Number: 5753080572666

Response (AIR) score [92] to support clinical decision making in case of a suspected AA, overcoming some limits of the Alvarado score and reducing the rate of unnecessary appendicectomies. Currently, the AIR score is one of those recommended by the guidelines of the World Society of Emergency Surgery (WSES)[1].

Laparoscopic appendicectomy became the gold standard for treating AA even in complex cases, with multiple RCTs and meta-analyses confirming the superiority of laparoscopic to open appendicectomy in both high-volume and regional centres [93].

Novel techniques have been introduced to improve the cosmetic results of conventional multiport laparoscopic appendicectomy (CMLA) and minimise complications, although many of these techniques have not been adopted in routine clinical practice due to longer learning curves, the need for dedicated instruments and higher costs.

Single-incision laparoscopic surgery (**SILS**) represented the first minimally invasive alternative to CMLA for appendicectomy. Initially, described in 1997 for cholecystectomy [94], this method involves the simultaneous use of multiple instruments through a single abdominal incision [95]. Studies have confirmed the efficacy of this technique (utilising both umbilical and suprapubic access), albeit at a higher cost and with an extended operative time [96, 97]. Recent trials have explored the use of reusable instruments and a "surgical glove port," indicating that with these modifications, costs become comparable to those of CMLA [98], and over time, operative times become similar [99].

During this period, **natural orifice transluminal endoscopic surgery (NOTES)** introduced another group of alternative surgical methods. With the advent of flexible operative endoscopies equipped with diverse instruments, including specialised devices for haemostasis and suturing [100], NOTES represented a significant innovation.

Trans-gastric appendectomy (TGAE), performed first among the NOTES procedures by Reddy and Rao in 2004 using an endoscope inserted through a minor gastric incision (published in 2016) [101], led the way. Other centres have reported successful applications [102, 103], although the total number of procedures remains limited, and many patients were laparoscopically assisted.

Transvaginal appendectomy (TVAE), introduced by Chinnusamy Palanivelu in 2008 [104], involves accessing the peritoneal cavity through a flexible operative endoscope inserted via an incision in the posterior vaginal fornix. This approach has advantages over TGAE in terms of operative time and conversion rate [105, 106].

The primary goals of NOTES include reducing wound infection and incisional hernia risks while achieving optimal cosmetic results (no visible scars). However, to date, only a small patient cohort has been treated with these techniques, as no significant studies have demonstrated its superiority over laparoscopy, and only a few centres possess

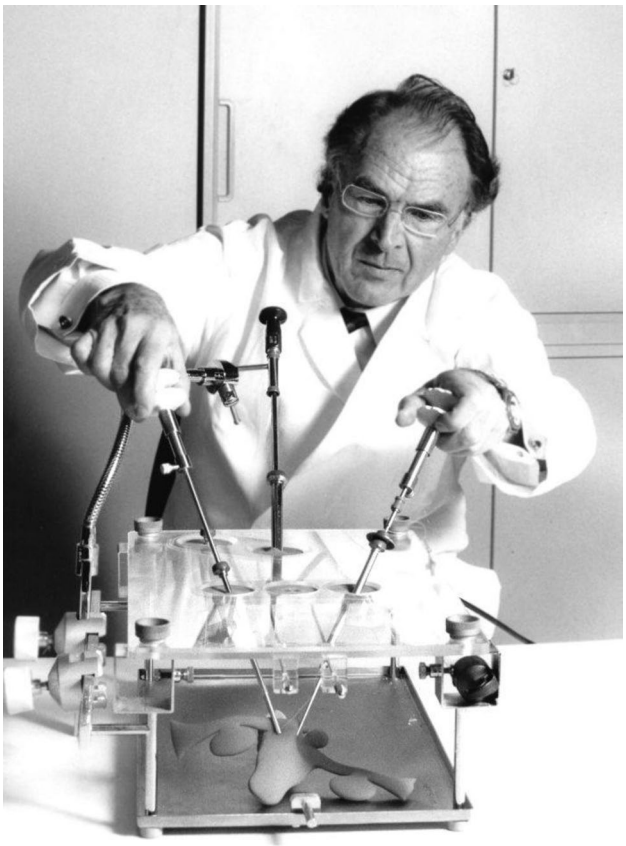

Fig. 19 Kurt Semm (1927–2003; Department of Obstetrics and Gynecology, University Clinic of Kiel) https://creativecommons.org/licenses/by-sa/3.0/de/deed.en

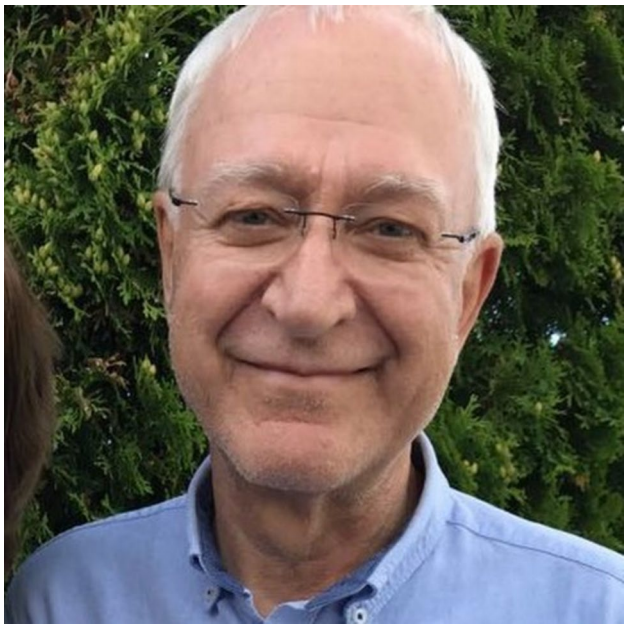

Fig. 20 Roland E. Andersson (courtesy of the same author)

the necessary skilled teams and equipment. Additionally, higher costs and increased procedural complexity hinder a widespread adoption.

The first case of endoscopic transcecal appendicectomy was reported by Wirtschafter and Kaufman in 1976. However, the procedure was involuntary because a totally inverted appendix mistaken for a polyp was identified postoperatively through histology [107].

This anecdotal case anticipated the first planned **endoscopic transcecal appendectomy (ETA)**, performed by Liu in 2018 [108].

Over the last decade, advancements in endoscopic techniques, such **as endoscopic submucosal dissection (ESD)**, **endoscopic mucosal resection (EMR)**, and **endoscopic full-thickness resection (EFTR)**, have expanded the range of endoscopically treatable lesions. However, the involvement of the appendiceal orifice poses a challenge due to difficulties in identifying the distal margin and the risk of postprocedural appendicitis.

ETA was developed to address these limitations, allowing for the complete removal of the appendix and mesoappendix through the caecum using a flexible endoscope, thereby avoiding any incision other than at the appendix's origin. Initially developed to treat low-grade tumours of the appendiceal ostium, the application of ETA has since expanded to include the treatment of chronic appendicitis and has been proposed for managing uncomplicated AA [109]. Currently, the application of ETA is limited to pilot centres, necessitating further studies to assess its feasibility and effectiveness.

Endoscopic retrograde appendicitis therapy (ERAT) is a new minimally invasive, endoscopic option for uncomplicated AA treatment. Liu first described this technique in 2012 [110], which, similarly to endoscopic retrograde cholangiopancreatography (ERCP), involves organ cannulation using a flexible endoscope. This process allows for the injection of contrast agent to perform endoscopic retrograde appendicography using a fluoroscope, helping in the differential diagnosis between suspected and actual AA. If an uncomplicated AA is confirmed, it can be treated through appendiceal stone extraction using a balloon catheter, appendiceal lumen irrigation and plastic stent insertion if needed. An alternative method using high-frequency ultrasound (HFUS) instead of X-ray has also been described [111].

In a recent meta-analysis [112], there were no significant differences in the technical success of ERAT at first hospital admission or in the effectiveness of treatment at a one-year follow-up compared to that of antibiotics or surgery, with a shorter operative time and length of stay. However, the reliability of these findings was compromised by a substantial risk of imprecision due to the quality of the studies included.

Fig. 21 Paulina Salminen (University of Turku, Finland). https://ifso2024.org/project/paulina-salminen/ (last accessed 20.th October 2024)

In 2018, ***Paulina Salminen*** (Fig. 21) published the 5-year results of the APPAC study [113], a randomised controlled trial comparing antibiotics (Intravenous ertapenem for 3 days, followed by a 7-day therapy of oral levofloxacin and metronidazole) versus surgery for uncomplicated AA, confirming the role of medical treatment and showing a significantly reduced overall complication rate in the antibiotic arm, although with a recurrence rate of 39.1%.

Similar findings (40%), albeit at a two-year follow-up, were reported in the CODA trial, another randomised trial by Flum et al. in 2021 [114]. The most commonly antibiotic regimens included at least a 24-h intravenous antibiotic (ertapenem, cefoxitin, or metronidazole plus one between ceftriaxone, cefazolin, or levofloxacin), followed by an oral regimen to complete a total of 10-day therapy (ciprofloxacin or cefdinir plus metronidazole).

However, the clinical implications of not removing occult appendiceal tumours in patients managed with antibiotics remain uncertain, with an estimated incidence of 0.5–1% among all cases of acute appendicitis [115, 116].

SARS-CoV-2 pandemic

In 2020, the COVID-19 pandemic exerted disruptive effects on surgical practice. In an effort to preserve healthcare resources for patients infected with SARS-CoV-2, scheduled surgeries and nonurgent outpatient activities were postponed or suspended [117]. In the case of AA, conservative treatment for uncomplicated forms was recommended whenever possible. In the first months of the pandemic, the potential risk of SARS-CoV-2 transmission through aerosolisation of viral particles in the smoke plume and pneumoperitoneum during laparoscopy led some authors and scientific societies to recommend a provisional shift to the open approach [118, 119].

Overall, in the first wave of the pandemic, the COVID-19 pandemic showed a substantial shift towards conservative management of AA, yielding satisfactory outcomes [120, 121]. However, in 2021, there was a resurgence in the preference for straightforward laparoscopy. This change likely stemmed from a better understanding of viral transmission and enhanced coordination within healthcare systems [1, 122]. Concurrently, the pandemic period saw a decline in hospital admissions, possibly attributable to an increase in the number of mild cases successfully managed conservatively at home [123], with the incidence of complicated AA remaining unchanged.

At the moment, we are assisting at a return to the pre-outbreak practice, with some preliminary evidences that, in the absence of a coprolite, uncomplicated AA might resolve even spontaneously with simple observation without antibiotics [124, 125].

Anecdotes

Historical records document several instances of auto-appendicectomy (or self-performing appendicectomy). The first known case was performed by the American surgeon ***Bertram F. Alden*** in 1912 under spinal anaesthesia, although the operation was completed by his assistant [126]. In 1921 **Evan O'Neill Kane** performed the surgery on himself using morphine and local anaesthesia [127].

Perhaps the most renowned episode of self-appendicectomy was by ***Leonid Ivanovich Rogozov***. As the sole surgeon on a Russian Antarctic expedition in 1961, Rogozov diagnosed himself with AA. After two days of worsening symptoms despite antibiotic therapy, he operated on himself using local anaesthesia, a mirror, and the aid of untrained assistants, successfully saving his own life [128].

Figure 22 shows a timeline summarising the key milestones in the history of acute appendicitis and its treatment.

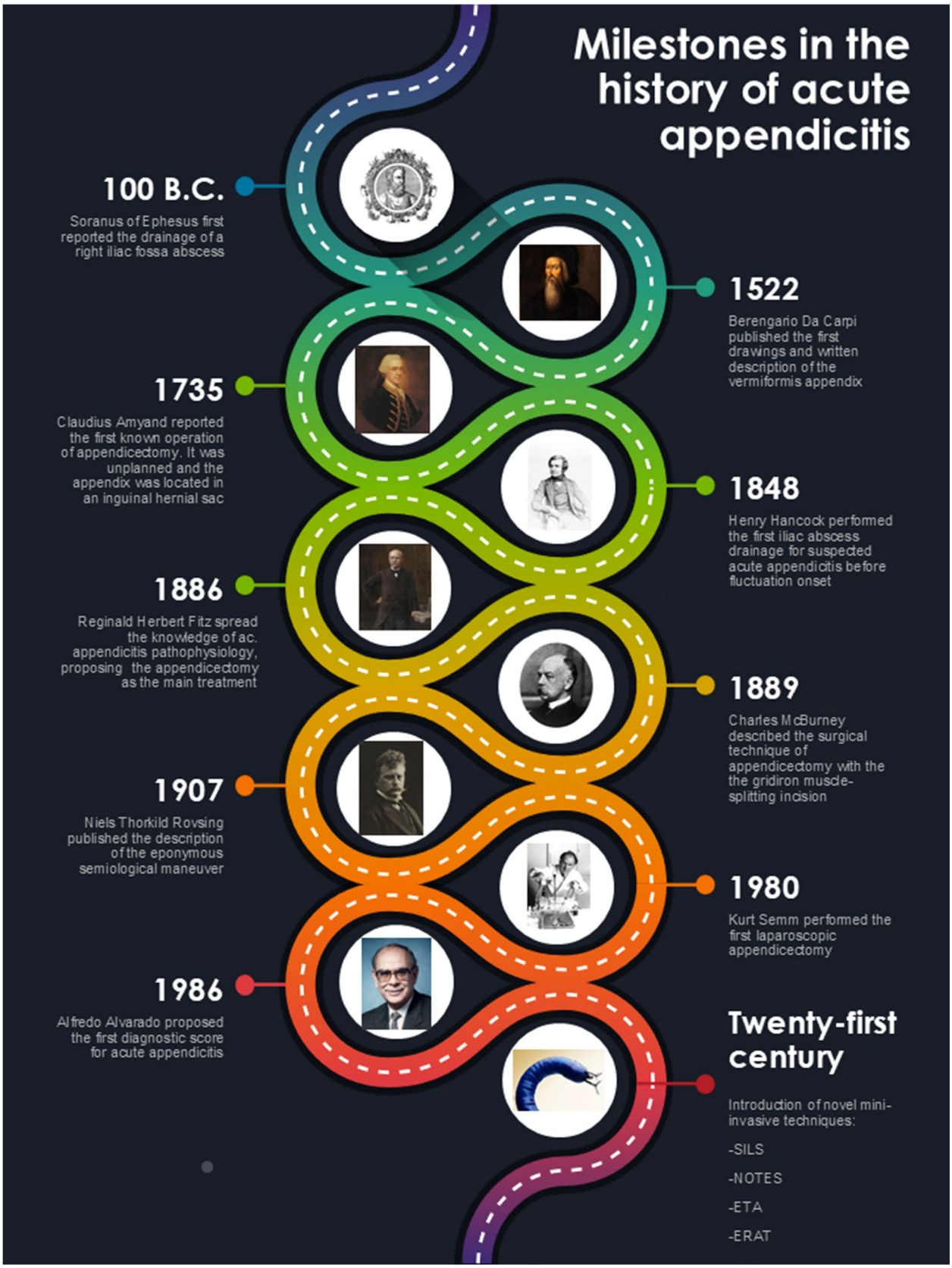

Fig. 22 Main steps in the knowledge of acute appendicitis and its treatment

Conclusions

The history of acute appendicitis and its treatment represents one of the most interesting topics in the surgical literature, as the disease was one of the first to benefit from the advancement of scientific revolution in the nineteenth century and the evolution of its treatment is representative of the historical evolution of surgery in the last three centuries.

Author contribution L.S. and F.P. conceive the idea of the manuscript. L.S., F.P., G.P, M.P, S.DS, G. DL, P.S, F.S. and B.N draft the manuscript and prepared Fig. 1–22. F.S. and B.N. supervise the drafting and revised it critically for important intellectual content. All authors reviewed and approved the final version.

Data availability No datasets were generated or analysed during the current study.

Declarations

Conflict of interest GP and FP are editors on this journal, but are recused from the Editorial peer review process of this article. None of the other authors has a conflict of interest to declare.

Ethics approval and consent to participate Not applicable.

Disclaimer The images from 1 to 17 that accompany the article are more than 75 years old and hence out with copyright rules. All sources have been attributed.

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