



Abdominal Sepsis in Surgery and does this "Diagnosis" Really Exist? Effective Surgical Therapy

José Luis García Hernández

Specialist in Surgery. Attached to the Department of Surgery General Hospital Iztapalapa "Dr. Juan Ramón de la Fuente" of the Ministry of Health of Mexico City. Graduated from the National Autonomous University of Mexico. Mexico City. Country Mexico

Morelos Adolfo García Sánchez

*Specialist in Surgery and with a Subspecialty in Colon and Rectal Surgery attached to the Department of Surgery of the of Surgery General Hospital "Dr. Rubén Leñero" of the Ministry of Health of Mexico City. Graduated from the National Autonomous University of Mexico, Mexico City. Country: Mexico

Gema Méndez Barrón

Specialist in Surgery. Attached to the Department of Surgery General Hospital "Dr. Rubén Leñero" of the Ministry of Health of Mexico City. Graduated from the National Autonomous University of Mexico. Mexico City. Country Mexico

Ivonne Alondra León Suárez

Specialist in Surgery. Attached to the Department of Surgery General Hospital "Dr. Rubén Leñero" of the Ministry of Health of Mexico City. Graduated from the National Autonomous University of Mexico. Mexico City. Country Mexico

José de Jesús Urbina Cabello

Specialist in Surgery. Attached to the Department of Surgery General Hospital "Dr. Rubén Leñero" of the Ministry of Health of Mexico City. Graduated from the National Autonomous University of Mexico. Mexico City. Country Mexico

ABSTRACT

Introduction: the medical area presents an accelerated advance in knowledge, as well as in technology, which has caused empty gaps that confuse, transcend and are filled or transformed into fiction or unfounded criteria; the specialty of Surgery tends to this phenomenon. **Objective:** 7 years of experience in the treatment of patients with abdominal sepsis in 3 hospitals. **Method:** a multicenter, retrospective, longitudinal, observational and descriptive study was conducted to review the records of patients surgically treated for abdominal sepsis over a period of 7 years. **Results:** 353 patients with abdominal sepsis treated surgically; 243 men (69%), 110 women (31%), with an age range of 18 to 81, mean 42; the first cause is biliary pathology, in 22.94% it does not start with an infectious process, diabetes mellitus occupies the 1st place as comorbidity 39%. Morbidity of 79% and mortality of 23.51%. **Discussion:** most deaths are caused by the "host response to the infection itself", it is not supported by evidence; this not only skews the science used to model it, but also the approaches to treat it, the accurate diagnosis of infectious diseases

is a complex process influenced by factors such as clinical judgment, diagnostic methods and the availability of resources. **Conclusions:** abdominal sepsis (infectious) does not exist as a real diagnosis, but is an inflammatory process of the individual, complex, multifactorial, where incorrect diagnosis and treatment impact the patient's life. In Mexico, a real situational diagnosis of the health sector must be carried out and a reengineering of processes in the quality of medical-surgical, administrative and research care must be carried out to initiate a beneficial/correct, efficient, effective change in mortality erroneously called abdominal sepsis.

Keywords: Abdominal sepsis, Infection, Surgery, Systemic inflammatory response, Chemical peritonitis, Immunological peritonitis.

INTRODUCTION

In the medical area it presents an accelerated advance and with titanic steps in knowledge, as well as in technology in recent times, all this has caused empty spaces or gaps that confuse, transcend and are filled or transformed into fiction or unfounded criteria and the Specialty of Surgery, therefore, does not escape from this phenomenon.

As far as the history of infection is concerned, signs of infection and infestation have been found in many fossils from all geological periods, so it follows that infectious diseases are as old as life itself on earth. [1] Historically the infection has only been documented when the impact is too much affecting large populations, this is exposed in the Bible around 1000 BC where the Hebrews exiled in Egypt, during the years that included the reign of Akhenaten (or Amenhotep IV) (c. 1379 BC) with the plagues suffered.

On the other hand, the gram-negative bacterium *Yersinia pestis* cocobacillus is an infectious agent that has been directly responsible for more human deaths than any other infectious disease: the first is the plague of Justinian (541-542 AD) that devastated Asia, North Africa, Arabia and part of Europe; the second is the so-called Black Death (1347-1351 AD). Which killed a third of the population of Europe, and finally the third pandemic (1855-1918), which began in China and India and ended up spreading to the rest of Asia, Africa and America. [2, 3] Girolamo Fracastoro, a physician-poet born in Verona, published in 1546: "De contagione et contagiosis morbis". [4] In 1796, the Englishman Edward Jenner discovered immunization by creating the smallpox vaccine. Holmes in 1843 and Semmelweis in 1847 inexplicably implemented hand washing, managing to exponentially reduce puerperal infection. In 1854, Filippo Pacini discovered choleric vibrio, a fact attributed to him by Robert Koch in 1883. [5] Anton van Leeuwenhoek discovered, what he would call "animacles" in 1675. But it was not until the genius of Louis Pasteur in 1859 that he linked these microorganisms to infectious disease: creating the "Microbial Theory of Disease" or "Germ Theory". [6] Dramatically changing the development of medicine.

The World Health Organization defines infection as "the presence and multiplication of the microorganism in the tissues of the host or in other words a process caused by the invasion of normally sterile tissues, fluids or cavities of the organism by pathogenic or potentially pathogenic microorganisms". [7] On the other hand, infection is defined as the "invasion of the organism by pathogenic germs, which establish themselves and multiply. Depending on the virulence of the germ, its concentration and the host's defenses, an infectious disease develops

(caused by local cell injury, toxin secretion or by the antigen-antibody reaction), a subclinical disease or an innocuous coexistence." [8] Bacteremia is the presence of viable bacteria in the blood, is the prelude to bloodstream infection, and evolves in various clinical spectrums, which is differentiated as sepsis and/or progressing to a systemic inflammatory response syndrome, sepsis, then septic shock, and a multiorgan dysfunction syndrome leading to the death of the patient. [9] Sepsis is defined as an infection that is clinically and/or microbiologically suspected or documented with one or more of the criteria for systemic inflammatory response syndrome. Finally, septic shock occurs when the infectious agent, its toxins and/or the release into the circulation of the mediators of inflammation produce a cardiovascular decompensation characterized by distributive shock with hypotension, decreased systemic vascular resistance and high cardiac output, with the consequent alteration of metabolism and cell death at the level of various organs that leads to multiorgan dysfunction syndrome and finally to the death. [10] Accurate identification of pathogens is crucial for the management of sepsis, traditional microbiological methods are time-consuming and have very limited sensitivity; they allow adjustments of antibiotic therapy that are based on pathogen identification, and only 17% were isolated. For this reason, the metagenomic clinic has been implemented, which achieves a sensitivity of 100% and a specificity of 87.1%. [11] The virulence of a microorganism greatly conditions its potential to establish an infection or on the genes of microorganisms called "pathogenicity islands". [12, 13]

In addition, the World Health Organization currently says that "the impact that healthcare-associated infections and antimicrobial resistance have on people's lives is incalculable. More than 24% of patients affected by nosocomial sepsis and 52.3% of those patients treated in an intensive care unit die each year. These deaths double or triple when infections are resistant to antimicrobials." [7] It should be noted that bacteriuria can exist without causing an infection, like bacteria on the skin or intestine (colonization). For this reason, it is essential to use cultures, which would be positive when 1 or 2 bacteria were present, to determine infection in the estimated amount of $\geq 10^{5\text{th}10}$ colony-forming units, depending on the anatomical site, the microorganism and the resources available for it. On the other hand, fungal isolates were specified according to growth rate, colony morphology, and pigment production on sabouraud dextrose agar plates. [14, 15] It should be noted that the pathogen cannot be analyzed directly from the sample and requires the cultivation of a pure colony, meaning that the standard protocol requires additional time, labor, consumables, and is much more complex when it comes to anaerobes. The virulence of *Clostridioides difficile* is mainly caused by two toxins, toxin A and toxin B, with a limited ability to measure the severity of infection based on the actual biochemical activity of the toxins and therefore their potency to cause harm. [16] *Klebsiella pneumoniae*, *Serratia marcescens*, *Klebsiella oxytoca*, *Pseudomonas aeruginosa*, *Enterobacter aerogenes*, *Staphylococcus aureus*, *Enterobacter cloacae*, *Acinetobacter baumannii*, *Escherichia coli*, and *Proteus mirabilis* have been isolated and confirmed by culture and sequencing. *Streptococcus pneumoniae*, *Branhamella catarrhalis*, *Haemophilus influenzae* and 3 bacterial toxins, ruling out *Mycoplasma pneumoniae* by culture, serology and molecular biology based on PCR that targets the gene of the toxin of the respiratory distress syndrome acquired in the community. [17]

However, it should be pointed out how elementary they are required for an infection:

- Infective dose (or degree of contamination): it is the necessary number of microorganisms necessary to produce infection. An inoculum can be defined as the

population of microorganisms or cells that is introduced into the fermentation medium, which is introduced into the body to cause or increase immunity to a specific disease or condition, or into the medium for different medical microbiological procedures. [18]

- Primary infection or the reactivation of a latent infection: it is conceptualized as the set of local and general reactions that occur in the human body, whose form of expression and severity will be conditioned by two opposing factors: number and virulence. [19]
- Immunity/host: to date there are viral infections where it is not yet clear how receptor binding leads to infection, including whether the receptor plays a structural or other role beyond being a simple anchor. [20] In one example, bacteriophages are the dominant members of the human enteric virome and can shape bacterial communities in the gut, new insights into the complex interactions between bacteriophages and the intestinal mucosa, which could underline the pathogenesis of the disease, exemplified in patients with Crohn's disease and ulcerative colitis. [21]
- Human genetic differences may play a role in the development of recurrent infections. [22] As well as the genetic differences of microorganisms, serotypes, their mutations and the genetic diversity of human isolates, an example of this is *Salmonella enterica*, which is the phenomenon in the infectious diversity it causes. [23]

OBJECTIVE

To present the experience of seven years in the treatment of patients with the diagnosis of abdominal sepsis, in research of three hospitals in Mexico City and the State of Mexico.

METHOD

It is a multicenter, retrospective, longitudinal, observational, and descriptive study. Where the records and files of all patients surgically treated for abdominal sepsis are reviewed, regarding complicated elective surgery and surgical emergency; over a seven-year period of surgical practice, in a multicenter study in three hospitals in Mexico City and the State of Mexico that are:

1. Specialty Hospital of Mexico City "Dr. Belisario Domínguez" of the Ministry of Health. Mexico City. Country: Mexico. 3rd Level of medical care.
2. "Dr. Rubén Leñero" General Hospital of the Ministry of Health. Mexico City. Country: Mexico. 2nd Level of medical care.
3. "Las Américas" General Hospital of Ecatepec. State of Mexico, of the Ministry of Health of the State of Mexico. Country: Mexico. 2nd Level of medical care.

In the study period that ran from December 2017 to December 2024. Age, sex, etiological and surgical diagnosis, pathological history and associated factors, time of evolution of the disease or of the first elective surgical intervention, previous surgical treatments/number of surgeries/complications/sequelae, quantified bleeding, surgical time, days of hospital stay, morbidity and mortality were documented. With subsequent follow-up until definitive discharge.

The study and presentation of the results is carried out using descriptive statistical procedures.

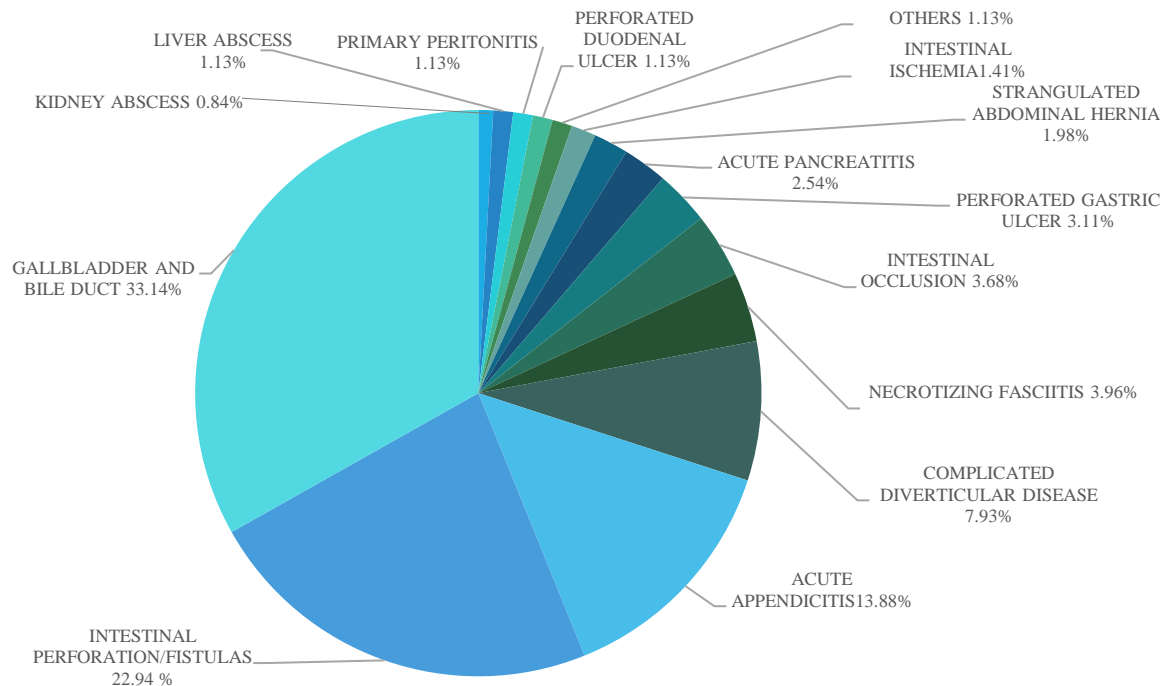
RESULTS

A total of 353 patients diagnosed with abdominal sepsis who were surgically treated in the study period were identified. A total of 243 (69%) and 110 women (31%) were men, with an

age range of 18 to 81 years, with a mean age of 42 years and a bimodal range of 32 and 49 years. Patients were classified according to the etiology of abdominal sepsis and expressed in number and percentage in see table and graph 1.

Table 1: Etiology of Patients with Abdominal Sepsis in the Multicenter Study from 2017 to 2024 Expressed in Number and Percentage

Etiology of Abdominal Sepsis	Number/%
Kidney Abscess	3/0.84
Liver Abscess	4/1.13
Intestinal Ischemia	5/1.41
Intestinal Occlusion	13/3.68
Strangulated Abdominal Hernia	7/1.98
Vesiculam And Bile Duct	117/33.14
Primary Peritonitis	4 /1.13
Acute Appendictis	49/13.88
Acute Pancreatitis	9 /2.54
Perforated Gastric Ulcer	11/3.11
Perforated Duodenal Ulcer	4/1.13
Complicated Diverticular Disease	28/7.93
Intestinal Perforation/Fistulas	81/22.94
Necrotizing Fasciitis	14/3.96
Other	4/1.13
Total	353/100



Graph 1: Etiology of Abdominal Sepsis

The individuals cataloged with the diagnosis of abdominal sepsis had a real origin of onset and as the first cause it was detected that gallbladder pathology currently occupies the first place with 117 patients representing 33.14%, where multiple variants are identified such as cholangitis, gallbladder cholecystitis, biliary fistula, emphysematous cholecystitis, pyocholecyst, gallbladder cancer, pneumobilia, biliary ileus. [24] The second most frequent pathology is intestinal perforation/fistula or the so-called enteroatmospheric fistula, which is multifactorial and in most cases is due to complications of elective/scheduled surgery or another cause, such as trauma or failing that due to the so-called open abdomen technique, [25] surgical washes, acute pancreatitis, internal hernias, etc. See figure 1

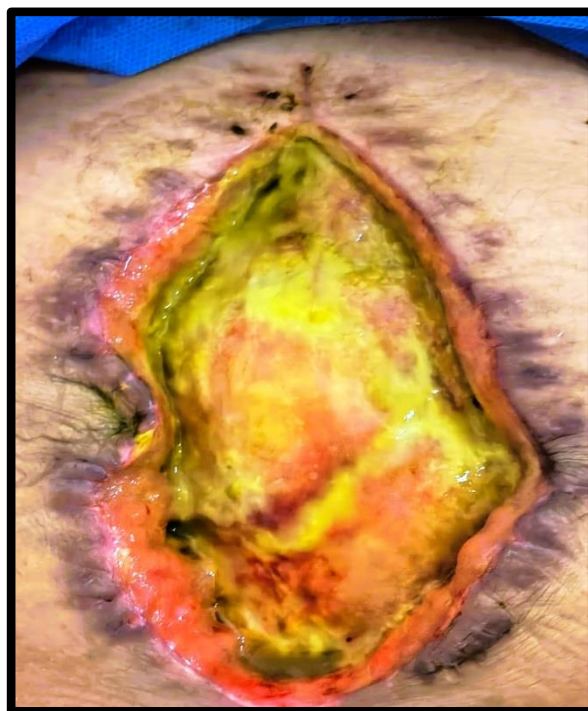


Figure 1: A 45-year-old woman operated on for complicated appendicitis, initially performed an appendectomy and right hemicolectomy with ileostomy that after 19 days presented with intestinal perforation. Image of open abdomen with secondary ileal intestinal fistula (chronic intestinal perforation).

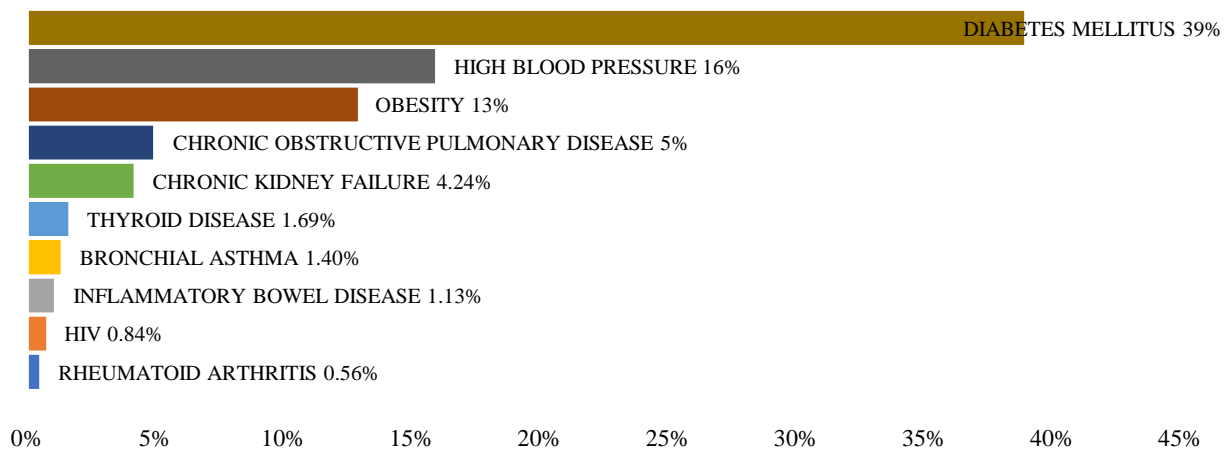
With an incidence of 81 patients representing 22.94%. That in the beginning there is no infectious process, but it is a chemical inflammatory (aseptic) "phenomenon", that over time there is massive bacteremia due to intestinal leakage, bacterial translocation, external contamination, etc., and that it is concluded by many clinicians to be classified as abdominal sepsis. The third cause of abdominal sepsis is acute appendicitis, where the original diagnoses written on the surgical sheets are acute perforated appendicitis with purulent/fecal peritonitis, residual abscess, stercoraceous fistula among others. [26] However, because they are the most frequent, they are not those with high morbidity/mortality, but they may present "controlled" morbidity (ileostomy, surgical wound infection, reoperation for residual abscess, prolonged hospital stay for antibiotic therapy in a residual abscess, etc.) except for enteroatmospheric fistula.

The comorbidities or factors identified in this group of researchers were diabetes mellitus in 39%, subsequent hypertension in 16%, obesity in 13% and chronic obstructive pulmonary disease in 5%. Regarding drug addiction, smoking ranks first with 41%, alcoholism in second place with 11% and drug addiction in third place with 6%. Table and graph 2 show the most frequent and significant documented comorbidities in this study group.

TABLE 2: COMORBIDITIES IN PATIENTS WITH ABDOMINAL SEPSIS. MULTICENTER STUDY FROM 2017 TO 2024, EXPRESSED IN NUMBER AND PERCENTAGE.

Comorbidity	Number	Percentage
Diabetes Mellitus	138	39 %
Arterial Hypertension	57	16 %
Chronic Obstructive Pulmonary Disease	18	5 %
Bronchial Asthma	5	1.4%
Obesity	46	13 %
Hiv	3	0.84%
Chronic Kidney Failure	15	4.24%
Rheumatoid Arthritis	2	0.56%
Inflammatory Bowel Disease	4	1.13%
Thyroid Disease	6	1.69%
Total	294	83.28%

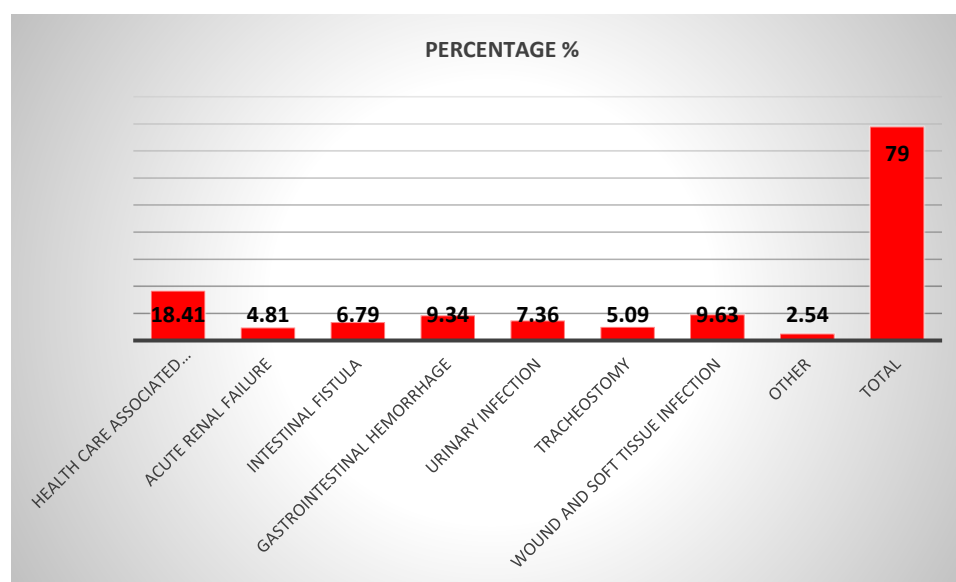
**GRAPHIC 2
COMORBIDITIES**



It should be clarified that the same patient may have two or more comorbidities at the same time and that this can greatly alter the patient's prognosis, both in terms of their actual and/or etiological diagnostic delay and consequently in their therapeutic strategic planning and survival, with a high risk of morbidity or mortality. Or on the contrary, exponentiating the systemic inflammatory response, which at the end of the day has a direct impact on the patient's survival. The documented hemorrhage ranged from 25 to 1,650 milliliters with an average of 125 milliliters and the surgical time varied from 28 minutes to 185 minutes with an average of 69 minutes. See table and graph 3. A total of 190 cases were excluded, where the file is incomplete and/or there is no diagnostic consistency.

Table 3: Morbidity Reported of Patients with Abdominal Sepsis in The Multicenter Study Expressed in Number and Percentage from 2017 To 2024.

Reported Morbidity in Abdominal Sepsis	Number/%
Health Care Associated Pneumonia	65/18.41
Acute Renal Failure	17/04.81
Intestinal Fistula	24/06.79
Gastrointestinal Hemorrhage	33/09.34
Urinary Infection	26/07.36
Tracheostomy	18/05.09
Wound and Soft Tissue Infection	34/09.63
Other	09/02.54
Total	226/79.00

**Graphic 3: Reported Morbidity in Abdominal Sepsis**

Morbidity was described by the events or complications that patients experienced in number and percentage of abdominal sepsis, including surgical wound infection as a consequence of the same surgical cause, and it should be understood that a single case or individual can present 2, 3 or more events of complications; concluding that there were a total of 226 events that represent 79%, so the risk of each patient is calculated with an incidence of morbidity of up to 28.25%. But the total number of patients detected for diseases associated with the underlying pathology in this study was 96 patients and representing 27.19%.

The days of hospital stay that were documented from the patient's admission to the emergency room or to the intensive care unit or on the operating floor, present an average of 24 days with the range of 9 to 71 days. The days tabulated in the intensive care unit that the patient attended were with an average of 6 days and a range of 4 to 15 days. The total mortality reported was very high, it was documented in 83 patients representing 23.51%, where it was detected in this work that necrotizing fasciitis, intestinal ischemia, renal abscess and complicated diverticular disease present a much higher risk of mortality, which is expressed up to 50% of the total number of patients, however, pneumonia is often the 1st cause of death and not abdominal sepsis previously diagnosed, treated, completed or with its chronic repercussions. See figure 2.

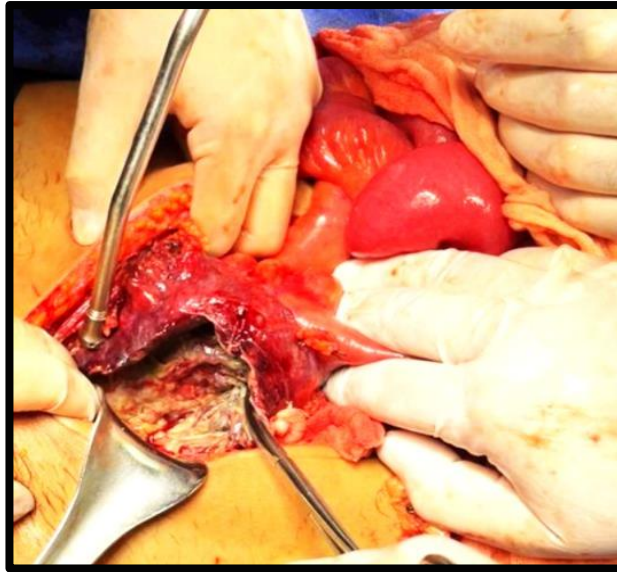


Figure 2: A 23-year-old male was diagnosed with acute intestinal/abdominal occlusion. Image with perforated sigmoid colon tumor (colon adenocarcinoma) with fecal peritonitis and secondary abdominal sepsis.

The second cause of death is intestinal fistula, which is not a septic problem as such, but a syndrome of brutal wear and tear (of the patient, health personnel and the institution) that together evokes a secondary infectious process that transgresses the subject's homeostasis until death. And thirdly, necrotizing fasciitis that culminates in septic shock with multiple multi-organ failure. See figure 3.



Figure 3: A 41-year-old man with type 2 diabetes mellitus presenting with Fournier's disease, due to rectal supralelevator abscess and sepsis. In the postoperative period, there is recurrent drainage, debridement and surgical lavage.

However, the annual adjusted mortality was only 3.35%. It should be noted that no necropsy was performed and that the diagnoses in the death certificate of the so-called abdominal sepsis previously documented do not coincide, nor is there any way to corroborate as in the past, when necropsies were routinely done.

EFFECTIVE SURGICAL THERAPY

A Perception of the Experience of the Author Dr. Morelos Adolfo García Sánchez

The objective of effective surgical treatment in the so-called abdominal sepsis is to carry out and comply with the essential, relative and absolute factors that increase a better chance of survival in terms of the patient's prognosis, with minimal morbidity/sequelae and that reduce mortality.

Essential Factors

1. Diagnosis: Determining that the patient has an urgent surgical pathology.
2. Time: Do not delay effective surgical intervention.

Relative Factors:

1. Urgent preoperative preparation:
 - a) Initiation of empirical antibiotic therapy based on the presumptive diagnosis, frequency/statistics and expertise of the surgeon, in an acclimatization to the specific local microbiome of the hospital or the community.
 - b) Initiation of immediate replacement of liquids and electrolytes.
 - c) Monitoring and initiation of placement/invasion of tubes, peripheral catheters, etc. (No real benefit of the central venous catheter has been documented and there is a risk of further morbidity)
 - d) Crossing and pilot of blood products, with initiation or projection of transfusion.
 - e) Apply phytomenadione 20 milligrams to the patient in a single dose intramuscularly or intravenously.
2. Deficient infrastructure and absent human capital or lack of competence/commitment.
3. Lower risk/morbidity. - In the surgical act, priority should be given to not using stomata, not leaving the abdomen open, packing, etc. Avoiding a new immediate, mediate or elective surgical procedure, for the same reason depending on the case or the emergency that arises.

Absolute Factors:

1. Control: In surgical intervention, absolute control of the contamination, inoculum or substance that causes the inflammatory process (septic) by means of Damage Control Surgery or by a definitive surgical technique, with the sole objective of the patient evolving well or that their results are equivalent. Prior sample of the substance involved. (Culture, Gram stain, Ziehl-Neelsen, cytological or cytopathological, cytochemical, biopsy culture, etc.)
2. Drainage: In emergency surgery, the contents (inoculum, abscess, fecal matter, bile, gastric/intestinal material, pancreatic, hematoma, etc.) must be drained, dissected, evacuated completely/absolutely.
3. Thorough surgical washing: It is imperative to perform a deep, thorough wash of the entire abdomen and/or its involved compartments, with an average capacity of five

liters of a subject according to the constitution, it is the minimum amount of preheated sterile water to correctly perform this phase.

4. Colocation of multiple drains: once the abdominal cavity is cleaned, it must be closed at any cost, despite the intestinal edema, with the respective probing and with the help of relaxation agreed with the anesthesia service; Then, soft drains are placed in both subphrenic spaces that cover both slides and culminate in the pelvic cavity, in a total of 4 that objectively achieve total coverage of the abdomen completely. However, the use of these drains should be adapted to the etiology of abdominal sepsis and/or palliative surgical procedures (stoma, gastrostomy, enterostomy, etc.).
5. The closing: Finally, before the closure of the surgical wound and change of gloves, after the closure of the aponeurosis, iodine is applied without removal in the subcutaneous cellular tissue, and partial or total closure of the skin with separate stitches.

It has been observed that the post-surgical evolution applying this effective surgical therapeutic conduct has greatly benefited patients, with a single surgical intervention, minimal bleeding on average less than 150 milliliters, without surgical reinterventions or residual abscesses, without infection of the surgical wound and with a very satisfactory evolution without sequelae, with discharge home in a short time. with minimal morbidity, combating mortality and with high-cost containment. This has occurred in 114 patients operated on by the author of this study group, which represents 32.29%.

DISCUSSION

Despite its numerous definitions, reviews, consensus statements, and clinical guidelines, the term "sepsis" is still considered a discrete clinical entity that is often claimed to be a direct cause of mortality. [27] Sepsis has been defined as "a life-threatening organ dysfunction due to a dysregulated host response to infection and used the Sequential Organ Failure Assessment score to operationalize it" [28]

Most deaths are caused by the "host response to the infection itself", it is not supported by evidence; this not only skews the science used to model it, but also the approaches to treat it. [29]

It continues to be argued that pathogen-directed therapy should be accompanied by some form of immune modulation, as the host's response to infection is clearly maladaptive; [30] On the other hand, "sterile sepsis" may occur only from inflammation. It may have developed severe acute pancreatitis and other life-threatening problems (noninfectious acute respiratory disease syndrome (ARDS), systemic inflammatory response syndrome (SIRS), or cytokine release syndrome [31, 32, 33]

The "World Health Organization declared sepsis a global health priority" [34] The most frequent sites of sepsis-associated infection are the lung (43%), urinary tract (16%), abdomen (14%), head (14%), and bloodstream/other (13%). [35] Other scientists point out that when there is an exaggerated and then uncontrolled host physiological response to microbe-based infections, sepsis develops, which is characterized by the presence of a cytokine storm, consisting of tumor necrosis factor (TNF), type I interferons (IFN), interleukins: IL-1, IL-6, IL-8, and IL-10. [36, 37] The first line of defense is the gut and associated local immune system, the

liver has essential functions in sepsis because it is considered the second line of defense in eliminating invading microorganisms, reducing the spread of infections. [38]

Diagnostic accuracy in infectious disease cases is crucial for proper patient management and public health interventions. Among 28,451 autopsied cases, 546 (1.9%) were diagnosed with infectious diseases. Pleuropulmonary infections were the most common cause of death (69.8%) as determined by autopsy, followed by bloodstream infections (14.1%) and intra-abdominal infections (10.0%). Discrepancies between clinical and autopsy diagnoses were identified in 22.4% of cases. Pleuropulmonary infections had the highest frequency of diagnostic discrepancies (29.1%), followed by central nervous system infections (15.8%). This study highlights the importance of autopsy to identify diagnostic discrepancies and improve clinical practice in cases of infectious diseases, since they died from them, reaching 1 in 5 misdiagnosed cases. [39] Diagnosing infectious diseases accurately and quickly remains a persistent challenge, as detecting infectious diseases is a complex process influenced by factors such as clinical judgment, diagnostic methods, and availability of resources, [39, 40]

In another study of 460 people (876 wounds) only 44 cases were identified, which is 5.02%, evidence that infection in this group delayed healing up to 12 weeks, along with other comorbidities, which were much higher than the 13% that further caused the delay in healing up to 22 weeks. [41] On the other hand, in an investigation of respiratory infections of the lower respiratory tract, in a group of 1,103 patients and ruling out immunosuppression and/or the low probability of isolating the microorganism; therefore, it was stated that there were only 504 were evaluated with a definitive microbiological diagnosis, where 280 cases were viral diseases, 129 with bacterial diseases and the remaining 95 had mixed viral and bacterial diseases. The most frequent viral detections were rhinovirus in 23%, influenza type A in 21% and respiratory syncytial virus in 10%, with few viral co-infections 4.1% with *Streptococcus pneumoniae* in 12%, *Haemophilus influenzae* in 7%, *Legionella* only 5% and 2% had multiple bacterial detections. [42] The most common causes of infection in hospitalized patients are the airways and central venous catheters, with *Escherichia coli* being isolated as the most common cause of gram-negative-associated bacteremia, while *Staphylococcus aureus* is the most common gram-positive organism isolated. [9]

Gastrointestinal diseases were the most common causes of sepsis at the abdominal level in a percentage of 50.63% of 241 patients, with perforation of the digestive tract being the most frequent etiology among them, with an incidence of 49.79% and 120 patients. Initial monotherapy with β -lactam antibiotics was the most frequently administered treatment (79.83%) and in 380 patients, cephalosporins ceftriaxone and carbapenems, mainly imipenem and meropenem, were the second most used. The in-hospital mortality rate was 7.56%, with three additional deaths during the subsequent 1-year follow-up. [43]

It is decisive that peritonitis is a surgical emergency due to the perforation or rupture of a hollow abdominal viscera, or it can also be spontaneous which are called primary; secondary are due to the initial statement described or tertiary peritonitis that do not respond to the treatment of primary peritonitis. [44, 45] Surgical interventions for peritonitis often result in high morbidity and sometimes mortality in severe cases. Infection of the surgical site is expected after surgery since there was already infection in the cavity and should not be taken as another morbidity, but as an extension of causal abdominal disease. [46]

On the other hand, it is necessary to reflect on whether the infection of microorganisms by anaerobes is real, since in the experience of the authors, isolation, its existence in the infectious process, in a culture or a real identification in the clinical-operative area, colonies; etc. It is only carried out by clinical or so-called immersed suspicion or by empirical induction, since its virulence or pathogenicity has never been verified. [47] And it has been reported that intra-abdominal infections are very significant and that it is the second most frequent cause of mortality from infection in the Intensive Care Unit. The classification of intra-abdominal infection can be made by its location, intraperitoneal or retroperitoneal or by the extent that affects the peritonitis, whether localized or diffuse, or according to the host's ability to collect the infection or intra-abdominal abscess or purulent peritonitis; and these infections can be monomicrobial if the pathogen responsible is unique or polymicrobial if multiple species are identified/isolated.

However, there is aseptic and/or chemical peritonitis, which occurs when irritating substances enter the abdominal cavity, where the inflammation of the peritoneal serosa is initially sterile. [46] Isolated pathogens, sometimes difficult to eradicate, and control of septic outbreak is of vital importance to ensure the effectiveness of supportive and antimicrobial therapy. Based on the latter, aggressive therapeutic modalities are used that must be applied to rigorously selected patients and by experienced physicians; however, there is empirical overtreatment of antibiotics due to the lack of accurate diagnostic tools or despite having the resources and knowledge, this medical malpractice is carried out due to arrogance, competence/ignorance, etc. [48, 49]

The World Health Organization advocates for the rational use of medicines, providing indicators for indications for drug use, assessing prescribing patterns and drug-related services; applying the parameters of the introduction of the Beers criteria, where numerous studies have examined prescribing patterns in comparison with these guidelines. Antibiotic prescribing practice was assessed using the 2023 World Health Organization Access, Watch and Reserve (AWaRe) classification system. [50, 51] In addition, judgments have been reached, as published in this report where it says that the study group of 64% received antibiotic treatment, even though only 28% presented symptoms consistent with the diagnostic criteria of the intensive care unit, the rest of the patients were diagnosed and treated despite not meeting the diagnostic criteria. This pattern of overdiagnosis leads to overtreatment, in short, medical malpractice. [52]

Antibiotics given within an hour of the incision reduce the incidence of surgical site infections in clean-contaminated abdominal surgeries. However, patients undergoing emergency surgery for an intra-abdominal infectious process often receive antibiotic treatment, they do not benefit from the pre-incisional antibiotic since it has been documented that they eventually have infection of the surgical wound. [53] The treatment of abdominal sepsis is initially with the use of antibiotic therapy, despite having a surgical etiology to be resolved, in addition to raising awareness of reducing the use of broad-spectrum antibiotics. [54] This line of treatment is expressed in the study of antibiotic therapy that focuses on prophylaxis, [55] post-surgery adjuvant, or empirical therapy in 4,530 patients in 23 hospitals; in patients with septic shock, microbiological samples were collected from 3,208 patients, or 70.8% patients, of which 3,041 were intra-abdominal samples and 48.8% were positive for *E. coli* (45.6%). The overall mortality rate was 5.13% (235/4350). [56]

In another report, early administration of appropriate antimicrobials is crucial to improve patient outcomes, where documented community-acquired infections were 85.66% of 286 patients, and the most common primary infection site was the urinary tract (24.48%), followed by respiratory tract infections (20.28%), and biliary and intra-abdominal infections (17.13%). The 30-day mortality rate of bloodstream infections was 16.08%. [57] A total of 286 pathogens representing 63.29% were isolated, including 181 Gram-negative bacteria, mainly *Escherichia coli*, *Klebsiella pneumoniae*, and *Pseudomonas aeruginosa*; 101 which are 35.31% were Gram-positive bacteria, mainly *Staphylococcus aureus*, *Staphylococcus epidermidis*, and *Streptococcus pneumoniae*; and only 4 cases that are 1.40% fungal isolates; the documented resistance rates were to penicillin G, rifampicin and cefoxitin reaching 74.7%, 4.2% and 50%. [57, 58]

With the cultures or isolation of microorganisms, the assertion that pathogens of normal biota (*Phocaeicola vulgatus*, *Eikenella corrodens*) are the cause of sepsis or abdominal septic shocks, is very risky; since there are reports of the pathogenicity of this microbiome that "are friends", and that according to another are brutal in their pathogenicity in some healthy subjects without neglecting immunosuppressed patients. this concept is questioned. [59, 60] and it is recalled that the virulence of a microorganism greatly conditions its potential to establish an infection. [12, 13]

Regarding the treatment of abdominal sepsis in the context of colorectal surgery, anastomotic leakage is one of the most feared complications, rescue failure is synonymous with the death of the patient with such a high rate of 15.7%, with surgery being the only possibility, survival option. [61] And where specified in the previously published study, which states that: "the majority of patients presenting with abdominal sepsis with abdominal distention and intestinal edema due to purulent, fecal, or chemical peritonitis, or a combination of two of the three, were considered candidates for the treatment of the open abdomen. However, when resolving the cause of sepsis or controlling it with adequate palliation in Damage Control Surgery or through energetic and thorough surgical washing, together with the placement of drains in strategic places and the use of nasogastric/bladder catheters to empty virtual spaces; together with the early initiation of frequent empirical antibiotics and, finally, the cooperation and/or participation in the surgery for the relaxation of the patient by the Anesthesia service in the closure of the cavity, the closure of the patient's abdominal cavity is achieved." [62] Open abdomen in surgery should be banned at any cost because of the brutal morbidity it entails and the high mortality. [25]

Nowadays in the medicine of the "artificial intelligence" era their concern is only to publish the possibility of determining the predictive value of patient mortality in abdominal sepsis; without providing any clinical, critical, analytical benefit that impacts the patient's survival in a positive way; for example, the elevation of C-reactive protein, procalcitonin and the canonical Notch ligand delta-1 type; which are relative/non-specific data that will depend on the infectious focus, the triggering pathogen and the severity of the disease, but at the end of the day it translates into an unnecessary increase in costs and that does not contribute to reducing mortality. [63]

Preclinical and animal research has revealed that cytokines derived from immune cells activate the hypothalamic-pituitary-adrenal axis, which plays a vital role in maintaining homeostasis

during the disease; on the other hand, the 2016 Sepsis Survival Campaign guidelines recommend intravenous hydrocortisone only if fluid resuscitation and vasopressor therapy fail to restore hemodynamic stability. [64]

There are two large-scale randomized trials (APROCCHSS trial and ADRENAL trial) that investigated adjuvant hydrocortisone in septic shock. The first APROCCHSS trial (enrolling 1,241 patients) found that patients randomly assigned to glucocorticoids exhibited lower mortality at 90 days. [65] In contrast, in the second ADRENAL, hydrocortisone treatment did not improve 90-day survival, but it reduced the duration of mechanical ventilation and shock. [66] In conclusion, the prophylactic use of glucocorticoids in hemodynamic status during surgical procedures identified patients who received a low-dose glucocorticoid of 200 to 300 mg of single-dose hydrocortisone during induction of anesthesia. [64]

OBSERVACIONES

1. In patients with the diagnosis of abdominal sepsis where the age, comorbidities or factors (smoking, alcoholism, immunosuppressant therapy, etc.) of this investigated group; drastically alter the patient's systemic inflammatory response, as in its clinical presentation in an indifferent or even unknown way; since they can be exponential in the systemic inflammatory response or the opposite, catapult to a minimum the real inflammatory process that exists at a very high final cost. This causes a diagnostic/therapeutic delay; without ceasing to be in a very serious or critical condition or dying without any treatment. That assertion supports them: does this diagnosis of "abdominal sepsis" really exist?
2. The second observation refers to the lack of real knowledge of the cause of death of the patient with a diagnosis of "abdominal sepsis"; since in Mexico for 25 years autopsies have not been routinely performed as they were previously done, now they are anecdotal.
3. It is simple to pigeonhole the patient and not question the brief misdiagnosis of "abdominal sepsis", since it must be pointed out that there are different diagnoses, one partially or completely resolved etiological, joint diagnoses, sequelae diagnoses, diseases potentiated by others or failing that, a new final diagnosis as a cause of death to the etiological, even without an autopsy, so it is necessary to have an analytical criterion.
4. Abdominal infection or sepsis that is believed to be caused by anaerobes is only by deduction/induction or illusion, since in 100% of cases in Mexico it is not objectively confirmed with cultures, colonies, etc., and there is no investigated scientific type I evidence of its existence. However, no patient is left without the application of antibiotic coverage for these pathogens.
5. There is a diagnosis of "sterile abdominal sepsis", which produces a systemic inflammatory response, multiple organ failure, and death; this occurs in chemical aseptic peritonitis, which occurs when irritating substances enter the abdominal cavity. Inflammation of the peritoneal serosa is initially sterile and fatal.
6. When analyzing that "abdominal sepsis" is called monomicrobial if the pathogen responsible is unique or polymicrobial if several species are identified. There are many variants to explain:
 - Who takes the sample

- How the sample is taken
- Where the sample is taken from, one or more sites, catheters or probes, fluids/fluids, etc.
- What resources are available for the sample, transfer, incubation, process, etc.
- Who processes the sample, the form and the inputs for it
- Period or time of resampling of the same site or other sites
- How the results are reported.

With all these variants and more to mention, without an institutional protocol and/or official Mexican standard for this complex process, it leaves a catastrophic void of the specific microbiological diagnostic reality.

7. The inappropriate, arbitrary and indiscriminate use of antibiotics by medical personnel, paramedics or the general population; it is another cadastral cause due to unequivocal/erroneous judgments and concepts due to poor competence of the responsible medical personnel, originating from the poor quality of teaching of medical schools in Mexico (there are faculties that do not even carry the subject of pharmacology), synergize exponentially with an advertising influence of the fashionable pharmacological emporiums; the easy accessibility of antibiotics by non-medical people, etc. The result is fatal, as it improves the effectiveness of the drug in mitigating infection and evokes multiple resistances of pathogens.
8. There are pathogens (infections) that are difficult to eradicate. Is this statement correct? For multifactorial causes:
 - The host or patient is suffering from wear and tears and has other diseases that have not yet been treated or treated. (anemia, malnutrition, avitaminosis, dehydration, pneumonia, etc.,)
 - Another cause is incomplete/poor quality reports due to poor crops, which do not report colonies, unrealistic or non-tropical susceptibility tests, etc.
 - The indiscriminate use of polypharmacy, escalation of unnecessary antibiotics empirically, with empirical overtreatment and, as if that were not enough, the incidence of the exponential increase in pseudomembranous colitis.
 - All the above is in most cases due to a lack of administrative expertise due to the lack of accurate diagnostic tools, resources, supplies, personnel, supply of medicines, academic updating, skills, etc.
9. The lack of real, reliable statistics or efficient epidemiological systems, updated and acclimatized to each specialty or area of medical care/hospital.
 - The most common surgical pathology is unknown and has surely changed.
 - In the format of death certificates, they are poorly made, obsolete and not very specific.
 - There is no correct system of epidemiological control that is agreed upon, validated, universal, scientific, efficient, available, etc., that allows economic and administrative resources to be concentrated on the real needs that to date are unknown in our country.
 - The total absence of real clinical practice guidelines, based on level I research in Mexico, carried out by current quality specialists in the area. Not the rehashes of other countries, with the empiricism of the lowest level V of clairvoyance or, failing that, by research without scientific value.

10. Another factor that has been observed to have changed the patient's prognosis and to reduce mortality since it avoids nosocomial pneumonia, is early estimation in the operating room at the end of emergency surgery; since if it is a shift change, there is room in intensive care, it is at night and avoids surveillance in anesthetic recovery; anesthesiologists for convenience and safety do not withdraw mechanical ventilatory assistance and this translates into pneumonia that in the end the cost is the patient's life.
11. Nowadays in medicine, fashion is the sad obsession with determining the predictive value of the patient's mortality risk in abdominal sepsis and not with modifying erroneous, absurd, misappropriate or even contradictory behaviors, fashions or therapies.

CONCLUSIONS

Effective surgical therapy applied to patients with life-threatening surgical pathology well applied can make a difference in morbidity and mortality. Abdominal sepsis (infectious) does not exist as a real diagnosis, since it is a complex, multifactorial inflammatory process of the individual, where incorrect diagnosis and treatment directly impact the patient's life. In Mexico, a real situational diagnosis of the health sector and a reengineering of processes in the quality of medical-surgical, administrative and research care must be carried out to initiate a beneficial/correct, efficient and effective change to abolish mortality, erroneously called abdominal sepsis.

Conflict of Interest

The authors stated that they had no potential conflicts of interest regarding the research, authorship, and/or publication of this article.

References

1. Sánchez-González M.A. Historia y futuro de las pandemias. *Revista médica clínica los Condes*. 2021; 32(1) 7-13.
2. Perry R.D., Fetherston J.D. *Yersinia pestis*-etiologic agent of plague. *Clin Microbiol Rev*. 1997; 10(1):35-66.
3. Margarita-López M., Cardona-Zorrilla A.F. La peste negra: el enemigo incorpóreo. <https://revistamedicina.net/index.php>. 2020 e.
4. Neri-Vela, R. Las enfermedades infecciosas en el hombre y su prevención a lo largo del tiempo. *Gaceta médica de México*. 2021; 157(5): 481-483.
5. Restrepo M. Anton Van Leeuwenhoek: Breve historia de un descubrimiento. *Hechos Microbiol*. 2012; 3(2); 99-102.
6. Sendrail M. Historia cultural de la enfermedad. Madrid: Espasa-Calpe. 1983.
7. Organización Mundial de la Salud. La OMS publica el primer informe mundial sobre prevención y control de infecciones (PCI). 2022 comunicado de prensa Ginebra. Revisado el 03/04/2025 en: <https://www.who.int/es/news/item/06-05-2022-who-launches-first-ever-global-report-on-infection-prevention-and-control>
8. Clínica Universidad de Navarra. Diccionario médico. 2025. Revisado el 03/04/2025 en: <https://www.cun.es/diccionario-medico/terminos/infeccion>.
9. Smith D.A., Nehring S.M. Bacteraemia. [Updated July 17, 2023]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; January 2025. Disponible en: <https://www.ncbi.nlm.nih.gov/books/NBK441979/>

10. Labbé V., Desnos C., Preau S., et al. Risk, rate or rhythm control for new onset supraventricular arrhythmia during septic shock: protocol for the CAFS multicentre, parallel-group, open-label trial. *BMJ Open*. 2025; 15(4):e090404.
11. Sun Q., Teng R., Shi Q et al. Clinical implement of Probe-Capture Metagenomics in sepsis patients: A multicentre and prospective study. *Clin Transl Med*. 2025; 15(4):e70297.
12. Nemati A., Gigliucci F., Morabito S., Badouei M.A. Virulence plasmids in edema disease: Insights from whole-genome analysis of porcine O139:H1 Shiga toxin-producing *Escherichia coli* (STEC) strains. *Front Cell Infect Microbiol*. 2025; 15:1528408.
13. Andreu A. Patogenia de las infecciones del tracto urinario. *Enfermedades Infecciosas y Microbiología Clínica*. Revisado e04/04/2025 en: <https://www.elsevier.es/es-revista-enfermedades-infecciosas-microbiologia-clinica-28-articulo-patogenia-infecciones-del-tracto-urinario-13091444>
14. Werter D.E., Schneeberger C., Geerlings S.E., et al. Diagnostic Accuracy of Urine Dipsticks for Urinary Tract Infection Diagnosis during Pregnancy: A Retrospective Cohort Study. *Antibiotics (Basel)*. 2024; 13(6):567.
15. Jd J.M.A., Ramalingam R. Clinicomycological Profile of Dermatophytosis in a Tertiary Care Hospital in Tamil Nadu, India. *Cureus*. 2025; 17(3):e79961.
16. Dvorak J., Fojtík L., Adámková L., et al. Proof-of-concept MALDI-TOF-MS assay for the detection of Toxin B enzymatic activity in *Clostridioides difficile* infection. *Microbiol Spectr*. 2025: e0245324.
17. Fang Y., Xie P., Zhang X., et al. Rapid detection of *Mycoplasma pneumoniae* CARDS toxin in clinical respiratory specimens by a loop-mediated isothermal amplification assay. *Front Cell Infect Microbiol*. 2025; 15:1496829.
18. Flores-Medina P. J., Garabay-Murillo P., Peñaloza Mendoza G. R. Automatización de inoculación en medios de cultivo para el laboratorio de microbiología. *Rev. Cienc. Tecnol*. 2023; 6(4), e285.
19. Carvalho N., Pereira A., Castro M., et al. Beyond the Lungs: A Case Report of Disseminated Tuberculosis With Multisystem Involvement. *Cureus*. 2025; 17(2):e78484.
20. Adu O.F., Sempere Borau M., Früh S.P., et al. Cell binding, uptake, and infection of influenza A virus using recombinant antibody-based receptors. *J Virol*. 2025: e0227524.
21. Varadan A.C., Grasis J.A. Filamentous bacteriophage M13 induces proinflammatory responses in intestinal epithelial cells. *Infect Immun*. 2025: e0061824.
22. Omosa-Manyonyi G.S., Ponce I.R., Rosati D., et al. Genetic susceptibility to recurrent vulvovaginal candidiasis in an African population from Nairobi, Kenya. *Sci Rep*. 2025; 15(1):12149.
23. Al Fadhli A.H., Jamal W.Y., Khodakhast F.B., et al. *Salmonella enterica* serotypes causing infection in Kuwait during 2018-2021, determined by multi-locus sequence typing or whole genome sequencing. *Microbiol Spectr*. 2025: e0224824.
24. Sáenz-Romero L.A., García-Sánchez M.A., Barrera-Zavala A., et al. A Difficult Diagnosis. *Journal of biomedical engineering and medical imaging*. 2020; 8(6): 1-5.
25. Lupio. G. B. R., García-Sánchez. M. A., Atzimba, Z. C. C., et al. Open Abdomen Is the Equal of Catastrophic or Hostile? *British Journal of Healthcare and Medical Research*. 2024: 11(2):182-200.
26. Herrera-Medina J.M., Retana-Márquez F.J., García-Sánchez M.A., y cols. Experiencia del tratamiento de la apendicitis aguda. *Revista Ocronos*. 2024;7(5): 982.7
27. Alverdy J. Unpacking the sepsis controversy. *Trauma Surg Acute Care Open*. 2025; 10(1):e001733. doi: 10.1136/tsaco-2024-001733.

28. Singer M., Deutschman C.S., Seymour C.W., et al. Third International Consensus on Definitions of Sepsis and Septic Shock (Sepsis-3). *JAMA*. 2016; 315:801–810.
29. Mellhammar L., Wollter E., Dahlberg J., et al. Estimating Sepsis Incidence Using Administrative Data and Clinical Medical Record Review. *JAMA Netw Open*. 2023;6:e2331168.
30. Lindell R.B., Meyer N.J. Interrogating the sepsis host immune response using cytomics. *Crit Care* 2023;27:93.
31. Jaramillo-Bustamante JC, Piñeres-Olave BE, González-Dambrauskas S. SIRS or not SIRS: Is that the infection? A critical review of the sepsis definition criteria. *Bol Med Hosp Infant Mex* 2020;77:293–302.
32. Andrews M.C., Duong C.P.M., Gopalakrishnan V., et al. Gut microbiota signatures are associated with toxicity to combined CTLA-4 and PD-1 blockades. *Nat Med* 2021;27:1432–41.
33. Thomas R.M., Jobin C. Microbiota in pancreatic health and disease: the next frontier in microbiome research. *Nat Rev Gastroenterol Hepatol* 2020;17:53–64.
34. Cassini Alessandro, et al. "Global Report on the epidemiology and burden on sepsis: current evidence, identifying gaps and future directions." *Global Report on the epidemiology and burden on sepsis: current evidence, identifying gaps and future directions*. 2020.
35. Vakkalanka J.P., Harland K.K., Swanson M.B., et al. Clinical and epidemiological variability in severe sepsis: an ecological study *J Epidemiol Community Health* 2018; 72: 741-745.
36. Parolini C. Sepsis and high-density lipoproteins: Pathophysiology and potential new therapeutic targets. *Biochim Biophys Acta Mol Basis Dis*. 2025; 1871(5):167761.
37. Cavaillon J., Marc Adib-Conquy, M., Fitting, C., et al. Cytokine cascade in sepsis. *Scandinavian Journal of Infectious Diseases*. 2003;35 (9), 535–544.
38. Schnab B., Brenner D.A. Interactions Between the Intestinal Microbiome and Liver Diseases. *Gastroenterology*. 2014; 146(6):1513-1524,
39. Eshaghi S, Sheybani F, Hedjazi A, Naderi H, Shirazinia M, Morovatdar N. Infectious Causes of Death: An Autopsy-Based Study of 546 Cases. *Open Forum Infect Dis*. 2025 Feb 4;12(2):ofaf065. doi: 10.1093/ofid/ofaf065. PMID: 39963699; PMCID: PMC11832044.
40. Suneja M., Beekmann S.E., Dhaliwal G., et al. Diagnostic delays in infectious diseases. *Diagnosis (Berl)*. 2022; 9(3):332-339.
41. Idensohn P.J., Gilbert K., Boodhoo K., et al. The Prevalence, aetiology and Healing Trajectories of Hard-To-Heal Wounds in South Africa. *Int Wound J*. 2025; 22(3):e70155.
42. Falsey A., Peterson D., Walsh E., et al. A Four-Gene Signature from Blood to Exclude Bacterial Etiology of Lower Respiratory Tract Infection in Adults. *Res Sq [Preprint]*. 2025 Feb 27:rs.3.rs-6033997. doi: 10.21203/rs.3.rs-6033997/v1.
43. Bennett N., Tanamas S.K., James R., et al . Healthcare-associated infections in long-term care facilities: a systematic review and meta-analysis of point prevalence studies. *BMJ Public Health*. 2024;2(1):e000504. doi: 10.1136/bmjph-2023-000504.
44. Gurguí M., Moreno A., y cols. Peritonitis y otras infecciones intrabdominales. *Sociedad Española de Enfermedades Infecciosas y Microbiología*. 2023. Guía de práctica clínica. Madrid, España.
45. Adeleke A.A., Wuraola F.O., Olasehinde O. Effect of Wound Irrigation with Povidone Iodine Versus Normal Saline on Superficial Incisional Surgical Site Infection Following Laparotomy for Peritonitis. *J West Afr Coll Surg*. 2025; 15(2):203-208.

46. Ikota M., Akahoshi T., Murata I., et al. [Perforation of Small Intestinal Gastrointestinal Stromal Tumor Required Emergency Surgery-A Case Report]. *Gan To Kagaku Ryoho*. 2025; 52(2):182-184.
47. García Sánchez M.A., Sáenz Romero L.A., De La Fuente González M., et al. Pneumoperitoneum! Is it a Diagnosis? *EC Gastroenterology and Digestive System*. 2021;8(1): 33-38.
48. García-Basulto M.J., García-Rodríguez M.E., Benavidez-Márquez A., y cols. Pacientes con infección intrabdominal en la unidad de cuidados intensivos. *Revista Cubana de Cirugía*. 2020; 59(3).
49. Dierikx T.H., Admiraal J, Nusman C.M., et al. The diagnostic accuracy of presepsin for late-onset neonatal sepsis: a multicenter prospective cohort study. *Pediatr Res*. 2025. doi: 10.1038/s41390-025-04008-x.
50. Malekzadeh M., Khadivi Y., Sohrevardi S.M., Afzal G. Drug prescription patterns and compliance with WHO and beers criteria in older patients. *BMC Geriatr*. 2025; 25(1):135.
51. Abdu N., Idrisnur S, Tewelde T., Tesfamariam E.H. Antibiotic prescribing practice using WHO Access, Watch and Reserve classification and its determinants among outpatient prescriptions dispensed to elderly population in six community chain pharmacies in Asmara, Eritrea: a cross-sectional study. *BMJ Open*. 2024; 14(6):e085743.
52. Murray K., Shimabukuro J., Khalfay N., et al. Antibiotic Overprescription for "Urinary Tract Infections" Is Associated With Poor Diagnostic Stewardship and Low Adherence to Guidelines. *Neurourol Urodyn*. 2025; 44(2):382-389.
53. Hendrix A., Kammien A., Maung A.A., et al. Antibiotics and Surgically Treated Acute Appendicitis, When, Where, and Why? *Surg Infect (Larchmt)*. 2025. doi: 10.1089/sur.2024.264.
54. Gallego-Navarro C., Beckermann J., Linnaus M.E., et al. Optimizing Antibiotic Management for Adult Patients Presenting with Acute Perforated Appendicitis: A Quality Improvement Study. *Surg Infect (Larchmt)*. 2025; 26(3):143-149.
55. Droogh D.H.M., de Boer M.G.J., van Prehn J., et al. Dutch Pancreatic Cancer Group. Standard versus Pre-emptive Antibiotic Treatment to Reduce the Rate of Infectious Outcomes after Whipple resection (SPARROW): a study protocol for a multicentre, open label, randomised controlled trial. *Trials*. 2025; 26(1):88.
56. Coccolini F., Brogi E., Ceresoli M., et al. Epidemiological analysis of intra-abdominal infections in Italy from the Italian register of complicated intra-abdominal infections-the IRIS study: a prospective observational nationwide study. *World J Emerg Surg*. 2025; 20(1):22.
57. Lang Y., Chen L., Xiao J., et al. A single-center retrospective study of pathogen distribution and antibiotic resistance of bloodstream infections in emergency department. *Zhong Nan Da Xue Xue Bao Yi Xue Ban*. 2024; 49(11):1799-1807.
58. Kato H., Hirai J., Takano T., et al. A systematic review and meta-analysis on the efficacy of carbapenems versus metronidazole combination therapy in patients infected with *Bacteroides* spp. *J Infect Chemother*. 2025; 31(5):102687.
59. Wang S., Niu W., Lv T., Xie K. Traceability of septic shock caused by *phocaeicola vulgatus*: a rare case report. *BMC Infect Dis*. 2025; 25(1):364.
60. Zhang H., Xia Y., Wang L., Zhang B. Septicemia caused by *Eikenella corrodens* in a previously healthy male: A case report. *Medicine (Baltimore)*. 2025; 104(13): e41849.
61. Rubio-García J.J., Mauri Barberá F., Villodre Tudela C., et al. Failure to rescue in colon surgery. *J Healthc Qual Res*. 2025; 40(4):101118.

62. García-Sánchez M.A., García-Hernández J.L., Urbina-Cabello J.J., et al. Damage Control Surgery: A Strategic Resource! *British Journal of Healthcare and Medical Research* 2025; 12, (02): 90-109.
63. Theobald V., Bloos F., Bauer M., et al. Host-derived Delta-like Canonical Notch ligand-1 in sepsis and septic shock: Infection site, pathogens and disease severity matter - Secondary analysis of data from a randomized controlled trial. *J Infect.* 2025; 90(4):106458.
64. Tao T., Shi Y., Ye X., et al. Intraoperative Low-Dose Glucocorticoids in Surgical Patients with Abdominal Sepsis: A Multicenter Retrospective Cohort Study. *Health Sci Rep.* 2025; 8(2): e70360. doi: 10.1002/hsr.2.70360. PMID: 39980824; PMCID: PMC11839392.
65. Annane D., Renault A., Brun-Buisson C., et al. CRICS-TRIGGERSEP Network. Hydrocortisone plus Fludrocortisone for Adults with Septic Shock. *N Engl J Med.* 2018 Mar 1;378(9):809-818.
66. Venkatesh B., Finfer S., Cohen J. et al. ADRENAL Trial Investigators and the Australian–New Zealand Intensive Care Society Clinical Trials Group. Adjunctive Glucocorticoid Therapy in Patients with Septic Shock. *N Engl J Med.* 2018; 378(9):797-808.