

# Management of secondary peritonitis

## Our experience



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### Management of secondary peritonitis: our experience

*Intra-abdominal infections are a common cause of nosocomial sepsis and are associated with a severe morbidity, mortality and sanitary economy implications, especially for decentralized sanitary structures.*

*Mortality due to diffuse suppurative peritonitis (from 10 to 20%) nowadays continues to be unacceptably high. Patients outcome is significantly influenced by early adequate surgery and/or peritoneal drainage: moreover, even early and adequate empiric antimicrobial therapy influences patients morbidity and mortality. Multiple empirical regimens have been proposed, but rarely supported by reliable randomized-controlled studies.*

*The authors report 201 cases of patients with fever and meaningful peritoneal involvement occurred since August 1999 up to August 2005: 110 cases were conservatively treated, 91 cases were surgically treated. The paper summarizes IDAB (Infection Disease Advisory Board) guidelines inheriting management of intra-abdominal infections: empiric antimicrobial therapy for the most common causes of abdominal infections is proposed for low-mid level risk patients, focusing on antibiotic treatment duration. High risk patients need to be evaluated paying particular attention to timely surgical infection source control.*

**CONCLUSION:** *Despite of the progress in antimicrobial agents and intensive care treatment, peritonitis is still one of the most important infectious problems that a surgeon has to face.*

**KEY WORDS:** Peritonitis, Secondary peritonitis, Surgery on peritonitis.

### Introduction

Peritonitis is currently one of the most important problems that a surgeon might face.

**Primary peritonitis** is a peritoneal diffuse infection that arises without any septic focus finding: it interests cirrhotic patients with ascites (decreased protein synthesis and decreased complement activity): sepsis, hepato-renal syndrome, diffuse encephalopathy, hypovolemia and intestinal hemorrhages are predisposing factors. Primary peritonitis in children, rare nowadays, is characterized by

Gram- (Escherichia coli) monomicrobial infection. Primary peritonitis occurring in young girls is caused by organisms that are believed to arise from the genital tract. Primary peritonitis is mainly monomicrobial and usually doesn't require a surgical approach.

**Secondary peritonitis** is caused by a chemical, physical or biological aggression of the peritoneal serosa.

It takes origin from flogistic, perforative, neoplastic, vascular pathology or from a trauma of an abdominal organ and/or from trauma of the wall.

It can be consequence of the spreading of a flogistic site: acute appendicitis, acute cholecystitis, diverticulitis, adnexitis, hepatic abscess, pancreatitis.

It can also derive from perforation of hollow organs: perforated peptic ulcers, perforation of diverticula, diastatic perforation located before an occlusion, gallbladder perforation, appendix perforation, toxic megacolon, perforation of the bladder, perforation as a result of neoplasia.

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sia infiltration and iatrogenic perforations in course of diagnostic procedures.

Moreover it can be consequence of hollow organs ischaemia with necrosis: intestinal stroke and necrosis, strangling, volvulus, intasate or incarcerated or strangled hernias.

Finally it can be consequence of direct or indirect surgical actions: anastomotic dehiscence, sieroematic cavity fluids collection, postoperative pancreatitis, intraoperative bacterial contamination, vascular lesions with ischaemia or necrosis of hollow organs <sup>1</sup>.

**Tertiary peritonitis** is defined as the persistence or recurrence of intraabdominal infection after adequate treatment for primary or secondary peritonitis (lack of response to surgical and antibiotic therapy): the most common infecting organisms are Enterococcus, Candida, Staphylococcus epidermidis and Enterobacter.

In a decreasing order of incidence common not-traumatic causes of peritonitis reported in literature are:

- appendicitis 35%
- acute cholecystitis 20%
- peptic ulcer perforation (duodenal/gastric 3:1) 15%
- intestinal ischemia/necrosis, gangrenous cholecystitis 10%
- postoperative complications 10%

- other causes (colon, diverticula perforations etc.) 9%
- iatrogenic visceral lesions. 1%

Despite improvements of antimicrobial therapy and great progresses inheriting intensive treatment, mortality due to diffused peritonitis interests from 10 up to 20% of cases in literature.

Necrotizing acute pancreatitis, and surgery-related diffuse purulent peritonitis are the most important causes of death. Literature indicates, in this specific group, a mortality of 50- 60% that nowadays continues to be unacceptably high <sup>2,3</sup>.

### Our experience

We have studied cases of hyperpyrexia with meaningful consensual peritoneal involvement that come to our observation between 1999 and 2005. On a total of 201 cases we have distinguished the subgroup of patients conservatively treated and healed with observation and antibiotic therapy (110 cases, 58%) and subgroup of patients treated with surgery and antibiotic therapy (91 cases, 42%).

In 21 cases of post-operative hyperpyrexia we have searched the responsible microorganism through coltural exams.

TABLE I

Cases	Conservative Tr.	Surgical Tr.
Acute appendicitis	20	23 (2 reintervention)
Acute cholecystitis	24	21
Cholangitis	9	2
Diverticulitis	12	5
Adnexitis	3	2
Crohn disease	6	3
Toxic megacolon	5	3
Gastroduodenal perforation	3	3
Intestinal Ischemia	3	3
Rectal perforation	3	3
Closed bowel perforation	6	6
Anastomotic Dehiscence	6	4
Evisceration	3	3
Wound infection	7	0
Abscessual endoperitoneal fluid collection		10 (US or TC driven drainage)
<b>Total</b>	<b>110</b>	<b>91</b>

TABLE II

Cases of post-operative hyperpyrexia whose responsible microorganism we have searched.	21
Negative search in coltural exam:	9
Positve search in coltural exam:	
E. Coli, Pseudomonas Aerug. Stafilococcus Epidermidis, Bacteriodes Fragilis, Candida.	12

The average age of patients in our series was 41 years: our surgical team is mainly addressed to elective abdominal pathology so MPI score, we have been collecting for 150 of the 201 patients along the treatment, has demonstrated a average score value of 19. Two patients died with a respective MPI score of 29 and 31.

## Discussion

### *Diagnosis*

The diagnosis of an abdominal infection requiring surgical management implies urgent indication to the etiological therapy, support and intensive care and surgical control of infection sources.

Fever, pain, lacking of peristalsis with no fecal or gas emissions remain the main signs in secondary peritonitis diagnosis even if nowadays they are integrated with laboratory, imaging and instrumental methods.

In some circumstances, the diagnosis of dangerous abdominal infections could be difficult: for example during early postoperative time, in immunocompromised patients and in patients with comorbidity.

Every case of post-operative hyperpyrexia could prelude to serious abdominal infection, however in many cases it is not found.

In our experience a variable percentage (from 15 to 40%) of patients who undergo abdominal surgery experiences hyperthermia: only 20-30% of these patients demonstrates a cultural microbial finding; common causes of post-operative hyperthermia are pulmonary atelectasia, urinary infections, wound infections and thrombophlebitises (4W: wind, water, wound, walking); other possible causes are venous catheters, hepatic suffering halothan-related or neoplastic hyperpyrexias especially in patients who undergo palliative surgical treatments.

Pain is a symptom whose valuation is difficult, especially during early postoperative time, in older patients, children, psychiatric patients, patients with advanced neuropathy and immunocompromised.

Although the pain remain one of the main signs: its characters, localization, irradiations, the modifications over time and its relations often suggest strong indications about the organ affected.

Hypomobility, cutaneous hyperaesthesia, tension of parietal muscles, rigidity, lack of hepatic dullness and auscultatory silence are the main physical signs suggesting peritonitis. Moreover we have to underline the role of rectal exploration and evocation of ileopsoas and otturatore muscle signs.

Diagnosis is enforced by haematological data (leukocytosis, metabolic acidosis), ultrasonographical data (acute cholecystitis, localized peritonitis, fluids collections acquired by ultrasound guided aspiration), traditional RX data and nowadays is enforced by tomographic data (collections, organ lesions, etc).

Diagnostic peritoneal lavage could be useful to unveil in drained collections leucocytes, amylase, bilirubin, microbial contamination, moreover not negligible is the role of diagnostic laparoscopy.

Transplants, chemotherapy, autoimmune diseases, cortisonic treatment expose patients to infections from CMV, Candida and opportunists microorganism (Proteus, Enterobacter, Pseudomonas, Enterococcus, Staphilococcus epidermidis), especially during alitiasic cholecystitis, diverticulitis, perforations, pancreatitis, and they hide, at the same time, symptoms.

The differential diagnosis of peritonitis implies exclusion of pulmonary pathologies (lobar inferior pneumonia), of cardiac pathology (acute myocardial infarction, angor), of neurological pathologies, of urological pathologies (pyelonephritis, urinary lithiasis) of gynecological pathologies (adnexitis, cysts), of toxic and metabolic pathologies (diabetes, uraemia, Addison disease, saturnism), of infectious pathologies (typhoid fever, TBC, spontaneous bacterial peritonitis), of haematological pathologies (porphyria, leukaemia, sickle cells anemia), of other diseases (familiar Mediterranean fever, peri-arthritis, cancer).<sup>4,5,6</sup>

### *Pathophysiology*

Peritoneal surface is extended 2 square meters and acts like a semipermeable membrane characterized by bidirectional electrolytes, water and small molecules exchanges.

The mechanisms of peritoneal defense can be distinguished in mechanisms of "removal" (peritoneal clearance of bacteria and toxins diaphragm-mediated, mechanisms of "killing" (macrophages, neutrophils, opsonin, C3b, IgC, CTL, Fibronectin), and mechanisms of "sequestration" (fibrin reticulum, fibrin-related adhesions of bowel and omentum to circumscribe septic process).

Mesothelial cells provide an intense biological answer and play an important role: they promote the clearance of contaminated fluid and induce formation of adhesions fibrin-mediated to circumscribe localization of microbial agents: a complex sequence of events evolved in order to protect life.<sup>7</sup>

Bacterial flora of secondary peritonitis is generally characterized by the prevalence of E.Coli, Enterococchi, Bacterioides and Clostridi. E.Coli and Bacterioides are more prone to determine septicaemia for their greater propension to reach blood circulation.

Anaerobi and opportunistic bacteria usually lead to circumscribed peritonitis.

Severe abdominal infections are characterized by an elevated level of bacterial endotoxins, that could prelude to systemic inflammatory syndrome (SIRS) often complicated because of multiorgan failures.<sup>8</sup>

## Treatment

### Triaging

The treatment of the surgical should be preceded by attribution to patients of some score (APACHE II, MPI) during clinical triaging.

A reproducible score system allows the surgeon to determine severity of peritonitis: this is essential in order to ratify the effectiveness of the treatments, in order to compare the intensive and surgical cures scientifically, in order to help in valuation of the risk and to select patients who could require a more aggressive approach; finally is important in order to inform the patient and their relatives with greater objectivity.

One of the most accepted systems is APACHE II: it calculates various physiological variables during the first 24 hours in hospital together with age and state of health of the patient.

This allows one stratification of the risk factors and a predictive equation of the survival but requires time.

Another wide adopted index is the Mannheim Peritonitis Index (MPI) based on the analysis of 17 possible factors of risk, 8 of which particularly important to obtain a prognosis: age, sex, organ damage, cancer, duration of the peritonitis, colon involvement, extension of the peritonitis and character (clean, purulent or faecal) of the peritoneal fluid. It has some advantages over apache II: it's simpler and provides the possibility to acquire retrospective data normally present in the surgical registries. Literature reports a statistically meaningful relation between the value of the score and potentiality of fatal evolution. Mortality increases with increasing of the ranges of the score.

Adopting three ranges "< 20", "from 20 to 30", and "> 30" MPI-score related mortality grows from 0% to 28% up to 81%. In relation to APACHE II score acquired in the first day of cure, mortality grows up from 20% to 46% up to 100%.<sup>9,10,11,12</sup>

Established the risk, the patient will receive colloids and liquids infusion while venous central pressure, diuresis, HCT, HGT, renal functionality, electrolytes and emogas will be monitored.

Parenteral total nutrition and empiric antibiotics therapy, waiting for antibiogram if possible, could be useful. The contribution of liquids and nutritional support pre and postoperative are crucial to favorable prognosis.

### Antimicrobial therapy

Experimental models have demonstrated that the infection will become, in nearly the totality of the cases polymicrobial, aerobica and anaerobic with a prevalence of gram negative (aerobic and anaerobic) and anaerobic cocci. During the first septicemic stage *Escherichia Coli* is main responsible of high percentage of death; over

time a second stage is observed where *Bacteriodes fragilis* is responsible of anaerobic abscesses. The role of *Enterococcus fecalis* is not clearly defined but should be considered in every case of septic shock.

The clinical evidence demonstrates that the adoption of a rapid correct empiric therapy and the adoption of antibiogram-guided definitive therapy (examining microbiological findings on the fluids of the patient) has a meaningful impact on the morbidity, mortality, duration of the hospitalization and therefore has also a great influence in sanitary economy.

Thank to the collaboration of organism like IDSA (Infectious Disease Society of America)<sup>13</sup>, Surgical Infection Society, American Society of Microbiology, the Society of Infectious Disease Pharmacists, some evidence based guidelines have been proposed.

In Europe similar guidelines have been composed by Infectious Disease Advisory Board (IDAB).<sup>14</sup> Empiric therapy of community acquired infections must have for target gram-negative aerobic germs, facultative bacteria, gram-positive cocci, and in cases of infections whose source is distal jejunum or colon, anaerobic bacilli should be considered. In mild-to-moderate community-acquired infections, antibiotics used to treat nosocomial infections should not be used: antibiotics with low toxicity like ampicillin/sulbactam, cefazolin, cefuroxime/metronidazole, ticarcillin/clavulanate ed ertapenem should be preferred. Aminoglycosides being nephrotoxic and ototoxic are not recommendable in community acquired infections and should be used only in patient with allergies to beta-lactamines.

Patients with severe disease or higher risk (higher APACHE II score, immunosuppressive treatment, antitlastic treatment, comorbidity, nutritional defect) should be treated against facultative bacteria and gram-negative aerobic: meropenem, imipenem/cilastatina, ceftriaxone, piperacillin/tazobactam, ceftazidime/metronidazole, cefotaxime, cefepime.

Nosocomial abdominal infections (hospital acquired) have more resistant bacterial flora that could include *Pseudomonas Aeruginosa*, *Enterobacter*, *Proteus*, *Candid*, *Enterococci* and *Stafilococcus Aureus*. Empiric antibiotic therapy for such infections should be guided by knowledge of the nosocomial flora (hospital-related) and its antimicrobial susceptibilities/resistances pattern: this is possible through periodical nosocomial samplings and helps to identify the presence of gram positive meticillin-resistant bacteria, vancomicine or ampicillin resistant *S. Aureus* or *Enterococci* and *Bacteriodes clindamicina*, cefotetan, ceftoxitin, and quinolon resistant.

Subsequently the treatment of severe hospital acquired infections should be modified in relation to microbiological findings on patient biological coltures and could imply combined antibiotic therapies (quinolon, carbapenem, aminoglicosids).

The duration of the therapy should be prolonged until signs of infection disappear (temperature, it leucocytosis,

and lacking peristalsis). Patients who need extended therapy (over 5-7 days) should undergo ulterior exams (echo, TC, coltures), and the opportunity of another surgical look should be considered.

Antifungine therapy against *Candida* is unnecessary unless the patient has received immunosuppressive therapy for neoplasm, transplantation, inflammatory disease or the patient has postoperative or recurrent intrabdominal infections. In these cases is important to establish the presence of fluconazolo-resistant *Candida* to treat with anfotericin B or voriconazole.

## Surgery

Surgery treatment could imply removal of the organ source of infection (cholecystectomy, appendicectomy), repair of perforative lesions (stomach, duodenum), bowel resections (diverticula, intestinal infarction, jejunum, colon, sigma perforations), the repair, where possible, of anastomotic dehiscence, temporary external derivation of faecal transit, peritoneal washing and debridement, placing of multiple peritoneal drainages. Some authors underline advantages of early diagnostic or therapeutic laparoscopy: according them it provides greater diagnosis accuracy and more accurate, rapid and effective treatment of acute abdominal pain reducing the percentage of inopportune laparotomies and the frequency of right iliac fossa useless surgical accesses. Another wide debated problem is inherent the opportunity of one stage intervention with a relaparotomy only if necessary instead of a programmed relaparotomy during first intervention.

Cases where the opportune choice is questionable require experience and common sense.

The factors that influence this choice are: opportunity to perform primary anastomosis based on the etiology, interested regions and organs, local extension of the process and opportunity of primary closure of the abdominal wall.<sup>15,16,17</sup>

The adoption of programmed relaparotomy or adoption of relaparotomy only if necessary appear to prelude to similar results in the treatment of the seriously diffused peritonitis: the primary objective remains the removal of infection source as soon as possible.

## Conclusion

The peritonitis are nowadays characterized by high mortality.

Early diagnosis, intensive supportive care, timely adoption of correct antimicrobial treatment (empirical and antibiogram-driven) and surgical control of infection sources as soon as possible play a fundamental role in prognosis of patients.

## Riassunto

Le infezioni intraddominali sono una causa comune di sepsi in ambito nosocomiale e sono associate ad una severa morbilità, mortalità e ad importanti implicazioni di economia sanitaria, specie per le strutture sanitarie decentrate.

L'attuale mortalità dovuta alle peritoniti suppurative diffuse varia dal 10 al 20%: continua pertanto ad essere inaccettabilmente alta.

La prognosi dei pazienti è significativamente influenzata da un trattamento chirurgico precoce e da un adeguato drenaggio chirurgico: anche una precoce e opportuna terapia antibiotica influenza la mortalità e la morbilità. In questo campo sono stati proposti molti schemi terapeutici antimicrobici, solo raramente supportati da studi randomizzati attendibili.

Gli autori riportano 201 casi di pazienti con sindrome febbrile e risentimento peritoneale trattati tra l'agosto 1999 e l'agosto 2005: di essi 101 sono stati trattati con terapia farmacologica, e i restanti 91 con antibiotici e trattamento chirurgico.

Il lavoro riassume le linee guida dell' Infectious Disease Advisory Board per il trattamento delle infezioni addominali: viene proposta una terapia antimicrobica empirica per i pazienti a rischio moderato ponendo particolare attenzione alla durata del trattamento.

I pazienti ad alto rischio andrebbero inoltre valutati ponendo particolare attenzione al controllo della sorgente di infezione.

CONCLUSIONE: Nonostante i progressi nel trattamento antimicrobico e in terapia intensiva, le peritoniti sono ancora oggi uno dei più importanti problemi che il chirurgo deve affrontare.

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