World Journal of Gastroenterology

Online Submissions: http://www.wjgnet.com/1007-9327office
wjg@wjgnet.com
doi:10.3748/wjg.v18.i9.865

*World J Gastroenterol* 2012 March 7; 18(9): 865-871
ISSN 1007-9327 (print) ISSN 2219-2840 (online)


EDITORIAL

# Antimicrobial management of intra-abdominal infections: Literature's guidelines

Massimo Sartelli, Fausto Catena, Federico Coccolini, Antonio Daniele Pinna

Massimo Sartelli, Department of General Surgery, Macerata Hospital, 62100 Macerata, Italy
Fausto Catena, Federico Coccolini, Antonio Daniele Pinna, Department of General, Emergency and Transplant Surgery, Sant'Orsola-Malpighi University Hospital, 40138 Bologna, Italy
Author contributions: All the authors contributed equally to this paper.
Correspondence to: Massimo Sartelli, MD, Department of General Surgery, Macerata Hospital, Via Santa Lucia 2, 62100 Macerata, Italy. m.sartelli@virgilio.it
Telephone: +39-733-2572486 Fax: +39-733-2572471
Received: February 10, 2011 Revised: March 29, 2011
Accepted: April 4, 2011
Published online: March 7, 2012

## Abstract

Antimicrobial management of severe intra-abdominal infections (IAIs) involves a delicate balance of optimizing empirical therapy, which has been shown to improve clinical outcomes, while simultaneously reducing unnecessary antimicrobial use. Two sets of guidelines for the management of intra-abdominal infections were recently published. In 2010, the Surgical Infection Society and the Infectious Diseases Society of America (SIS-IDSA) created guidelines for the diagnosis and management of complicated IAIs. The new SIS-IDSA guidelines replace those previously published in 2002 and 2003. The World Society of Emergency Surgery (WSES) guidelines represent additional contributions, made by specialists worldwide, to the debate regarding proper antimicrobial drug methodology. These guidelines represent the conclusions of the consensus conference held in Bologna, Italy, in July 2010 during the first congress of the WSES.



**Key words:** Intra-abdominal infections; Antimicrobial therapy; Literature's guidelines

**Peer reviewers:** Marcelo A Beltran, MD, Chairman of surgery, Hospital La serena, PO BOX 912, La Serena, IV REGION, Chile; Martin D Zielinski, MD, Department of Trauma, Critical Care and General Surgery, Mayo Clinic, 1216 2nd St Sw, Rochester, MN 55902, United States

Sartelli M, Catena F, Coccolini F, Pinna AD. Antimicrobial management of intra-abdominal infections: Literature's guidelines. *World J Gastroenterol* 2012; 18(9): 865-871 Available from: URL: http://www.wjgnet.com/1007-9327/full/v18/i9/865.htm DOI: http://dx.doi.org/10.3748/wjg.v18.i9.865

## INTRODUCTION

Intra-abdominal infections (IAIs) encompass a variety of pathological conditions, ranging from uncomplicated appendicitis to fecal peritonitis. Cases of IAI are further subcategorized as being either uncomplicated or complicated[1].

In the event of an uncomplicated case of IAI, the infection only involves a single organ and does not extend to the peritoneum. Patients with such infections can be treated with either surgical resection or antibiotics. When the infection is effectively resolved by surgical excision, 24-h perioperative prophylaxis is typically sufficient. Patients with IAIs, including acute diverticulitis and certain forms of acute appendicitis, may be treated non-operatively by means of antimicrobial therapy.

In the event of complicated IAI, the infectious process proceeds beyond the organ, causing either localized or diffuse peritonitis. The treatment of patients with complicated IAIs involves both source control and antibiotic therapy.

Antimicrobial therapy plays an integral role in the management of IAIs, especially in critically ill patients who require immediate empiric antibiotic therapy. An insufficient or otherwise inadequate antimicrobial regimen is one of the variables most strongly associated with unfavorable outcomes[2,3].

Various studies have demonstrated that inappropriate

antimicrobial use is common. Excessive antimicrobial use has contributed to the emergence and spread of drug-resistant microorganisms and has simultaneously increased overall treatment costs[4-9].

An antimicrobial-based approach to treating IAIs always involves a delicate balance between the optimization of empirical therapy, which has been shown to improve clinical outcomes, and the reduction of excessive antimicrobial use, which has been proven to increase the rate of emergence of antimicrobial-resistant strains.

The threat of antimicrobial resistance has been identified as one of the major challenges in the management of complicated IAIs.

In the past few decades, an increased prevalence of infections caused by antibiotic-resistant pathogens, including methicillin-resistant *Staphylococcus aureus*, vancomycin-resistant *Enterococcus* species, carbapenem-resistant *Pseudomonas aeruginosa* (*P. aeruginosa*), extended-spectrum β-lactamase (ESBL)-producing *Escherichia coli* (*E. coli*) and *Klebsiella* species, and multidrug-resistant *Acinetobacter* species, has been observed, especially in IAIs.

To resolve the medical community's tendency to overuse antibiotics, a set of guidelines outlining the proper use of antimicrobial therapy has been implemented, which contains specific directions for addressing IAIs.

Two different sets of guidelines outlining the clinical management of IAIs were recently published.

In 2010, the Surgical Infection Society (SIS) and the Infectious Diseases Society of America (IDSA) instituted standardized guidelines for the diagnosis and management of complicated IAIs[10].

The new SIS and IDSA guidelines replace those previously published in 2002 and 2003.

The World Society of Emergency Surgery (WSES) guidelines[11] represent an additional contribution to the debate by specialists worldwide. These guidelines represent the conclusions reached by the consensus conference held in Bologna, Italy, in July 2010, during the first congress of the WSES; in attendance at this event were surgeons, infectious disease specialists, pharmacologists, radiologists and intensivists, all of whom wished to define and streamline a standardized set of recommendations for the early treatment and management of IAIs[11].

## GUIDELINES BY SIS AND IDSA: ANTIMICROBIAL MANAGEMENT FOR COMPLICATED INTRA-ABDOMINAL INFECTIONS

In the SIS and IDSA guidelines, selection of the appropriate antimicrobial regimen is based primarily on the "risk factor" of the potential failure of the treatment in question.

"High risk" describes patients with an increased likelihood of treatment failure and a greater potential severity of infection according to clinical assessment criteria. Such patients include those with anatomically unfavorable infections or health care-related infections[10].

Clinical factors predicting failure of treatment for IAIs include: (1) delay in the initial stages of intervention (24 h ); (2) high severity of illness (Acute Physiology and Chronic Health Evaluation Ⅱ score > 15); (3) advanced age of patient; (4) comorbidity involving organ dysfunction; (5) low albumin levels; (6) poor nutritional status; (7) peritoneal involvement or diffuse peritonitis; (8) inability to achieve adequate debridement or control of drainage; (9) presence of malignancy; and (10) health care-related infection.

Health care-related infections refer to a spectrum of adult patients treated in acute care hospitals or monitored in chronic care settings. These patients increase their risk of infection due to the emergence of multidrug-resistant bacteria. Health care-related infections have higher risks of complication and mortality than community-acquired disease.

Guidelines developed by the SIS and the IDSA have recommended various single-agent and combination regimens for patients with different levels of risk.

### *Extra-biliary community-acquired intra-abdominal infections*

In the treatment of patients with community-acquired IAIs, empiric antimicrobial therapy should protect against common gram-negative and anaerobic enteric bacteria.

The SIS and IDSA guidelines classify community-acquired IAIs as being mild, moderate, or severe on the basis of the patient's assessed risk factors.

For high severity infections, those cases for which adequate empirical therapy helps reduce the rate of mortality, regimens having a broader spectrum of antimicrobial activity are recommended.

For adult patients with mild-to-moderate community-acquired infections, the SIS-IDSA guidelines recommend the use of ticarcillin-clavulanate, cefoxitin, ertapenem, moxifloxacin, or tigecycline as single-agent therapies; the guidelines also advocate combinations of metronidazole with cefazolin, cefuroxime, ceftriaxone, cefotaxime, or levofloxacin, as opposed to single agents featuring broader antimicrobial activity.

The empiric use of antimicrobial regimens with broad-spectrum activity against gram-negative organisms, which include meropenem, imipenem-cilastatin, doripenem, piperacillin-tazobactam as single-agent therapies, or ciprofloxacin, levofloxacin ceftazidime, cefepime each combined with metronidazole, is recommended by the SIS-IDSA guidelines for treating high-severity community-acquired IAIs.

(Due to the increasing resistance of *E. coli* to fluoroquinolones, local population susceptibility profiles and, if available, isolate susceptibilities should be reviewed).

The SIS-IDSA guidelines do not recommend the routine use of agents effective against enterococci in community-acquired infections, even if infections caused by these organisms may be associated with poorer clinical outcomes[10].

Additionally, antifungal protection is not required for community-acquired infections.

According to the guidelines, Amynoglicosides should be reserved for patients allergic to b-lactam agents and, even in these cases, they are "last resort" options that should be used only when quinolone-based regimens are unavailable. That said, depending on the local susceptibility patterns of nosocomial gram-negative bacilli, Aminoglycosides may be a reasonable choice for the empiric or definitive treatment of certain patients with health care-related IAIs.

### *Health care-associated intra-abdominal infections*

Health care-related infections are commonly caused by more resistant strains, which may include the non-fermenting gram-negative *P. aeruginosa, Acinetobacter* species, *E. coli*, *Enterobacter* species, *Proteus* species, *methicillin resistant Staphylococcus aureus*, enterococci, *Candida* species, and extended spectrum β-lactamase-producing *Klebsiella*. For these infections, given that adequate empiric therapy appears to be a crucial factor affecting postoperative complications and mortality rates, complex multidrug regimens are recommended.

According to the SIS-IDSA guidelines, antibiotic selection should always be tailored to address the nosocomial microorganisms known to be present at the facilities in which the patient developed the infection.

### *Biliary intra-abdominal infections*

For patients with complicated biliary IAIs, selection of a specific antimicrobial therapy should be based on the origin of the infection (community versus health care), on the severity of illness, and on the presence or absence of a biliary-enteric anastomosis.

For biliary infections, anaerobic therapy is not recommended unless a biliary-enteric anastomosis is present.

Regarding community-acquired biliary infections, antimicrobial activity against enterococci is not required because such strains have not proven to be pathogenic. For certain immunosuppressed patients, however, particularly for those who have undergone extensive hepatic-related procedures or liver transplants, enterococcal infections can be clinically significant and may require treatment.

For community-acquired acute cholecystitis of mild-to-moderate severity, the SIS and IDSA guidelines recommend treatment regimens of cefazolin, cefuroxime, or ceftriaxone. On the other hand, for community-acquired acute cholecystitis causing severe physiologic disturbance, advanced age, and/or immunocompromise, the IDSA guidelines recommend Imipenem-cilastatin, meropenem, doripenem, piperacillin-tazobactam as single-agent therapies, or ciprofloxacin, levofloxacin, cefepime, each in combination with metronidazole. Contrastingly, for acute cholangitis of any severity grade following bilio-enteric anastomosis, the SIS-IDSA guidelines recommend Imipenem-cilastatin, meropenem, doripenem, piperacillin-tazobactam as single-agent therapies, or ciprofloxacin, levofloxacin, cefepime, each in combination with metronidazole. For health care-related biliary infection of any severity grade, the IDSA guidelines recommend Imipenem-cilastatin, meropenem, doripenem, piperacillin-tazobactam, or ciprofloxacin, levofloxacin, cefepime, each in combination with metronidazole, supplementing them with vancomycin.

(Due to the increasing resistance of *E. coli* to fluoroquinolones, local population susceptibility profiles and, if available, isolate susceptibilities should be assessed and systematically reviewed).

## GUIDELINES BY WSES: ANTIMICROBIAL MANAGEMENT FOR INTRA-ABDOMINAL INFECTIONS

Patients with IAIs are classified by SIS-IDSA guidelines into low risk and high risk.

However the definition of "risk" in IAIs remains too vague. Dividing patients with IAIs into lower and higher risk categories may be not easy, and attempting to assess a patient's risk of treatment failure may be not sufficient to optimize an antimicrobial treatment plan.

In order to stratify the patients with IAIs, WSES guidelines stratify patients with IAIs according to the specific risk for antimicrobial resistant bacteria and to the clinical patient's severity.

In order to better identify the pathogens present and evaluate the associated resistance patterns, infections are classified as being either community- or hospital-acquired.

In the past two decades, the incidence rate of hospital-acquired infections caused by resistant microorganisms has risen significantly, a finding that is probably correlated with higher levels of antibiotic exposure and an increasing number of patients with one or more predisposing conditions such as recent exposure to antibiotics, high severity of illness, advanced age, comorbidity, degree of organ dysfunction, low albumin level, poor nutritional status, immunocompromise, and the presence of malignancy.

In the last years, the level of resistance has become significant also in the community acquired infections. The main resistance problem in IAIs is represented by ESBL producers Enterobacteriaceae, even today frequently found in community acquired infections[12,13].

The available therapeutic options for the treatment of ESBL-associated infections are limited by drug resistance conferred by the ESBLs[14,15].

The third generation cephalosporins, recommended by SIS-IDSA for high risk patients in association with metronidazole, should not be used to treat suspected infections with ESBL producing organisms because clinical outcome is poor even in the presence of apparent susceptibility[14].

Also cefepime should not be used as the first line therapy against ESBL-producing organisms[14].

Piperacillin-tazobactam, recommended by SIS-IDSA guidelines for high risk patients, is not regarded as suitable first line therapy for serious infections caused by ESBL producer[14].

Ciprofloxacin has been a potential antimicrobial option for the treatment of infections caused by ESBL producing enterobacteriaceae; however, in recent years, the usage of ciprofloxacin has risen, and ESBL-producing isolates resistant to fluoroquinolones has increased over time also in *E. coli*[14].

For two decades Carbapenems have been the antibiotics of first choice for ESBLs.

The increased carbapenem consumption has been associated to increasing of carbapenem-resistant bacterial species[13].

The rapid spread of carbapenemases in *Klebsiella pneumoniae* (*K. pneumoniae*)[16] emphasizes the concept that the usage of carbapenems should be optimized in terms of indication and exposure.

Therefore, group 2 carbapenems should be used in community acquired IAIs only in critically ill patients where inadequate antimicrobial therapy may have a significant impact on the patients mortality, independently by the site of infection.

The choice of the antimicrobial regimen poses serious problems for the management of critically ill patients. In patients with severe sepsis or septic shock an early correct empirical antimicrobial therapy has a significant impact on the outcome, independently by the site of infection.

It is confirmed by a recent prospective observational study, involving 180 consecutive patients with secondary generalized peritonitis, by Riché *et al*[17] that demonstrated, a significantly higher mortality rate in septic shock (35% *vs* 8% for patients without shock).

Recently published international guidelines outlining the proper management of severe sepsis and septic shock (Surviving Sepsis Campaign)[3] recommend the intravenous administration of antibiotics within the first hour following diagnosis; the use of broad-spectrum agents that can effectively penetrate the presumed site of infection; and the daily reassessment of the antimicrobial regimen in order to optimize treatment efficacy, prevent the development of drug resistance, avoid drug-induced toxicity, and minimize the overall cost of hospitalization.

For years, antibiotics have typically been used as single-agent therapies; only once microbiological cultures and susceptibility tests had been performed were more potent compounds then administered. The traditional approach, however, may no longer be appropriate for critically ill patients in the current context of increasing antibiotic resistance.

Increasing rates of antibiotic resistance and a better understanding of the inflammatory process together prompted the medical community to begin advocating the use of broad-spectrum regimens initially when treating critically ill patients.

This two-stage approach, consisting of aggressive initial therapy followed by a less intense follow-up treatment, allows for the immediate and effective treatment of serious infections while simultaneously avoiding the overuse of antibiotics, potential microbial resistance, and excessive hospitalization costs.

### *Community-acquired intra-abdominal infections*

Empirical antibiotic treatment of community-acquired IAIs should be conducted in accordance with the most frequently isolated germs and the local trends of antibiotic resistance. The major pathogens involved in community-acquired IAIs are enterobacteriaceae, streptococci, and anaerobes. The primary problems with resistance stem from ESBL-producing enterobacteriaceae, which are frequently found in community-acquired infections[12,13].

Many factors can increase the risk of ESBL selection, but prior exposure to antibiotics (mainly third generation cephalosporins) and comorbidities that continuously require antibiotic treatment regimens, are among the most significant predisposing criteria[18].

In the event of community-acquired IAIs, antimicrobial therapy for enterococci should be considered on a patient-by-patient basis, mainly for critically ill and immunocompromised patients as well as patients with valvular heart disease or prosthetic implants.

Community-acquired IAIs may be treated with either single or multiple antimicrobial regimens depending on the patient's condition as well as the predominant risk factors for specific microorganisms and resistance patterns. For stable, non-critical patients presenting with no ESBL-associated risk factors, amoxicillin/clavulanate and ciprofloxacin plus metronidazole regimens are recommended. Contrastingly, for critically ill patients presenting with no ESBL-associated risk factors, treatments of piperacillin/tazobactam are recommended.

On the other hand, for stable, non-critical patients presenting with ESBL-associated risk factors, ertapenem or tigecycline treatments are recommended. Contrastingly, for critically ill patients presenting with ESBL-associated risk factors, meropenem or imipenem plus fluconazole regimens (the latter in the event of risk factors for *Candida*) are recommended.

Antimicrobial regimens recommended by WSES[11] for treating extra-biliary community-acquired IAIs was summarized in Table 1.

### *Biliary intra-abdominal infections*

Antibiotics are always recommended when treating complicated cholecystitis and advanced uncomplicated cholecystitis.

The most important factors for antimicrobial drug selection in biliary infections are the following: antimicrobial activity against causative bacteria, the clinical condition of the patient in question, and the biliary levels of the antimicrobial agents.

An antibiotic's in-bile efficacy as well as the manner in which it is ultimately secreted into the bile are also important selection criteria when choosing an appropriate drug regimen.

The microorganisms that are most often isolated in biliary infections are the gram-negative aerobes, *E. coli* and *K. pneumoniae,* and several anaerobes, especially *Bacteroides fragilis*. Activity against enterococci is not typically required since their pathogenicity in biliary tract infections remains unclear[19,20].

**Table 1 Antimicrobial regimens recommended by the World Society of Emergency Surgery recommendations for treating extra-biliary community-acquired intra-abdominal infections**

| | Antimicrobial agents | Dosage |
|---|---|---|
| In stable, non-critical patients | | |
| With no ESBL-associated risk factors | Amoxicillin/clavulanate | 2.2 g every 6 h (2-h infusion time) |
| | Ciprofloxacin | 400 mg every 8 h (30-min infusion time) |
| | + | |
| | Metronidazole | 500 mg every 6 h (1-h infusion time) |
| With ESBL-associated risk factors | Ertapenem | 1 g every 24 h (2-h infusion time) |
| | Tigecycline | 100 mg LD then 50 mg every 12 h (2-h infusion time) |
| In critically ill patients presenting | | |
| With no ESBL-associated risk factors | Piperacillin/tazobactam | 9 g LD then 18 g per day *via* continuous infusion or 4.5 g every 6 h (4-h infusion time) |
| With ESBL-associated risk factors | Meropenem | 500 mg every 6 h (6-h infusion time) |
| | or | |
| | Imipenem | 500 mg every 4 h (3-h infusion time) |
| | + | |
| | Fluconazole | 600 mg LD then 400 mg every 24 h (2-h infusion time) |

ESBL: Extended-spectrum β-lactamase; LD: Loading dose.

**Table 2 Antimicrobial regimens recommended by the World Society of Emergency Surgery recommendations for treating biliary intra-abdominal infections**

| | Antimicrobial agents | Dosage |
|---|---|---|
| In stable, non-critical patients | | |
| With no ESBL-associated risk factors | Amoxicillin/clavulanate | 2.2 g every 6 h (2-h infusion time) |
| | Ciprofloxacin | 400 mg every 8 h (30-min infusion time) |
| | + | |
| | Metronidazole | 500 mg every 6 h (1-h infusion time) |
| With ESBL-associated risk factors | Tigecycline | 100 mg LD then 50 mg every 12 h (2-h infusion time) |
| In critically ill patients | | |
| With no ESBL-associated risk factors | Piperacillin/tazobactam | 9 g LD then 18 g per day *via* continuous infusion or 4.5 g every 6 h (4-h infusion time) |
| With ESBL-associated risk factors | Piperacillin | 8 g LD then 16 g/d *via* continuous infusion or 4 every 6 h (4-h infusion time) |
| | + | |
| | Tigecycline | 100 mg LD then 50 mg every 12 h (2-h infusion time) |
| | +/- | |
| | Fluconazole | 600 mg LD then 400 mg every 24 h (2-h infusion time) |

ESBL: Extended-spectrum β-lactamase; LD: Loading dose.

The efficacy of antibiotics in treating biliary infections depends largely on the drugs' resulting biliary concentrations[21-23].

However, there are no clinical or experimental data available from which to infer the antimicrobial dosage that would safely maximize biliary duct penetration, and as such, no standardized recommendations have been established.

For stable, non-critical patients presenting with no ESBL-associated risk factors, amoxicillin/clavulanate or ciprofloxacin plus metronidazole regimens are recommended.

For stable, non-critical patients presenting with ESBL-associated risk factors, Tigecycline is recommended.

For critically ill patients presenting with no ESBL-associated risk factors, Piperacillin/tazobactam is recommended.

For critically ill patients presenting with ESBL-associated risk factors, tygecycline plus piperacillin (plus fluconazole in the event of risk factors for *Candida*) is the recommended drug regimen.

Antimicrobial regimens recommended by WSES[11] for treating biliary IAIs was summarized in Table 2.

### Hospital-acquired intra-abdominal infections

Hospital-acquired IAIs are, by definition, infections that were not present upon hospital admission but become evident at least 48 h following admission in patients hospitalized for a reason other than IAIs.

The threat of antimicrobial resistance has been identified as one of the major challenges in the management of complicated IAIs.

Hospital-acquired infections are commonly caused by more resistant strains, and for these infections, complex multi-drug regimens are usually recommended.

The use of anti-enterococcal drugs in empirical antibiotic regimens to treat nosocomial IAIs is always warranted if directed against *Enterococcus faecalis*.

**Table 3 Antimicrobial regimens recommended by the World Society of Emergency Surgery recommendations for hospital-acquired intra-abdominal infections**

| | Antimicrobial agents | Dosage |
|---|---|---|
| In stable, non-critical patients | Piperacillin | 8 g LD then 16 g/d *via* continuous infusion or 4 every 6 h (4-h infusion time) |
| | + | |
| | Tigecycline | 100 mg LD then 50 mg every 12 h (2-h infusion time) |
| | + | |
| | Fluconazole | 600 mg LD then 400 mg every 24 h (2-h infusion time) |
| In critically ill patients | Piperacillin | 8 g LD then 16 g/d *via* continuous infusion or 4 every 6 h (4-h infusion time) |
| | + | |
| | Tigecycline | 100 mg LD then 50 mg every 12 h (2-h infusion time) |
| | + | |
| | Echinocandin | |
| | Caspofungin | (loading dose of 70 mg, then 50 mg daily) |
| | Anidulafungin | (loading dose of 200 mg, then 100 mg daily) |
| | Micafungin | (100 mg daily) |
| | Meropenem | 500 mg every 6 h (6-h infusion time) |
| | or | |
| | Imipenem | 500 mg every 4 h (3-h infusion time) |
| | or | |
| | Doripenem | 500 mg every 8 h (4-h infusion time) |
| | + | |
| | Teicoplanin | 1.6 g *via* continuous infusion or 400 mg every 6 h (4-h infusion time) |
| | + | |
| | Echinocandin | |
| | Caspofungin | (loading dose of 70 mg, then 50 mg daily) |
| | Anidulafungin | (loading dose of 200 mg, then 100 mg daily) |
| | Micafungin | (100 mg daily) |

LD: Loading dose.

The recently published IDSA guidelines for the treatment of invasive candidiasis don't explicitly address candidal peritonitis[24]. However, the use of echinocandins is generally favored as a first-line empirical therapy in treating critically ill patients, while fluconazole is typically used for patients with less severe conditions. Consequently, by applying these trends to the context of IAIs one might suggest the prescription of echinocandins as a first-line treatment for cases of severe nosocomial IAIs.

For stable, non-critical patients presenting with risk factors for multidrug-resistant pathogens, fluconazole and tigecycline plus piperacillin are recommended.

In critically ill patients presenting with risk factors presenting for multidrug-resistant pathogens meropenem, imipenem/cilastatin, and doripenem (plus an echinocandin and Teicoplanin) or Tigecycline (plus an Echinocandin and Piperacillin) are recommended.

Antimicrobial regimens recommended by WSES[11] for hospital-acquired IAIs was summarized in Table 3.

## CONCLUSION

Proper empiric antimicrobial therapy has an enormous effect on the morbidity and mortality rates of patients suffering from IAIs, especially those who are critically ill. Inappropriate antibiotic treatments of IAIs may result in poor patient outcome. Furthermore, the selection of an appropriate antimicrobial agent has become a significant challenge due to the emerging resistances of target organisms to commonly prescribed antibiotics.

To more effectively customize antimicrobial treatment regimens, guidelines outlining the proper therapeutic protocol for administering antimicrobial drugs have been developed to help clinicians to better and more efficiently treat IAIs.

## REFERENCES


1 **Menichetti F**, Sganga G. Definition and classification of intra-abdominal infections. *J Chemother* 2009; **21** Suppl 1: 3-4

2 **Paul M**, Shani V, Muchtar E, Kariv G, Robenshtok E, Leibovici L. Systematic review and meta-analysis of the efficacy of appropriate empiric antibiotic therapy for sepsis. *Antimicrob Agents Chemother* 2010; **54**: 4851-4863

3 **Dellinger RP**, Levy MM, Carlet JM, Bion J, Parker MM, Jaeschke R, Reinhart K, Angus DC, Brun-Buisson C, Beale R, Calandra T, Dhainaut JF, Gerlach H, Harvey M, Marini JJ, Marshall J, Ranieri M, Ramsay G, Sevransky J, Thompson BT, Townsend S, Vender JS, Zimmerman JL, Vincent JL. Surviving Sepsis Campaign: international guidelines for management of severe sepsis and septic shock: 2008. *Crit Care Med* 2008; **36**: 296-327

4 **Hecker MT**, Aron DC, Patel NP, Lehmann MK, Donskey CJ. Unnecessary use of antimicrobials in hospitalized patients: current patterns of misuse with an emphasis on the anti-anaerobic spectrum of activity. *Arch Intern Med* 2003; **163**: 972-978

5 **Rüttimann S**, Keck B, Hartmeier C, Maetzel A, Bucher HC. Long-term antibiotic cost savings from a comprehensive intervention program in a medical department of a university-affiliated teaching hospital. *Clin Infect Dis* 2004; **38**: 348-356

6 **Cattan P**, Yin DD, Sarfati E, Lyu R, De Zelicourt M, Fagnani F. Cost of care for inpatients with community-acquired intra-abdominal infections. *Eur J Clin Microbiol Infect Dis* 2002; **21**: 787-793

7 **Montravers P**, Gauzit R, Muller C, Marmuse JP, Fichelle A,

Desmonts JM. Emergence of antibiotic-resistant bacteria in cases of peritonitis after intraabdominal surgery affects the efficacy of empirical antimicrobial therapy. *Clin Infect Dis* 1996; **23**: 486-494
8 **Mosdell DM**, Morris DM, Voltura A, Pitcher DE, Twiest MW, Milne RL, Miscall BG, Fry DE. Antibiotic treatment for surgical peritonitis. *Ann Surg* 1991; **214**: 543-549
9 **Sturkenboom MC**, Goettsch WG, Picelli G, in 't Veld B, Yin DD, de Jong RB, Go PM, Herings RM. Inappropriate initial treatment of secondary intra-abdominal infections leads to increased risk of clinical failure and costs. *Br J Clin Pharmacol* 2005; **60**: 438-443
10 **Solomkin JS**, Mazuski JE, Bradley JS, Rodvold KA, Goldstein EJ, Baron EJ, O'Neill PJ, Chow AW, Dellinger EP, Eachempati SR, Gorbach S, Hilfiker M, May AK, Nathens AB, Sawyer RG, Bartlett JG. Diagnosis and management of complicated intra-abdominal infection in adults and children: guidelines by the Surgical Infection Society and the Infectious Diseases Society of America. *Clin Infect Dis* 2010; **50**: 133-164
11 **Sartelli M**, Viale P, Koike K, Pea F, Tumietto F, van Goor H, Guercioni G, Nespoli A, Tranà C, Catena F, Ansaloni L, Leppaniemi A, Biffl W, Moore FA, Poggetti R, Pinna AD, Moore EE. WSES consensus conference: Guidelines for first-line management of intra-abdominal infections. *World J Emerg Surg* 2011; **6**: 2
12 **Hawser SP**, Bouchillon SK, Hoban DJ, Badal RE. In vitro susceptibilities of aerobic and facultative anaerobic Gram-negative bacilli from patients with intra-abdominal infections worldwide from 2005-2007: results from the SMART study. *Int J Antimicrob Agents* 2009; **34**: 585-588
13 **Hawser SP**, Bouchillon SK, Hoban DJ, Badal RE, Cantón R, Baquero F. Incidence and antimicrobial susceptibility of Escherichia coli and Klebsiella pneumoniae with extended-spectrum beta-lactamases in community- and hospital-associated intra-abdominal infections in Europe: results of the 2008 Study for Monitoring Antimicrobial Resistance Trends (SMART). *Antimicrob Agents Chemother* 2010; **54**: 3043-3046
14 **Paterson DL**. Recommendation for treatment of severe infections caused by Enterobacteriaceae producing extended-spectrum beta-lactamases (ESBLs). *Clin Microbiol Infect* 2000; **6**: 460-463
15 **Bradford PA**, Cherubin CE, Idemyor V, Rasmussen BA, Bush K. Multiply resistant Klebsiella pneumoniae strains from two Chicago hospitals: identification of the extended-spectrum TEM-12 and TEM-10 ceftazidime-hydrolyzing beta-lactamases in a single isolate. *Antimicrob Agents Chemother* 1994; **38**: 761-766
16 **Vatopoulos A**. High rates of metallo-beta-lactamase-producing Klebsiella pneumoniae in Greece--a review of the current evidence. *Euro Surveill* 2008; **13**: pii: 8023
17 **Riché FC**, Dray X, Laisné MJ, Matéo J, Raskine L, Sanson-Le Pors MJ, Payen D, Valleur P, Cholley BP. Factors associated with septic shock and mortality in generalized peritonitis: comparison between community-acquired and postoperative peritonitis. *Crit Care* 2009; **13**: R99
18 **Ben-Ami R**, Rodríguez-Baño J, Arslan H, Pitout JD, Quentin C, Calbo ES, Azap OK, Arpin C, Pascual A, Livermore DM, Garau J, Carmeli Y. A multinational survey of risk factors for infection with extended-spectrum beta-lactamase-producing enterobacteriaceae in nonhospitalized patients. *Clin Infect Dis* 2009; **49**: 682-690
19 **Westphal JF**, Brogard JM. Biliary tract infections: a guide to drug treatment. *Drugs* 1999; **57**: 81-91
20 **Järvinen HJ**. Biliary bacteremia at various stages of acute cholecystitis. *Acta Chir Scand* 1980; **146**: 427-430
21 **Sinanan MN**. Acute cholangitis. *Infect Dis Clin North Am* 1992; **6**: 571-599
22 **Blenkharn JI**, Habib N, Mok D, John L, McPherson GA, Gibson RN, Blumgart LH, Benjamin IS. Decreased biliary excretion of piperacillin after percutaneous relief of extrahepatic obstructive jaundice. *Antimicrob Agents Chemother* 1985; **28**: 778-780
23 **van den Hazel SJ**, de Vries XH, Speelman P, Dankert J, Tytgat GN, Huibregtse K, van Leeuwen DJ. Biliary excretion of ciprofloxacin and piperacillin in the obstructed biliary tract. *Antimicrob Agents Chemother* 1996; **40**: 2658-2660
24 **Pappas PG**, Kauffman CA, Andes D, Benjamin DK, Calandra TF, Edwards JE, Filler SG, Fisher JF, Kullberg BJ, Ostrosky-Zeichner L, Reboli AC, Rex JH, Walsh TJ, Sobel JD. Clinical practice guidelines for the management of candidiasis: 2009 update by the Infectious Diseases Society of America. *Clin Infect Dis* 2009; **48**: 503-535

**S- Editor** Sun H **L- Editor** Stewart GJ **E- Editor** Xiong L