Management of Intra-Abdominal Infections Free Online Course

MIFOC

1

Epidemiology

2

CIAO Study


Sartelli et al. World Journal of Emergency Surgery 2012, 7:36
http://www.wjes.org/content/7/1/36

WORLD JOURNAL OF EMERGENCY SURGERY

RESEARCH ARTICLE Open Access

Complicated intra-abdominal infections in Europe: a comprehensive review of the CIAO study

The CIAO Study ("Complicated Intra-Abdominal infections Observational" Study) is a multicenter study performed in 69 medical institutions throughout Europe over the course of a 6-month observational period (January - June 2012).

CIAO Study
Inclusion criteria

Patients with both community-acquired and healthcare-associated complicated intra-abdominal infections

CIAO Study
Primary end-points

Clinical profiles of intra-abdominal infections in Europe

Epidemiological profiles worldwide in Europe

Management profiles worldwide in Europe

5

CIAO Study
2152 patients

Mean age	53.8 years (range 4–98)
Sex	
Women	996 (46.3%)
Men	1,156 (53.7%)
Setting of acquisition	
Community acquired	1,701 (79%)
Healthcare-associated	451 (21%)
Diffusion	
Localized peritonitis	1,365 (63.5%)
Generalized peritonitis	787 (36.5%)
Clinical condition at admission	
Critical condition (severe sepsis/septic shock)	282 (13.1%)

6

CIAO Study
Source of infections

Source of Infection	Patients N° 2152 (100%)
Appendicitis	798 (37%)
Cholecystitis	289 (13.4%)
Post-operative	342 (15.,9%)
Colonic non diverticular perforation	158 (7.3%)
Gastroduodenal perforations	156 (7.3%)
Diverticulitis	166 (7.7%)
Small bowel perforation	103 (4.8%)
Others	110 (5.1%)
PID	18 (0.8%)
Post traumatic perforation	12 (0.6%)

7

CIAO Study
Aerobic bacteria from intra-operative peritoneal fluid

Total	1,525 (100%)
Aerobic Gram-negative bacteria	**1,041 (69.2%)**
Escherichia coli	632 (41.4%)
(Escherichia coli resistant to third generation cephalosporins)	64 (4.2%)
Klebsiella pneuumoniae	109 (7.1%)
(Klebsiella pneumoniae resistant to third generation cephalosporins)	37 (2.4%)
Enterobacter	63 (4.1%)
Proteus	33 (2.1 %)
Pseudomonas	80 (5.2%)
Others	124 (8.1%)
Aerobic Gram-positive bacteria	**484 (31.7%)**
Enterococcus faecalis	169 (11%)
Enterococcus faecium	72 (4.7%)
Staphylococcus Aureus	56 (3.7%)
Streptococcus spp.	100 (6,6%)
Others	87 (5.7%)

8

CIAO Study

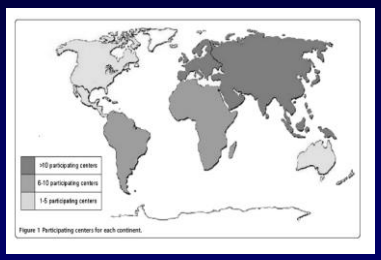
Multivariate analysis: risk factors for occurrence of death during hospitalization

Risk factors	Odds Ratio	95%CI	p
Age	3.3	2.2-5	<0.0001
Severe sepsis in the immediate post-operative course	27.6	15.9-47.8	<0.0001
Septic shock in the immediate post-operative course	14.6	8.7-24.4	<0.0001
Colonic non diverticular perforation	4.7	2.5-8	<0.0001
Complicated diverticulitis	2.3	1.5-3.7	<0.0001
Small bowel perforation	21.4	8-57.4	<0.0001
Delayed initial intervention	2.4	1.5-3.7	0.0001

Stepwise multivariate analysis, PR=0.005 E PE=0.001 (Hosmer-Lemeshow chi 2(8)=1.68, area under ROC curve=0.9465)

9

CIAOW Study



The CIAOW Study ("Complicated Intra-Abdominal infection Observational" Study worldwide) is a multicenter investigation performed in 57 medical institutions worldwide over the course of a 6-month observational period (October 2012 – March 2013).

10

CIAOW Study
(1898 patients)

Mean age	51.6 years (range 18-99)
Sex	
Women	777 (41%)
Men	1,121 (59%)
Setting of acquisition	
Community acquired	1,645 (86.7%)
Healthcare-associated	253 (13.3%)
Diffusion	
Localized peritonitis	1071 (56.4%)
Generalized peritonitis	827 (43.6%)
Clinical condition at admission	
Critical condition (severe sepsis/septic shock)	296 (14.2%)

11

CIAOW Study
Source of infections

Source of Infection	**1898 (100%)**
Appendicitis	633 (33.3%)
Cholecystitis	278 (14.6%)
Post-operative	170 (15.,9%)
Colonic non diverticular perforation	115 (9.9%)
Gastroduodenal perforations	253 (13.3%)
Diverticulitis	106 (5.6%)
Small bowel perforation	145 (7.6%)
Others	122 (6.4%)
PID	30 (1.6%)
Post traumatic perforation	46 (2.4%)

12

CIAOW Study

Aerobic bacteria from intra-operative peritoneal fluid

Total	**1.330 (100%)**
Escherichia coli	548 (41.2%)
(Escherichia coli resistant to third generation cephalosporins)	75 (5.6%)
Klebsiella pneuumoniae	140 (10.5%)
(Klebsiella pneumoniae resistant to third generation cephalosporins)	26 (1.4%)
Klebsiella oxytoca	11 (0.8%)
(Klebsiella oxytoca resistant to third generation cephalosporins)	2 (0.1)
Enterobacter	64 (4.8%)
Proteus	47 (3.5 %)
Pseudomonas	74 (5.6%)
Others	73 (5.6%)
Enterococcus faecalis	153 (11.5%)
Enterococcus faecium	58 (4.4%)
Staphylococcus Aureus	38 (2.8%)
Streptococcus spp.	85 (6,4%)
Others	39 (2.9%)

13

CIAOW Study

Multivariate analysis: risk factors for occurrence of death during hospitalization

Risk factors	**Odds Ratio**	**95%CI**	**p**
Age	1	1.00-1.04	<0.0001
Small bowel perforation	3	1.5-6	<0.0001
Delayed initial intervention	1.8	1.2-2.1	<0.0001
ICU admission	5.9	3.6-9.5	<0.0001
Immunosuppression	3.8	2.1-6.7	<0.0001

Stepwise multivariate analysis, PR=0.005 E PE=0.001 (Hosmer-Lemeshow chi 2(8)=1.68, area under ROC curve=0.9465)

14

WISS study

World Journal of Emergency Surgery

RESEARCH ARTICLE — Open Access

Global validation of the WSES Sepsis Severity Score for patients with complicated intra-abdominal infections: a prospective multicentre study (WISS Study)

The WISS study (WSES cIAIs Score Study) is a multicenter observational study underwent in **132** medical institutions worldwide during a four-month study period (October 2014-February 2015) from **54** different countries 4533 patients with a mean age of 51.2 years (range 18-99) were enrolled in the WISS study.

15

WISS Study

Source of infection

Source of infection	4553 (100%)
Appendicitis	1553 (34.2%)
Cholecystitis	837 (18.5%)
Post-operative	387 (8.5%)
Colonic non diverticular perforation	269 (5.9%)
Gastro-duodenal perforations	498 (11%)
Diverticulitis	234 (5.2%)
Small bowel perforation	243 (5.4%)
Others	348 (7.7%)
PID	50 (1.1%)
Post traumatic perforation	114 (2.5%)
Missing	

16

WISS Study

Mortality according to the clinical condition

No sepsis	1.2%
Sepsis	4.4%
Severe sepsis	**27.8%**
Septic shock	**67.8%**

17

WSES sepsis severity score for patients with complicated Intra-abdominal infections (Range: 0 - 18)

Clinical condition at the admission

Severe sepsis (acute organ dysfunction) at the admission	**3 score**
Septic shock (acute circulatory failure characterized by persistent arterial hypotension. It always requires vasopressor agents) at the admission	**5 score**

Setting of acquisition

Healthcare associated infection	**2 score**

Origin of the IAIs

Colonic non-diverticular perforation peritonitis	**2 score**
Small bowel perforation peritonitis	**3 score**
Diverticular diffuse peritonitis	**2 score**
Post-operative diffuse peritonitis	**2 score**

Delay in source control

Delayed initial intervention [Preoperative duration of peritonitis (localized or diffuse) > 24 h)]	**3 score**

Risk factors

Age>70	**2 score**
Immunosuppression (chronic glucocorticoids, immunosuppresant agents, chemotherapy, lymphatic diseases, virus)	**3 score**

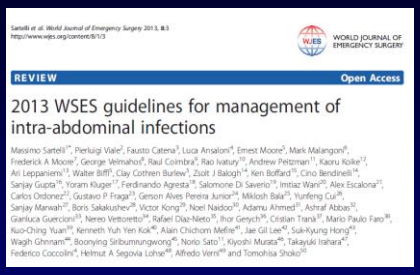
18

Mortality

CIAO Study	7.5% (163/2.152)
CIAOW study	10.5% (199/1.898)
WISS Study	9.2% (416/4.533)

19

Management of intra-abdominal infections



Sartelli et al. World Journal of Emergency Surgery 2013, 8:3
http://www.wjes.org/content/8/1/3

WORLD JOURNAL OF EMERGENCY SURGERY

REVIEW Open Access

2013 WSES guidelines for management of intra-abdominal infections

Massimo Sartelli[1*], Pierluigi Viale[2], Fausto Catena[3], Luca Ansaloni[4], Ernest Moore[5], Mark Malangoni[6], Frederick A Moore[7], George Velmahos[8], Raul Coimbra[9], Rao Ivatury[10], Andrew Peitzman[11], Kaoru Koike[12], Ari Leppaniemi[13], Walter Biffl[9], Clay Cothren Burlew[9], Zsolt J Balogh[14], Ken Boffard[15], Cino Bendinelli[16], Sanjay Gupta[16], Yoram Kluger[17], Ferdinando Agresta[18], Salomone Di Saverio[19], Imtiaz Wani[20], Alex Escalona[21], Carlos Ordonez[22], Gustavo P Fraga[23], Gerson Alves Pereira Junior[24], Miklosh Bala[25], Yunfeng Cui[26], Sanjay Marwah[27], Boris Sakakushev[28], Victor Kong[29], Noel Naidoo[30], Adamu Ahmed[31], Ashraf Abbas[32], Gianluca Guercioni[33], Nereo Vettoretto[34], Rafael Diaz-Nieto[35], Ihor Gerych[36], Cristian Trana[37], Mario Paulo Faro[38], Kuo-Ching Yuan[39], Kenneth Yuh Yen Kok[40], Alain Chichom Mefire[41], Jae Gil Lee[42], Suk-Kyung Hong[43], Wagih Ghnnam[44], Boonying Siribumrungwong[45], Norio Sato[11], Kiyoshi Murata[46], Takayuki Irahara[47], Federico Coccolini[4], Helmut A Segovia Lohse[48], Alfredo Verri[49] and Tomohisa Shoko[50]

Sartelli et al. World Journal of Emergency Surgery (2017) 12:29
DOI 10.1186/s13017-017-0141-6

World Journal of Emergency Surgery

REVIEW Open Access

The management of intra-abdominal infections from a global perspective: 2017 WSES guidelines for management of intra-abdominal infections

Massimo Sartelli[1*], Alain Chichom-Mefire[2], Francesco M. Labricciosa[3], Timothy Hardcastle[4], Fikri M. Abu-Zidan[5], Abdulrashid K. Adesunkanmi[6], Luca Ansaloni[7], Miklosh Bala[8], Zsolt J. Balogh[9], Marcelo A. Beltrán[10], Offir Ben-Ishay[11], Walter L. Biffl[12], Arianna Birindelli[13], Miguel A. Cainzos[14], Gianbattista Catalini[1], Marco Ceresoli[7], Ari Che Jusoh[15], Osvaldo Chiara[16], Federico Coccolini[7], Raul Coimbra[17], Francesco Cortese[18], Zaza Demetrashvili[19], Salomone Di Saverio[13], Jose J. Diaz[20], Valery N. Egiev[21], Paula Ferrada[22], Gustavo P. Fraga[23], Wagih M. Ghnnam[24], Jae Gil Lee[25], Carlos A. Gomes[26], Andreas Hecker[27], Torsten Herzog[28], Jae Il Kim[29], Kenji Inaba[30], Arda Isik[31], Aleksandar Karamarkovic[32], Jeffry Kashuk[33], Vladimir Khokha[34], Andrew W. Kirkpatrick[35], Yoram Kluger[36], Kaoru Koike[37], Victor Y. Kong[38], Ari Leppaniemi[39], Gustavo M. Machain[40], Ronald V. Maier[41], Sanjay Marwah[42], Michael E. McFarlane[43], Giulia Montori[7], Ernest E. Moore[44], Ionut Negoi[45], Iyiade Olaoye[46], Abdelkarim H. Omari[47], Carlos A. Ordonez[48], Bruno M. Pereira[49], Gerson A. Pereira Júnior[49], Guntars Pupelis[50], Tarcisio Reis[51], Boris Sakakhushev[52], Norio Sato[53], Helmut A. Segovia Lohse[40], Vishal G. Shelat[54], Kjetil Søreide[55,56], Waldemar Uhl[19], Jan Ulrych[58], Harry Van Goor[31], George C Velmahos[59], Kuo-Ching Yuan[39], Imtiaz Wani[60], Dieter G. Weber[61], Sanoop K. Zacharias[62] and Fausto Catena[63]

Sartelli et al. World Journal of Emergency Surgery (2017) 12:22
DOI 10.1186/s13017-017-0132-7

World Journal of Emergency Surgery

REVIEW Open Access

Management of intra-abdominal infections: recommendations by the WSES 2016 consensus conference

Massimo Sartelli[1*], Fausto Catena[2], Fikri M. Abu-Zidan[3], Luca Ansaloni[4], Walter L. Biffl[5], Marja A. Boermeester[6], Marco Ceresoli[3], Osvaldo Chiara[7], Federico Coccolini[3], Jan J. De Waele[8], Salomone Di Saverio[9], Christian Eckmann[10], Gustavo P. Fraga[11], Maddalena Giannella[12], Massimo Girardis[13], Ewen A. Griffiths[14], Jeffry Kashuk[15], Andrew W. Kirkpatrick[16], Vladimir Khokha[17], Yoram Kluger[18], Francesco M. Labricciosa[19], Ari Leppaniemi[20], Ronald V. Maier[21], Addison K. May[22], Mark Malangoni[23], Ignacio Martin-Loeches[24], John Mazuski[25], Philippe Montravers[26], Andrew Peitzman[27], Bruno M. Pereira[11], Tarcisio Reis[28], Boris Sakakushev[29], Gabriele Sganga[30], Kjetil Soreide[31], Michael Sugrue[32], Jan Ulrych[33], Jean-Louis Vincent[34], Pierluigi Viale[12] and Ernest E. Moore[35]

Classification

Diagnosis

Source control

Antimicrobial therapy

Sepsis control

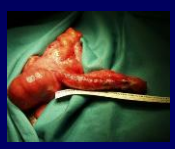
23

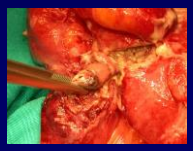
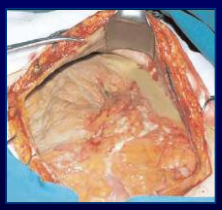
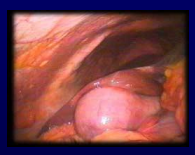
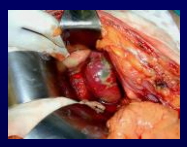
Classification

24

Intra-abdominal infections

Intra-abdominal infections (IAIs) include many pathological conditions, ranging from uncomplicated appendicitis to faecal peritonitis.



25

Classification

The term “intra-abdominal infections” (IAIs) describes a wide heterogeneity of clinical conditions. The anatomical extent of infection, the presumed pathogens involved, risk factors for major resistance patterns, and the patient's clinical condition should be assessed independently so as to classify patients.

26

Classification

Uncomplicated IAIs

In uncomplicated IAIs the infectious process only involves a single organ and does not proceed to peritoneum.

Complicated IAIs

In complicated IAIs, the infectious process proceeds beyond the organ and causes either localized peritonitis or diffuse peritonitis, depending on the ability of the host to contain the process within a part of the abdominal cavity

27

Classification

Uncomplicated IAIs

Patients with uncomplicated infections can be treated with either surgical resection or antibiotics. In patients with acute appendicitis and acute cholecystitis when the infection is effectively resolved by surgical excision, pre-operative therapy is typically sufficient.

Complicated IAIs

Patients with complicated IAIs, can be treated with both source control and antibiotic therapy.

28

Classification

Community-acquired IAIs

Hospital-acquired IAIs

They are characterized by increased mortality because of both underlying patient health status and increased likelihood of infection caused by multi drugs resistant organisms

29

Peritonitis

- **Primary peritonitis** is a diffuse bacterial infection without loss of integrity of the gastrointestinal tract. It is rare. It mainly occurs in infancy and early childhood and in cirrhotic patients.
- **Secondary peritonitis**, the most common form of peritonitis, is an acute peritoneal infection resulting from loss of integrity of the gastrointestinal tract or from infected viscera. It is caused by perforation of the gastrointestinal tract (e.g. perforated duodenal ulcer) by direct invasion from infected intra-abdominal viscera (e.g. gangrenous appendicitis). Anastomotic dehiscences are common causes of peritonitis in the postoperative period.
- **Ongoing or persistent (Tertiary) peritonitis** is a recurrent infection of the peritoneal cavity that follows either primary or secondary peritonitis.

30

Secondary peritonitis (origin)

Stomach
Peptic ulcer perforation
Malignancy
Trauma (mostly penetrating)
Duodenum
Peptic ulcer perforation
Trauma (blunt and penetrating)
Iatrogenic
Biliary tract
Cholecystitis
Stone perforation from gallbladder (ie, gallstone ileus) or common duct
Malignancy
Trauma (mostly penetrating)
Iatrogenic
Small bowel
Ischemic bowel
Incarcerated hernia (internal and external)
Closed loop obstruction
Crohn disease
Malignancy (rare)
Meckel diverticulum
Trauma (mostly penetrating)
Large bowel and appendix
Ischemic bowel
Diverticulitis
Malignancy
Ulcerative colitis and Crohn disease
Appendicitis
Colonic volvulus
Trauma (mostly penetrating)
Iatrogenic
Salpinx, and ovaries
Pelvic inflammatory disease
Post-operative
Anastomotic leaks
Infected haematoma

31

Classification

The grading of the clinical severity of patients with cIAIs has been well described by the sepsis definitions.

The data from WISS study showed that mortality was significantly affected by sepsis status when divided into four categories. Mortality rates increase in patients developing organ dysfunction and septic shock. Mortality by sepsis status was as follows: no sepsis 1.2%, sepsis only 4.4%, severe sepsis 27.8%, and septic shock 67.8%.

Sartelli M, Abu-Zidan FM, Catena F, Griffiths EA, Di Saverio S, Coimbra R, et al. Global validation of the WSES Sepsis Severity Score for patients with complicated intraabdominal infections: a prospective multicenter study (WISS Study). World J Emerg Surg. 2015;10:61.

32

Classification

Sepsis is now defined as a life-threatening organ dysfunction caused by a dysregulated host response to infection. Organ dysfunction can be represented by an increase in the Sequential [sepsis-related] Organ Failure Assessment (SOFA) score of 2 points or more. Septic shock should be defined as a subset of sepsis and should be clinically identified by a vasopressor requirement to maintain a mean arterial pressure of 65 mmHg or greater and serum lactate level greater than 2 mmol/L in the absence of hypovolemia.

Singer M, Deutschman CS, Seymour CW, Shankar-Hari M, Annane D, Bauer M, et al. The Third International Consensus Definitions for Sepsis and Septic Shock (Sepsis-3). JAMA. 2016;315:801–10.

33

Sepsis-3 definitions

Uncomplicated infection

Sepsis

Septic Shock

Singer M, Deutschman CS, Seymour CW, Shankar-Hari M, Annane D, Bauer M, et al. The Third International Consensus Definitions for Sepsis and Septic Shock (Sepsis-3). JAMA. 2016;315:801–10.

34

The new definition of sepsis requiring the presence of organ failure has lost its predictive potential and may hinder the awareness of the importance of early recognition and treatment of sepsis, de-emphasizing intervention at earlier stages when it is most treatable and leading to a higher risk of delayed diagnosis.

35

Diagnosis

36

Diagnosis

Early clinical evaluation is essential for diagnosing IAIs. It helps to optimize diagnostic testing and can result in earlier implementation of a proper management plan.

A step-up approach for diagnosis should be used and tailored to the clinical setting, resources, patient's age beginning with clinical and laboratory examination and progressing to imaging examinations.

37

Clinical presentation

Abdominal pain

It may be acute or insidious. Initially, the pain may be dull and poorly localized (visceral peritoneum) and often progresses to steady, severe, and more localized pain (parietal peritoneum).

Systemic inflammatory manifestations

Core body temperature > 38° C or < 36° C, heart rate > 90 beats per minute, respiratory rate > 20 breaths per minute (not ventilated) or $PaCO_2$ < 32 mm Hg (ventilated), WBC > 12,000, < 4,000 or > 10% immature forms (bands).
Hypotension and hypoperfusion signs such as lactic acidosis, oliguria, and acute alteration of mental status are indicative of evolution to severe sepsis.

Abdominal rigidity

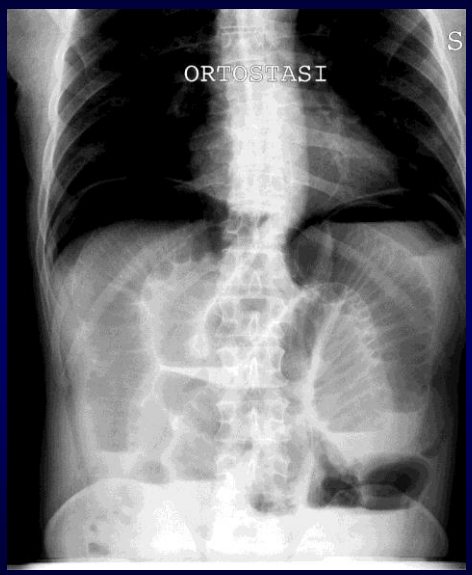
It suggests peritonitis and the need for urgent laparotomy.

38

Abdominal X-ray

- **Look for free gas, bowel obstruction, or subtle signs of intestinal ischaemia**
- Water-soluble contrast studies can show leaks
- Injection of contrast into drains, fistulae or sinus tracts may help demonstrate anatomy of complex infectios and help monitor adequacy of abscess drainage

39



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Ultrasound

- Advantage of being portable and almost risk-free
- Useful for:
  - identifying abscesses and fluid collections
  - guidance of percutaneous drainage procedures
  - detection of free fluid
  - evaluation of biliary tree
- Disadvantages:
  - operator dependent
  - difficult to perform in patients who have abdominal dressings or paralytic ileus

41

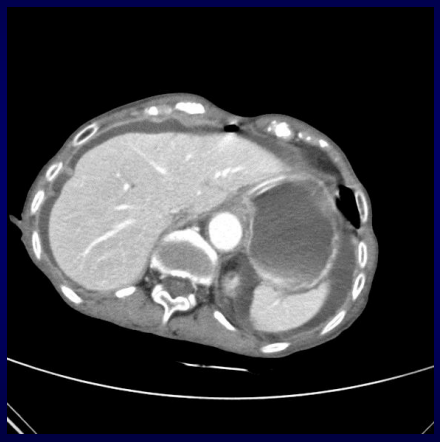
CT abdomen

CT of the abdomen and the pelvis, when it is possible to perform it, remains the diagnostic study of choice for intra-abdominal infections. CT can detect small quantities of fluid, areas of inflammation, and other GI tract pathology, with a very high sensitivity.

Although CT has higher sensitivity and specificity, concerns about radiation exposure have recently prompted reappraisal of the roles of sonography including performance by surgeons.

42

CT abdomen



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Source control

44

Most patients with cIAIs and sepsis/septic shock should undergo an urgent source control procedure; source control can be delayed in less severely-ill patients when the circumstances are appropriate.

45

Source control encompasses all the measures undertaken to eliminate the source of infection and to control ongoing contamination. Timing and adequacy of source control are currently the most important issues in the management of IAIs because inadequate and late operation may have a negative effect on outcome.

46

Surviving Sepsis Campaign: International Guidelines for Management of Sepsis and Septic Shock: 2016

The 2016 Surviving Sepsis Campaign guidelines suggest that a specific anatomic diagnosis of infection requiring emergent source control should be identified or excluded as rapidly as possible in patients with sepsis or septic shock.

47

An operative intervention remains the most viable therapeutic strategy for managing intra-abdominal sepsis. Surgical source control entails resection or suture of a diseased or perforated viscus (e.g., diverticular perforation, gastroduodenal perforation), removal of the infected organ (e.g., appendix, gallbladder), debridement of necrotic tissue, resection of ischemic bowel, and repair/resection of traumatic perforations with primary anastomosis or exteriorization of the bowel.

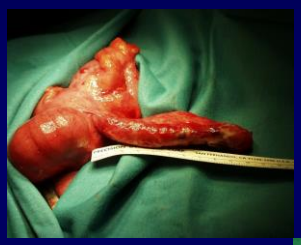
However, some data indicate highly selected patients can be managed without definitive source control if responding satisfactorily to antimicrobial therapy alone.

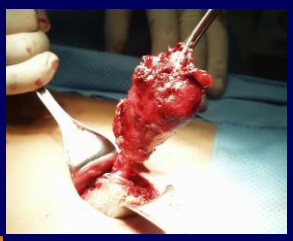
48

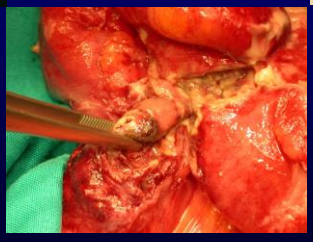
Highly selected patients with perforated diverticulitis (including those with an abscess <4 cm in diameter), a peri-appendiceal mass, or a perforated peptic ulcer can be managed without definitive source control if responding satisfactorily to antimicrobial therapy and other supportive measures.

49

Acute appendicitis







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Appendectomy Vs. conservative treatment

Appendectomy remains the treatment of choice also for acute appendicitis. Antibiotic therapy is a safe means of primary treatment for patients with uncomplicated acute appendicitis, but it is less effective in the long-term due to significant recurrence rates and probably needs the certainty of a CT proven diagnosis of uncomplicated appendicitis.

Sallinen V, Akl EA, You JJ, Agarwal A, Shoucair S, Vandvik PO, et al. Meta-analysis of antibiotics versus appendicectomy for non-perforated acute appendicitis. Br J Surg. 2016;103:656–67.

51

Open Vs. Laparoscopy

Both open and laparoscopic appendectomies are viable approaches to surgical treatment of acute appendicitis.

52

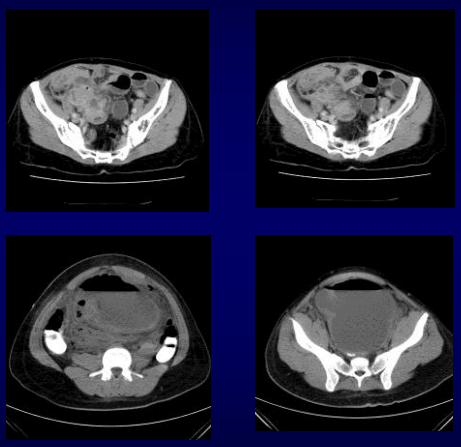
Recent WSES guidelines for diagnosis and treatment of acute appendicitis stated that laparoscopic appendectomy (LA) is the first choice where laparoscopic equipment and skills are available. In the Sauerland et al. review, wound infections were less likely after LA than after open appendectomy (OA) (OR 0.43; CI 0.34–0.54); however, the incidence of intra-abdominal abscesses was increased (OR 1.87; CI 1.19–2.93). Despite evidence showing that LA is safe in pregnancy, advantages are minor (less pain, less infections, less early deliveries) if compared to the risk of fetal loss.

Di Saverio S, Birindelli A, Kelly MD, Catena F, Weber DG, Sartelli M, et al. WSES Jerusalem guidelines for diagnosis and treatment of acute appendicitis. World J Emerg Surg. 2016;11:34.

Sauerland S, Jaschinski T, Neugebauer EA. Laparoscopic versus open surgery for suspected appendicitis. Cochrane Database Syst Rev. 2010;10:CD001546.

53

Periappendiceal abscess

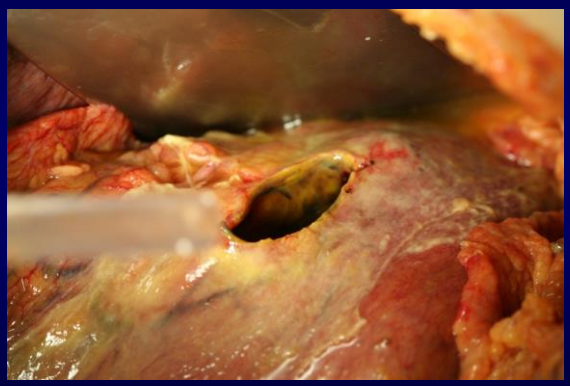


Periappendiceal abscess

Patients with a periappendiceal abscess can be managed with percutaneous image-guided drainage in surgical departments with ready access to diagnostic and interventional radiology. When percutaneous drainage is not available surgery is suggested.

55

Gastro-duodenal perforation



56

Gastro-duodenal perforation

Surgery is the treatment of choice for perforated peptic ulcers.

Simple closure with or without an omental patch is a safe and effective procedure to address small perforated ulcers (<2 cm).

57

There is no evidence of any significant advantages between laparoscopic and open repair of perforated peptic ulcer (PPU). However, laparoscopy has less postoperative pain and shorter hospital stay.

58

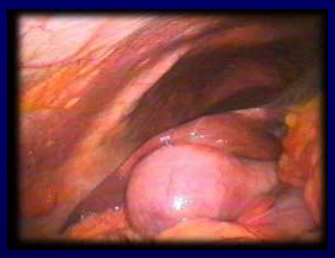
A systematic review was published in 2013 including randomized clinical trials comparing laparoscopic surgery versus open surgery for the repair of perforated peptic ulcer using any mechanical method of closure (suture, omental patch, or fibrin sealant).

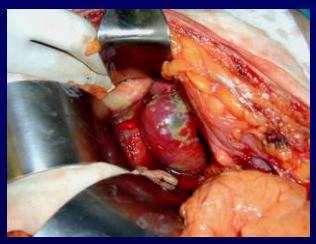
The authors concluded that laparoscopic surgery results are not clinically different from those of open surgery, but there is clearly a selection bias in the studies performed to date and there is a need of more randomized controlled trials with a larger number of patients.

Sanabria A, Villegas MI, Morales Uribe CH. Laparoscopic repair for perforated peptic ulcer disease. Cochrane Database Syst Rev. 2013;2:CD004778.

59

Acute cholecystitis





60

Timing of cholecystectomy

Early cholecystectomy: Surgery + antimicrobial prophylaxis

Delayed Cholecystectomy: Antimicrobial therapy + delayed surgery

Acute cholecystitis

Early cholecystectomy is a safe treatment for acute cholecystitis and generally results in shorter recovery time and hospitalization compared to delayed cholecystectomies.

Ansaloni L, Pisano M, Coccolini F, Peitzmann AB, Fingerhut A, Catena F, et al. 2016 WSES guidelines on acute calculous cholecystitis. World J Emerg Surg. 2016;11:25.

62

Acute cholecystitis

Laparoscopic cholecystectomy is a safe and effective treatment for acute cholecystitis.

It is the first choice for patients with acute cholecystitis where adequate resources and skill are available. Some risk factors may predict the risk for conversion to open cholecystectomy.

Ansaloni L, Pisano M, Coccolini F, Peitzmann AB, Fingerhut A, Catena F, et al. 2016 WSES guidelines on acute calculous cholecystitis. World J Emerg Surg. 2016;11:25.

63

Recent 2016 WSES guidelines for the management of acute calculous cholecystitis (AAC) stated that early cholecystectomy is the gold standard for treatment of ACC. Laparoscopic approach should initially be attempted except in cases of absolute anesthesiology contraindications or septic shock. Many prospective trials have demonstrated that the laparoscopic cholecystectomy is a safe and effective treatment for A**CC**.

A recently published meta-analysis demonstrated that laparoscopic cholecystectomy for ACC is the preferred approach having lower mortality and morbidity, significantly shorter post-operative hospital stay, and reduced rate of pneumonia and wound infections, compared with the open technique. Conversion rate ranged from 8 to 35%.

Coccolini F, Catena F, Pisano M, Gheza F, Fagiuoli S, Di Saverio S, et al. Open versus laparoscopic cholecystectomy in acute cholecystitis. Systematic review and meta-analysis. Int J Surg. 2015;18:196–204.

64

Acute diverticulitis

65

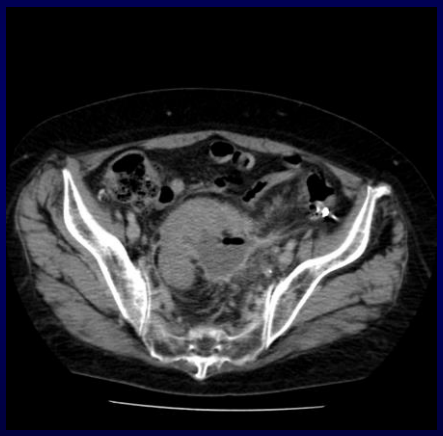
Uncomplicated diverticulitis

Antibiotics can be avoided in patients with CT findings of uncomplicated ALCD and without significant comorbid conditions or signs of sepsis. Patients should be clinically monitored to assess for resolution of the inflammatory processes.

Chabok A, Påhlman L, Hjern F, Haapaniemi S, Smedh K, AVOD Study Group. Randomized clinical trial of antibiotics in acute uncomplicated diverticulitis. Br J Surg. 2012;99:532–9.

66

Diverticular abscesses



Diverticular abscesses

On the basis of clinical conditions, patients with diverticular smaller abscesses may be treated by antibiotics alone.

Patients with abscesses having a large diameter should be treated by percutaneous drainage and intravenous antibiotics.

Whenever percutaneous drainage of the abscess is not feasible or not available, based on the clinical conditions patients with large abscesses can be initially treated by antibiotic therapy alone. However careful clinical monitoring is mandatory.

68

Diverticular peritonitis

Hartmann's procedure remains useful in the management of diffuse peritonitis in critically ill patients. However, in clinically stable patients, primary resection with anastomosis, with or without a diverting stoma, may be performed.

69

Laparoscopic lavage is not recommended in Hinchey IV diverticulitis because it can not achieve adequate source control. Laparoscopic lavage is safe and not inferior to sigmoid resection in case of Hinchey III but it is not considered the preferred choice, given the lack of evidence of major benefits.

Laparoscopic sigmoid resection is feasible and safe in selected patients, hemodynamically stable, without significant comorbidities and with onset of peritonitis <12-24 hours, only if specific advanced laparoscopic colorectal expertise is available.

70

A conservative approach using laparoscopic peritoneal lavage and drainage has been debated in recent years as an alternative to colonic resection. Great debate is still open on this topic, mainly due to the discrepancy and sometime disappointing results of the latest prospective trials such as SCANDIV, Ladies, and DILALA trials.

Angenete E, Thornell A, Burcharth J, Pommergaard HC, Skullman S, Bisgaard T, et al. Laparoscopic lavage is feasible and safe for the treatment of perforated diverticulitis with purulent peritonitis: the first results from the randomized controlled trial DILALA. Ann Surg. 2016;263:117–22.

Angenete E, Thornell A, Burcharth J, Pommergaard HC, Skullman S, Bisgaard T, et al. Laparoscopic lavage is feasible and safe for the treatment of perforated diverticulitis with purulent peritonitis: the first results from the randomized controlled trial DILALA. Ann Surg. 2016;263:117–22.

Vennix S, Musters GD, Mulder IM, Swank HA, Consten EC, Belgers EH, et al. Laparoscopic peritoneal lavage or sigmoidectomy for perforated diverticulitis with purulent peritonitis: a multicentre, parallel-group, randomised, open-label trial. Lancet. 2015;386:1269–77.

71

Colonic carcinoma perforation

Treatments for perforated colonic carcinoma should both stabilize the emergency condition of the peritonitis and fulfil the technical objectives of oncological intervention.

72

Colonic perforation following colonoscopy

Patients presenting with diffuse peritonitis caused by colonoscopic perforation should undergo immediate surgical intervention, which typically involves primary repair or resection

73

Small bowel perforations

Surgery is the treatment of choice for patients with small bowel perforations.

74

Small bowel perforations

There are many methods of surgical treatment of small bowel perforation, including primary closure, excision and closure, resection and primary anastomosis, limited right hemicolectomy, and stoma creation. Primary repair should be performed for patients with minor symptoms and with perioperative findings of minimal peritoneal contamination of the peritoneal cavity. In the setting of typhoidal perforation, although closure in two layers of single perforation with relatively healthy tissue after refreshment of the edge seems an acceptable option, resection of the unhealthy tissue segment with primary anastomosis of healthy edges about 10 cm on each side of the perforation is recommended.

In delayed cases with diffuse peritonitis, there can be severe inflammation and oedema of the bowel, resulting in friable tissue which precludes anastomosis, and therefore, an ileostomy should be performed as a life saving measure

75

Post-operative abscess

On the basis of the clinical conditions, the size of the abscess and the access to interventional radiology, antibiotics and/or percutaneous drainage may be suggested to treat post-operative localized intra-abdominal abscesses when there are no signs of generalized peritonitis

76

Post-operative peritonitis

Prompt surgical source control should be performed following diagnosis of post-operative peritonitis. Ineffective control of the septic source is associated with significantly elevated mortality rates.

77

Anastomotic dehiscence

Leak is associated with an increased likelihood of mortality.
Factors associated with intra-abdominal intestinal anastomotic leak are:

- Anastomotic tension
- Hypoxia
- Intra-operative or postoperative RBC transfusion
- Iron deficiency
- Ischemia
- Malnutrition
- Preoperative radiation therapy
- Prolonged duration of operation
- Renal failure
- Shock
- Steroid therapy
- Tobacco use

Re-laparotomy strategy

79

Ongoing Infections

In some patients, peritoneal infection may quickly lead to an excessive inflammatory response, causing organ failure. In these patients, an early re-intervention with surgical lavage of the peritoneal cavity and evacuation of toxic content and inflammatory cytokines may be crucial for stopping the septic cascade. This allows better control of the local inflammatory response and improved outcomes.

Koperna T, Schulz F: Relaparotomy in peritonitis: prognosis and treatment of patients with persisting intraabdominal infection. World J Surg 2000, 24(1):32–37. 92.

Lamme B, Mahler CW, van Ruler O, Gouma DJ, Reitsma JB, Boermeester MA: Clinical predictors of ongoing infection in secondary peritonitis: systematic review. World J Surg 2006, 30(12):2170–2181. 94.

80

Re-laparotomy strategy

Three methods of local mechanical management of abdominal sepsis following initial laparotomy for source control are currently debated:

(1) Open-abdomen
(2) planned relaparotomy,
(3) on-demand relaparotomy

81

Re-laparotomy strategy

On demand relaparotomy may be considered the preferred surgical strategy in patients with severe peritonitis because it has a substantial reduction in relaparotomies, health care utilization, and medical costs.

van Ruler O, Mahler CW, Boer KR, Reuland EA, Gooszen HG, Opmeer BC, de Graaf PW, Lamme B, Gerhards MF, Steller EP, van Till JW, de Borgie CJ, Gouma DJ, Reitsma JB, Boermeester MA; Dutch Peritonitis Study Group. Comparison of on-demand vs planned relaparotomy strategy in patients with severe peritonitis: a randomized trial. JAMA. 2007 Aug 22;298(8):865-72.

82

The on-demand strategy implies a vigilant observation of the patient and includes re-operation when patients show clinical deterioration or do not improve. However, these conditions are not well defined and often re-laparotomy may be performed too late. In patients with severe sepsis and septic shock.

83

Open abdomen and damage control surgery

In patients with severe abdominal sepsis the OA concept is closely linked to damage control surgery.

After source control abdominal closure may be temporary. In ICU patients resuscitation is optimized and patients are stabilized.

Early treatment with aggressive hemodynamic support can limit the damage of sepsis-induced tissue hypoxia and may limit the over stimulation of endothelial activity.

Following the early hemodynamic support, in principle after 24–48 h, reoperation may be performed with or without final abdominal closure

84

Damage Control Surgery

Initial control of contamination

Resuscitation to normal physiology in the intensive care unit

Subsequent re-exploration

85

Open abdomen and abdominal sepsis

- To control early any persistent source of infection removing more effectively infected or cytokine-loaded peritoneal fluid
- To prevent abdominal compartment syndrome and,
- To defer definitive intervention and anastomosis until the patient is hemodynamically stable and thus better able to heal

86

Open abdomen

Rapid closure with the assistance of negative pressure therapy should be the primary objective in the management of patients with open abdomen, in order to prevent severe morbidity such as fistulae, loss of domain and massive incisional hernias

Early closure

Delayed closure

87

Damage Control Surgery

There is insufficient evidence to advocate damage control surgery as general strategy in patients with secondary peritonitis.

Damage control surgery may be an option in selected significantly physiologically deranged patients with ongoing sepsis

88

Antimicrobial therapy

89

Antimicrobial therapy

The treatment of patients with complicated IAI involves both timely source control and antimicrobial therapy.

Empiric antimicrobial therapy is important in the management of intra-abdominal infections and must be broad enough to cover all likely organisms. Adequate source control is mandatory in the management of complicated IAIs.

90

Antimicrobial therapy

Antimicrobial therapy plays an integral role in the management of intra-abdominal infections. The choice of an inadequate antimicrobial agent is a cause of therapeutic failure.

91

Sartelli et al. World Journal of Emergency Surgery (2016) 11:33
DOI 10.1186/s13017-016-0089-y

World Journal of Emergency Surgery

REVIEW — Open Access

Antimicrobials: a global alliance for optimizing their rational use in intra-abdominal infections (AGORA)

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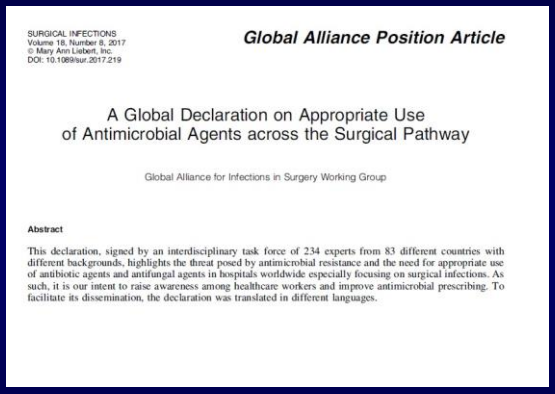

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Global Alliance Position Article

A Global Declaration on Appropriate Use of Antimicrobial Agents across the Surgical Pathway

Global Alliance for Infections in Surgery Working Group

Abstract

This declaration, signed by an interdisciplinary task force of 234 experts from 83 different countries with different backgrounds, highlights the threat posed by antimicrobial resistance and the need for appropriate use of antibiotic agents and antifungal agents in hospitals worldwide especially focusing on surgical infections. As such, it is our intent to raise awareness among healthcare workers and improve antimicrobial prescribing. To facilitate its dissemination, the declaration was translated in different languages.

Antibiotics can be life-saving when treating bacterial infections but are often used inappropriately, specifically when unnecessary or when administered for excessive durations or without consideration of pharmacokinetic principles. Large variations in antibiotic consumption exist between countries and whilst excessive use remains a major problem in some areas of the world, elsewhere there is lack of access to many antimicrobial agents. Antibiotic resistance (ABR) is a natural phenomenon that occurs as microbes evolve. However, human activities have accelerated the pace at which bacteria develop and disseminate resistance. Inappropriate use of antibiotics in humans and food-producing animals, as well as poor infection prevention and control practices, contribute to the development and spread of ABR.

Peritoneal specimens

95

Obtaining microbiological cultures from blood or fluid/tissue allows:

- to expand antimicrobial regimen if the initial choice is too narrow;
- perform a de-escalation is the empirical regimen is too broad.

When a microorganism is identified in clinical cultures, antimicrobial susceptibility testing (AST) should always be performed and reported to guide antibiotic therapy.

96

Intra-operative cultures should be always performed in patients with HA-IAs or with CA- at risk for resistant pathogens or in critically ill patients.

When a microorganism is identified in clinical cultures, antimicrobial susceptibility testing (AST) should always be performed and reported to guide antibiotic therapy

97

Microbiological identification in community-acquired IAI rarely influence the patient management

In post-operative peritonitis peri-operative cultures are routinely indicated as causative pathogens are less predictable

98

Empiric antimicrobial regimen

The choice of empiric antibiotic regimens in patients with IAI should be based on the clinical condition of the patients, the individual risk for infection by resistant pathogens, and the local resistance epidemiology.

99

Knowledge of local rates of resistance should be always an essential component of the clinical decision-making process when deciding on which antimicrobial regimen to use for empirical treatment of infection.

100

Predicting the pathogens and potential resistance patterns of a given infection begins by establishing whether the infection is community-acquired or hospital-acquired.
For patients with community-acquired intra-abdominal infections, agents with a narrower spectrum of activity are preferred. However, in CA-IAI patients at risk for extended-spectrum beta-lactamases (ESBLs) producing Enterobacteriaceae infections, anti-ESBL-producer coverage may be warranted. For patients with hospital-acquired infections, antibiotic regimens with broader spectra of activity are preferred.

101

Community-acquired IAIs

The major pathogens involved in community-acquired intra-abdominal infections are Enterobacteriaceae (especially *E. coli, K pneumoniae*, *Enterobacter*) Streptococcus species, and anaerobes (especially *B. fragilis*).

102

Community-acquired IAIs and ESBL

However, if CA-IAI patients have prior exposure to antibiotics or serious comorbidities requiring concurrent antibioitic therapy, anti-ESBL-producer coverage may be warranted.

Ben-Ami R, Rodriguez-Bano J, Arsian 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 β-lactamaseproducing Enterobacteriaceae in nonhospitalized patients. Clin Infect Dis 2009, 49:682–690.

103

Hospital-acquired IAIs

For patients with Hospital acquired infections, the pathogens are often unusual and antimicrobial regimens with broader spectra of activity are preferred

104

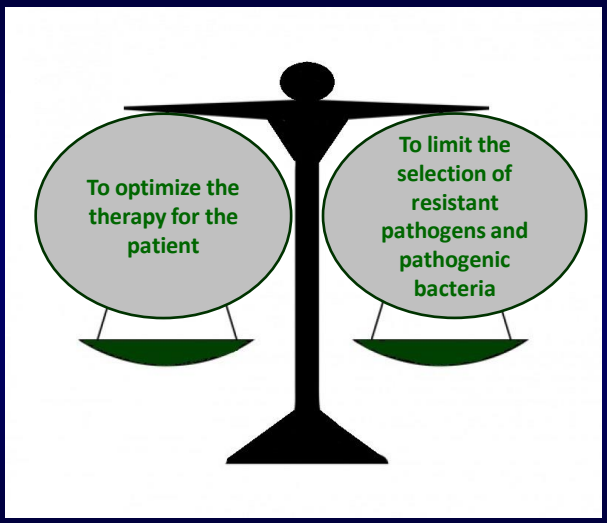
In the past 20 years, the incidence of healthcare-associated infections caused by drug-resistant microorganisms has risen dramatically, probably in correlation with escalating levels of antibiotic exposure and increasing frequency of patients with one or more predisposing conditions, including elevated severity of illness, advanced age, degree of organ dysfunction, low albumin levels, poor nutritional status, immunodepression, presence of malignancy, and other comorbidities.

105

Antibiotics use: finding the right balance

On one hand clinicians should offer optimal therapy for the individual patient under their care; on the other hand they should limit the impact of the antibiotic in order to prevent the selection of resistant pathogens and pathogenic bacteria such as *C. difficile*.

Antibiotics use: finding the right balance



Antimicrobial resistance

The problem of antimicrobial resistance (AMR) is widespread worldwide. Clinicians should be aware of their role and responsibility for maintaining the effectiveness of current and future antimicrobials. Health workers can help tackle resistance by:

- enhancing infection prevention and control;
- prescribing and dispensing antimicrobials when they are truly needed; and
- prescribing and dispensing the right antimicrobial(s) to treat the illness.

Extended-spectrum beta-lactamases (ESBLs)

In the event of intra-abdominal infection the main problem with antimicrobial resistance is posed by ESBL-producing Enterobacteriaceae, which may be identified in community-acquired infections

109

Extended-spectrum beta-lactamases (ESBLs)

- Extended-spectrum beta-lactamases (ESBLs) are mutant enzymes with a broader range of activity than their parent molecules
- ESBLs
  - Hydrolyze 3rd and 4th gen cephalosporins and aztreonam

110

ESBLs

- ESBL genes are often carried on plasmids that also encode resistance to multiple classes of antimicrobials
  - Aminoglycosides, Fluoroquinolones
- Antimicrobial armamentarium:
  - ß-lactam/inhibitor combinations (Pipercillin/tazobactam) +/-
  - Carbapenems
  - Tigecycline
  - Ceftolozane/tazobacta
  - Ceftazidime/avibactam

111

Carbapenem-resistant *Klebsiella pneumoniae*

Carbapenems offer a wide spectrum of antimicrobial activity against gram-positive and gram-negative aerobic and anaerobic pathogens (with the exception of MDR resistant gram-positive cocci). For more than 2 decades, carbapenems have been considered the agents of "last resort" for multidrug-resistant infections caused by Enterobacteriaceae. In the last decade, increased carbapenem consumption has been associated with an increased emergence of carbapenem resistance among Enterobacteriacea, particularly in *Klebsiella pneumoniae*.

112

Among carbapenems the best option for targeting ESBLs (though with no coverage of *P. aeruginosa*) is ertapenem, a once daily administered carbapenem that otherwise shares the activity of imipenem, meropenem and doripenem against most species, including ESBL producing pathogens. Imipenem/cilastatin, meropenem and doripenem provide coverage for Gram-negative non-fermenting bacteria. **However, inappropriate use of carbapenems should be avoided.**

113

The role of β-lactam/β-lactamase inhibitor (BLBLI) combinations towards ESBLs has been debated and controversial even if recent reports suggest their use in ESBL infections.

Although tigecycline does not feature in vitro activity against *P. aeruginosa* or certain Enterobacteriaceae (*Proteus spp., Serratia spp., Morganella morganii, Providencia stuartii*), it is still an option for complicated IAIs because of its favorable in vitro activity against anaerobic organisms, enterococci, several ESBLs, and some strains of carbapenemase-producing Enterobacteriaceae. Because of poor plasma concentrations, tigecycline performs poorly in bacteremic patients, with a much higher risk of failing to clear bacteremia. Tigecycline should not be considered as first-line therapy in patients with healthcare-associated pneumonia and bacteremia.

114

The recent challenges in the management of Gram-negative MDROs infections, especially in critically ill patients, have revived the clinical use of polymyxins and fosfomycin. There are still open questions about the need of combination therapy and the role of carbapenems, administered at high doses and by extended infusions, in the treatment of infections with carbapenem-resistant entetobacteriaceae.

Ceftolozane/tazobactam and ceftazidime/avibactam have recently been approved for the treatment of IAIs.

115

Antibiotics in critically ill patients

An inadequate empiric antimicrobial regimen is associated with unfavorable outcomes in critical ill patients. In these patients the following strategies should be always implemented to obtain an optimal response to therapy:

- Early source control procedures when indicated;
- Early initiation of therapy (ideally, within 1 h);
- Correct dosing;
- Considering risk factor for MDRO; and
- Avoiding use of identical antibiotic and the same antibiotic class administered in the preceding 3 months.

116

Antibiotics in critically ill patients

In critically ill patients antimicrobial therapy should be started as soon as possible.

In these patients to ensure timely and effective administration of antibiotics, clinicians should always consider the pathophysiological status of the patient as well as the pharmacokinetic properties of the employed antibiotics.

117

Correct dose in critically ill patients

The correct dose and correct administration of antimicrobials should include:

1) loading dose when indicated;
2) extended or prolonged infusion for beta-lactam antibiotics.

118

Loading dose

Higher than standard loading doses (LD) of hydrophilic agents such as beta-lactams should be administered to ensure optimal exposure at the infection site, maintaining a therapeutic threshold that considers the effects of renal function

119

pharmacokinetics / pharmacodynamics

- **Pharmacokinetics (PK)**
  - serum concentration profile
  - penetration to site of infection
- **Pharmacodynamics (PD)**
  - **susceptibility – MIC**

120

Time-dependent antibiotics

Beta-lactams exhibit time-dependent activity and exert optimal bactericidal activity when drug concentrations are maintained above the Minimum Inhibitory Concentration (MIC).

121

Concentration-dependent antibiotics

Antibiotics such aminoglycosides, polienes, and echinocandins exhibit concentration-dependent activity; as such, the dose should be administered in a once-a-day manner (or with the lowest possible daily administrations) in order to achieve zenithal plasma levels.

122

- Insufficient β-lactam concentrations in the early phase of severe sepsis/septic shock has been reported without the use of LD.

Taccone FS et al. Crit Care. 2010;14(4):R126

- Continuous infusion of beta-lactam antibiotics in severe sepsis has been associated with higher clinical cure in a multicenter RCT of 60 pts, but no difference was observed in the same study with 432 pts

Dulhunty JM et al. Clin Infect Dis. 2013;56:236-44
Dulhunty JM et al. Am J Respir Crit Care Med. 2015;192:1298-305

123

Recommended dosing regimen according to renal function

Table 2 Recommended dosing regimens (according to renal function) of the most commonly used renally excreted antimicrobials [248]

	Renal function			
Antibiotic	**Increased**	**Normal**	**Moderately impaired**	**Severely impaired**
Piperacillin/tazobatam	16/2 g q24 h CI or 3.375 q6 h EI over 4 hours	4/0.5 g q6 h	3/0.375 g q6 h	2/0.25 g q6 h
Imipenem	500 mg q4 h or 250 mg q3 h over 3 hours CI	500 mg q6 h	250 mg q6 h	250 mg q12 h
Meropenem	1 g q6 h over 6 hours CI	500 mg q6 h	250 mg q6 h	250 mg q12 h
Ertapenem	ND	1 g q24 h	1 g q24 h	500 mg q24 h
Gentamycin	9 to 10 mg/kg q24 h[b]	7 mg/kg q24 h	7 mg/kg q36–48 h	7 mg/kg q48–96 h
Amikacin	20 mg/kg q24 h	15 mg/kg q24 h	15 mg/kg q36–48 h[b]	15 mg/kg q48–96 h
Ciprofloxacin	600 mg q12 h or 400 mg q8 h	400 mg q12 h	400 mg q12 h	400 mg q24 h
Levofloxacin	500 mg q12 h	750 mg q24 h	500 mg q24 h	500 mg q48 h
Vancomycin	30 mg/kg q24 h CI	500 mg q6 h	500 mg q12 h	500 mg q24–72 h
Teicoplanin	LD 12 mg/kg q12 h for 3 to 4 doses; MD 6 mg/kg q12 h	LD 12 mg/kg q12 h for 3 to 4 doses; MD 4 to 6 mg/kg q12 h	LD 12 mg/kg q12 h for 3 to 4 doses; MD 2 to 4 mg/kg q12 h	LD 12 mg/kg q12 h for 3 to 4 doses; MD 2 to 4 mg/kg q24 h
Tigecycline	LD 100 mg; MD 50 mg q12 h	LD 100 mg; MD 50 mg q12 h	LD 100 mg; MD 50 mg q12 h	LD 100 mg; MD 50 mg q12 h

Sartelli M, Viale P, Catena F, Ansaloni L, Moore E, Malangoni M, Moore FA, Velmahos G, Coimbra R, Ivatury R, Peitzman A, Koike K, Leppaniemi A, Biffl W, Burlew CC, Balogh ZJ, Boffard K, Bendinelli C, Gupta S, Kluger Y, Agresta F, Di Saverio S, Wani I, Escalona A, Ordonez C, Fraga GP, Junior GA, Bala M, Cui Y, Marwah S, Sakakushev B, Kong V, Naidoo N, Ahmed A, Abbas A, Guercioni G, Vettoretto N, Díaz-Nieto R, Gerych I, Tranà C, Faro MP, Yuan KC, Kok KY, Mefire AC, Lee JG, Hong SK, Ghnnam W, Siribumrungwong B, Sato N, Murata K, Irahara T, Coccolini F, Lohse HA, Verni A, Shoko T. 2013 WSES guidelines for management of intra-abdominal infections. World J Emerg Surg. 2013 Jan 8;8(1):3.

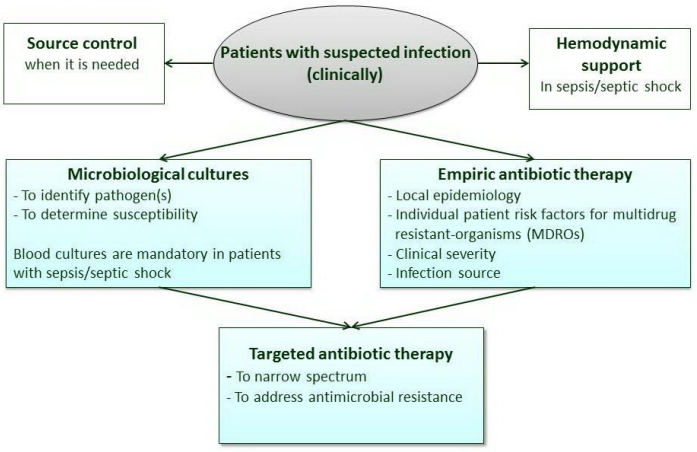
124

Antimicrobial de-escalation or withdrawal

The patient should be reassessed when the results of microbiological testing are available. Antimicrobial de-escalation or withdrawal should be always considered.

125

Rational use of antibiotics in surgery



126

Duration of antibiotic therapy

127

In the setting of uncomplicated acute cholecystitis and acute appendicitis post-operative antibiotic therapy is not necessary

Regimbeau JM, Fuks D, Pautrat K, Mauvais F, Haccart V, Msika S, et al. Effect of postoperative antibiotic administration on postoperative infection following cholecystectomy for acute calculous cholecystitis: a randomized clinical trial. JAMA. 2014;312:145–54.

128

In patients with complicated IAIs, when patients are not severely ill and when source control is complete, a short course (3–5 days) of post-operative therapy is suggested.

Sawyer RG, Claridge JA, Nathens AB, Rotstein OD, Duane TM, Evans HL, et al. Trial of short-course antimicrobial therapy for intraabdominal infection. N Engl J Med. 2015;372:1996–2005.

129

Patients who have ongoing signs of peritonitis or systemic illness (ongoing infection) beyond 5 to 7 days of antibiotic treatment, should warrant a diagnostic investigation.

130

In patients with ongoing or persistent IAIs, the decision to continue, revise, or stop antimicrobial therapy should be made on the basis of clinician judgment and laboratory information .

Recently, procalcitonin (PCT) has been suggested as a novel biomarker that may be useful in guiding therapeutic decision making in the management of sepsis. It may be a helpful tool to determine the timing and appropriateness of escalation of antimicrobial therapy in sepsis.

Carr JA. Procalcitonin-guided antibiotic therapy for septic patients in the surgical intensive care unit. J Intensive Care. 2015;3:36

131

Antibiotic armamentarium

The choice of empiric antibiotics in patients with IAI should be based on the severity of the infection, the individual risk for infection by resistant pathogens, and the local resistance epidemiology. Amoxicillin/clavulanate or cephalosporins in combination with metronidazole, are still good options for the treatment of non-severe IAIs, with piperacillin/tazobactam being a better choice if P. aeruginosa coverage is needed. The use of carbapenems should be limited so as to preserve activity of this class of antibiotics because of the concern of emerging carbapenem-resistance. Ciprofloxacin and levofloxacin are no longer appropriate first-line choices for empiric treatment in many regions because of the prevalence of fluoroquinolone resistance. Other options include aminoglycosides, particularly for suspected infections by Gram negative bacteria, and tigecycline especially when MDRO are suspected, though caution is advised for the latter, in the situation of a bacteremia.

Recent challenges in the management of multi-drug resistant Gram-negative infections, especially in critically ill patients, have reviewed the use of “old” antibiotics, such as polymyxins and fosfomycin.

Ceftolozone/tazobactam and ceftazidime/avibactam are new antibiotics that have been approved for treatment of cIAI infections (in combination with metronidazole) including infection by ESBLs and P. aeruginosa, though their role for the empirical therapy remains to be defined.

132

Intra-abdominal candidiasis

133

Candida

The presence of *Candida spp.* in the peritoneal samples is a factor of poor prognosis.

No study has specifically evaluated the efficacy of antifungal therapy in IAIs. In recent randomized trials focusing on antifungal therapy of invasive candidiasis, the proportion of patients with a diagnosis of abdominal candidiasis was low. The need for an early adequate systemic antifungal therapy in candida peritonitis is based on the assumption that delayed antifungal therapy initiation is associated to poorer outcome, particularly among those with candidaemia. However, a deleterious impact of delayed systemic antifungal therapy initiation has never been demonstrated in candida intra-abdominal infection.

134

Candida

Empiric antifungal therapy should be considered in patients with clinical evidence of intra-abdominal infection and significant risk factors for candidiasis:

- recent abdominal surgery;
- anastomotic leaks;
- necrotizing pancreatitis; and
- failure of treatment for bacterial infections.

135

Preferred empiric therapy in critically ill patients or those previously exposed to an azole is an echinocandin (caspofungin: loading dose of 70 mg, then 50 mg daily; micafungin:100 mg daily; anidulafungin: loading dose of 200 mg, then 100 mg daily). However, fluconazole, 800-mg (12 mg/kg) loading dose, then 400 mg (6 mg/kg) daily, should be still considered first-line antifungal therapy, in hemodynamically stable patients who are colonized with azole susceptible Candida species or who have no prior exposure to azoles.

The duration of therapy should be determined by adequacy of source control and clinical response.

Pappas PG, Kauffman CA, Andes D, Benjamin DK, Calandra TF, Edwards JE, et al. Clinical practice guidelines for the management of candidiasis: 2009 update by the Infectious Diseases Society of America. Clin Infect Dis. 2009;48:503–535. doi: 10.1086/596757.

136

Interventions to improve antibiotic prescribing practices for patients with IAIs

Patient level which includes clinical severity, epidemiological exposures, PK/PD factors, comorbidities, prior antibiotic exposure, prior infection, or colonization with MDROs and infection source.

Hospital level including presence of in-hospital antimicrobial stewardship programs, availability of local guidelines and updated microbiological data, infection control policy, educational activities, and structural resources (like computer-assisted order entry).

137

Although most antimicrobial use occurs in the community, the intensity of use in hospitals is far higher; hospitals are therefore particularly important in the containment of antimicrobial resistance.

Hospital based Antibiotic Stewardship Programs (ASPs) can help clinicians both to optimize the treatment of infections and reduce adverse events associated with antibiotic use.

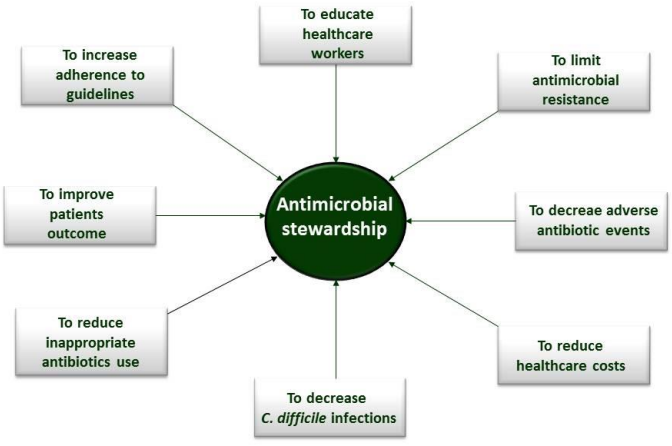
Given the urgent need to improve antimicrobial use in healthcare all acute care hospitals should implement Antibiotic Stewardship Programs.

138

Since physicians are primarily responsible for the decision to use antibiotics, educating them and changing the attitudes and knowledge that underlie their prescribing behavior are crucial for improving antimicrobial prescription. The ultimate goal of an ASP should be to stimulate a behavioral change in prescribing practice. Educational interventions should include any attempt to persuade physicians to modify their clinical practice.

139

The 8 goals of the antimicrobial stewardship programs

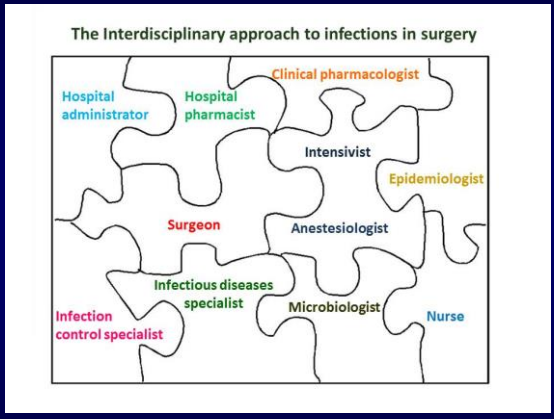


140

Promotion of ASPs across clinical practice is crucial to their success to ensure standardization of antibiotic use within an institution. We propose that the best means of improving antimicrobial stewardship should involve collaboration among various specialties within a healthcare institution including prescribing physicians.

Successful ASPs should focus on collaboration between all healthcare professionals to shared knowledge and widespread diffusion of practice. Involvement of prescribing physicians in ASPs may rise their awareness on antimicrobial resistance.

141



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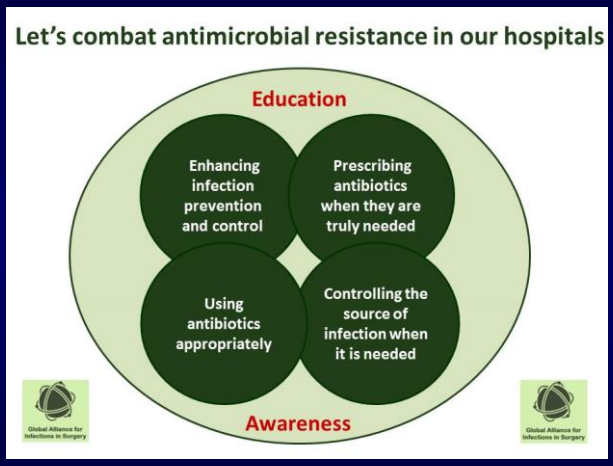

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Abdominal sepsis

144

Sepsis is a complex, multifactorial syndrome which can evolve into conditions of varying severity. If left untreated, it may lead to the functional impairment of one or more vital organs or systems.

Abdominal sepsis represents the host's systemic inflammatory response to bacterial or yeast peritonitis.

145

Patients with severe sepsis or septic shock of abdominal origin require early hemodynamic support, source control, and antimicrobial therapy.

146

Patients with at least two of three clinical abnormalities including Glasgow coma score of 14 or less, systolic blood pressure of 100 mmHg or less, and respiratory rate 22/min or greater may have poor outcome typical of sepsis. Importantly, qSOFA does not define sepsis but provides simple bedside criteria to screen adult patients with suspected infection.

Singer M, Deutschman CS, Seymour CW, Shankar-Hari M, Annane D, Bauer M, et al. The Third International Consensus Definitions for Sepsis and Septic Shock (Sepsis-3). JAMA. 2016;315:801–10

147

Sepsis is now defined as a life-threatening organ dysfunction caused by a dysregulated host response to infection. It can be clinically represented by an increase in the SOFA score of 2 points or more.

Singer M, Deutschman CS, Seymour CW, Shankar-Hari M, Annane D, Bauer M, et al. The Third International Consensus Definitions for Sepsis and Septic Shock (Sepsis-3). JAMA. 2016;315:801–10

148

PaO2/FiO2 (mmHg)	
< 400	1
< 300	2
< 200 and mechanically ventilated	3
< 100 and mechanically ventilated	4
Glasgow coma scale	
13–14	1
10–12	2
6–9	3
< 6	4
Mean arterial pressure OR administration of vasopressors required	
MAP < 70 mm/Hg	1
dop <= 5 or dob (any dose)	2
dop > 5 OR epi <= 0.1 OR nor <= 0.1	3
dop > 15 OR epi > 0.1 OR nor > 0.1	4
Bilirubin (mg/dl) [µmol/L]	
1.2–1.9 [> 20-32]	1
2.0–5.9 [33-101]	2
6.0–11.9 [102-204]	3
> 12.0 [> 204]	4
Platelets×103/µl	
< 150	1
< 100	2
< 50	3
< 20	4
Creatinine (mg/dl) [µmol/L] (or urine output)	
1.2–1.9 [110-170]	1
2.0–3.4 [171-299]	2
3.5–4.9 [300-440] (or < 500 ml/d)	3
> 5.0 [> 440] (or < 200 ml/d)	4

SOFA score

149

Septic shock is defined as a subset of sepsis in which particularly profound circulatory, cellular, and metabolic abnormalities who are associated with higher risk of mortality than with sepsis alone. Patients with septic shock can be clinically identified by requirement for vasopressors to maintain a mean arterial pressure of 65 mmHg or greater and serum lactate level greater than 2 mmol/L (>18 mg/dL) in the absence of hypovolemia.

Singer M, Deutschman CS, Seymour CW, Shankar-Hari M, Annane D, Bauer M, et al. The Third International Consensus Definitions for Sepsis and Septic Shock (Sepsis-3). JAMA. 2016;315:801–10

150

Fluid therapy is needed to improve microvascular blood flow through an increased cardiac output as an essential part of the treatment of sepsis. A fluid challenge should incorporate four determinant elements: (1) crystalloid solutions should be the first choice because they are well tolerated and cheap; (2) fluids should be infused rapidly to induce a quick response but not so fast that an artificial stress response develops; (3) the goal should be an increase in systemic arterial pressure; and (4) avoidance of pulmonary edema which is the most serious complication of fluid infusion through appropriate monitoring that is necessary to prevent edema occurrence.

Vincent JL, De Backer D. Circulatory shock. N Engl J Med. 2013;369:1726–34.

151

Early identification of sepsis and prompt administration of intravenous fluids and vasopressors are always mandatory.

Hypotension is the most common indicator of inadequate perfusion.

152

Prompt administration of intravenous fluids for resuscitation is critical in patients with an ongoing sepsis. This initial resuscitation should be titrated to the clinical response, and not solely guided by a predetermined protocol. Vasopressor agents may serve to augment and assist fluid resuscitation, particularly where this therapy alone is failing.

153

Fluid overload should be avoided in patients with generalized peritonitis.

154

Particularly in patients with abdominal sepsis, requiring urgent surgical intervention, overly aggressive fluid resuscitation may increase intra-abdominal pressure and worsen the inflammatory response, which is associated with a high risk of complications

155

The systemic inflammatory response syndrome, increased vascular permeability, and aggressive crystalloid resuscitation predispose to fluid sequestration and collection in the peritoneum. Patients with advanced sepsis commonly develop bowel edema. These changes along with an associated forced closure of the abdominal wall may result in increased IAP ultimately leading to intra-abdominal hypertension (IAH). Elevated IAP may reduce both regional and global perfusion resulting in significant organ failure. An uncontrolled IAH, with an IAP exceeding 20 mmHg, and new organ failure onset leads to abdominal compartment syndrome (ACS). ACS is a potentially lethal complication affecting splanchnic, cardiovascular, pulmonary, renal, and central nervous systems.

Sartelli M, Catena F, Di Saverio S, Ansaloni L, Malangoni M, Moore EE, et al. Current concept of abdominal sepsis: WSES position paper. World J Emerg Surg. 2014;9:22.

156

When fluid challenge fails to restore adequate arterial pressure and organ perfusion, clinicians should resort to vasopressor agents.

Vasopressor drugs maintain adequate blood pressure and preserve perfusion pressure, thereby optimizing blood flow in various organs.

157

Norepinephrine is now the first-line vasopressor agent which is used to correct hypotension in the event of septic shock. It is more efficacious than dopamine and is more effective for reversing hypotension in patients with septic shock

De Backer D, Aldecoa C, Njimi H, Vincent JL. Dopamine versus norepinephrine in the treatment of septic shock: a meta-analysis. Crit Care Med. 2012;40:725–30

158

Norepinephrine is more efficacious than dopamine and may be more effective for reversing hypotension in patients with septic shock. Dopamine may cause more tachycardia and may be more arrhythmogenic than norepinephrine, and as an alternative vasopressor agent to norepinephrine, it should be used only in patients with low risk of tachyarrhythmias and absolute or relative bradycardia.

159

Delay in first antibiotic administration is associated with increased in-hospital mortality in patients with severe sepsis and septic shock.

Ferrer R, Martin-Loeches I, Phillips G, Osborn TM, Townsend S, Dellinger RP, et al. Empiric antibiotic treatment reduces mortality in severe sepsis and septic shock from the first hour: results from a guideline-based performance improvement program. Crit Care Med. 2014;42:1749–55.

160

Principal determinants of antibiotic choice in critically ill patients are based on three parameters:

1) Severity of illness,
2) local ecology, and
3) risk factors of the host. Previous antibiotic use is associated with a higher development of multidrug resistant organisms (MDROs).

Broad-spectrum antibiotic therapy, including combination of different antibiotic classes should be recommended in patients with septic shock, settings with high rates of MDRO, and previous antibiotic administration

161

Thanks

Together we can impact millions of people!

162

Designed and performed by Massimo Sartelli MD
No conflict of interest to declare

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163