Algorithm for the treatment of secondary peritonitis

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Secondary peritonitis

• Perforation of hollow viscus

• Acute infection of intra-abdominal or pelvic viscus

• Transmural bowel necrosis with perforation or established peritonitis or abscess

• Post-trauma (stab wound, perforation or contusion)

• Post-operative and nosocomial
Surviving Sepsis Campaign: International guidelines for management of severe sepsis and septic shock: 2008

R. Phillip Dellinger, MD; Mitchell M. Levy, MD; Jean M. Carlet, MD; Julian Bion, MD; Margaret M. Parker, MD; Roman Jaeschke, MD; Konrad Reinhart, MD; Derek C. Angus, MD, MPH; Christian Brun-Buisson, MD; Richard Beale, MD; Thierry Calandra, MD, PhD; Jean-Francois Dhainaut, MD; Herwig Gerlach, MD; Maurene Harvey, RN; John J. Marini, MD; John Marshall, MD; Marco Ranieri, MD; Graham Ramsay, MD; Jonathan Sevransky, MD; B. Taylor Thompson, MD; Sean Townsend, MD; Jeffrey S. Vender, MD; Janice L. Zimmerman, MD; Jean-Louis Vincent, MD, PhD; for the International Surviving Sepsis Campaign Guidelines Committee
2 Major Goals

Source control
Antibiotic therapy

= Appropriateness
Quality of the procedure
On time
Timing of Initiation of Antimicrobial Therapy

8. Antimicrobial therapy should be initiated once a patient receives a diagnosis of an intra-abdominal infection or once such an infection is considered likely. For patients with septic shock, antibiotics should be administered as soon as possible (A-III).

9. For patients without septic shock, antimicrobial therapy should be started in the emergency department (B-III).
We recommend that initial empirical anti-infective therapy include one or more drugs that have activity against all likely pathogens (bacterial and/or fungal) and that penetrate in adequate concentrations into the presumed source of sepsis (grade 1B).
Pharmacokinetics in the peritoneal fluid

Ceftazidime 1.5g X 3/24 H

Serum
Peritoneal exsudate

Buijk SLCE et al. J Antimicrob Chemother; 2002;49:121-128
The issues to consider

• Ecology and geographic location
• Type of infection
• Severity of the case
  – Risk of failure of source control
• Risk of resistant pathogens
• Risk of *Enterococcus* species
• Risk of *Candida* species

IDSA GUIDELINES
E. coli resistance
3G Cephalosporins

E. faecium resistance
vancomycin

Appropriate antibiotic therapy

Community-acquired Infection (CAI)

Health-care associated Infection (HCAI)

Broad spectrum AB

Community micro-organisms

Nosocomial Micro-organisms
Severity of the case

Mild to moderate severity

High-risk patients = risk of adverse outcome (death)
- High APACHE II score
- Poor nutritional status
- Significant cardiovascular disease
- Inability to obtain adequate source control
- Immunosuppressed (transplant, cancer, inflammation)

Septic shock or organ failure

Factors predicting failure of source control

Delayed initial intervention (> 24h)
High severity of the illness (APACHE II ≥15)
Advanced age
Comorbidity and degree of organ dysfunction
Low albumine level
Poor nutritional status
Degree of peritoneal involvement or diffuse peritonitis
Inadequate debridement or control of drainage
Presence of malignancy

Increased risk of resistant pathogens

- Foreign travel risk of contamination (CAI)
  

- Epidemiology and local ecology (CAI)
  
  Canton R et al. Rev Esp Quimioter 2011;24:223-32
  Nejmi H et al. Med Mal Infect 2010 .11015

- Prolonged preoperative hospital stay (CAI-HCAI)

- Preoperative antibiotic therapy (CAI-HCAI)

- Resistant bacteria at the time of initial intervention (HCAI)

ESBLs (%) in intra-abdominal pathogens, SMART Asia, 2008

Hsueh et al., IJAA 2010; 34: 408
Increased risk of enterococcal infection

- Heath care associated infection or postoperative infection
- Previous use of cephalosporins
- Previous use of other antimicrobial agents selecting enterococcus species
- Immunocompromised patients (transplant patients)
- Patients with valvular heart disease
- Patients with prosthetic intravascular materials

Table 2. Agents and Regimens that May Be Used for the Initial Empiric Treatment of Extra-biliary Complicated Intra-abdominal Infection

<table>
<thead>
<tr>
<th>Regimen</th>
<th>Community-acquired infection in adults</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Mild-to-moderate severity: perforated or abscessed appendicitis and other infections of mild-to-moderate severity</td>
</tr>
<tr>
<td>Single agent</td>
<td>Cefoxitin, ertapenem, moxifloxacin, tigecycline, and ticarcillin-clavulanic acid</td>
</tr>
<tr>
<td>Combination</td>
<td>Cefazolin, cefuroxime, ceftriaxone, cefotaxime, ciprofloxacin, or levofloxacin, each in combination with metronidazole&lt;sup&gt;a&lt;/sup&gt;</td>
</tr>
</tbody>
</table>

<sup>a</sup>Metronidazole is especially useful against anaerobic infections.
Clinical and microbiological profiles of community-acquired and nosocomial intra-abdominal infections: results of the French prospective, observational EBIIA study

Philippe Montravers, Alain Lepape, Luc Dubreuil, Rémy Gauzit, Yves Pean, Daniel Benchimol and Hervé Dupont

Etude épidémiologique Bactério-clinique des Infections Intra-Abdominales (EBIIA)

Microbiological and clinical epidemiology of intra-abdominal infections

• 6 months January-June 2005
• 11 university and 14 non-university hospitals
• ICU and surgical ward
• Patients > 18 years
• Abdominal surgery (open/coelioscopic) for peritonitis with purulent material
• Microbiological culture of peroperative intra-abdominal samples

Community-acquired infection

**FIRST LINE THERAPY**

**Monotherapy:**
(cefoxitin, ticarcillin/clav), moxifloxacin, ertapenem, tigecycline

**Combination:**
amoxicillin/clav (sulbactam) + aminoglycosides
 ticarcillin/clav + aminoglycosides
 cefotaxime/ceftriaxone/(fluoroquinolones) + metronidazole

**Resistant pathogens**
- moxifloxacin, ertapenem, tigecycline
- ESBL strains?
- amoxicillin/clav + aminoglycosides
- ticarcillin/clav + aminoglycosides
- (fluoroquinolones + aminoglycosides + metronidazole)
Resistant pathogens

Community-acquired infection

Yes

(moxifloxacin, ertapenem, tigecycline)

Imipenem, meropenem, doripenem

Imipenem, meropenem, doripenem + aminoglycosides

piperacillin/tazo ± aminoglycosides

cefepime/ceftazidime + metronidazole

No

Yes

Yes

Imipenem, meropenem, doripenem + aminoglycosides

piperacillin/tazo + aminoglycosides

cefepime/ceftazidime + aminoglycosides + metronidazole

Signs of severity
## Recommendations for Empiric Antimicrobial Therapy for Health Care–Associated Complicated Intra-abdominal Infection

<table>
<thead>
<tr>
<th>Organisms seen at the local level</th>
<th>Penems</th>
<th>Pip/taz</th>
<th>Ceftazidime Cefepime + metronidazole</th>
<th>Amino glycoside</th>
<th>Vanco</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;20% R- <em>P. aeruginosa</em>, Acinetob ESBL or other MDR GNB</td>
<td></td>
<td></td>
<td></td>
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<td></td>
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<tr>
<td>ESBL</td>
<td></td>
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<td></td>
</tr>
<tr>
<td>&gt;20% <em>P. aeruginosa</em> R cefta</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>MRSA</td>
<td></td>
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</tbody>
</table>

- **Recommended**
- **Not recommended**

Risk factors for multidrug resistant bacteria and optimization of empirical antibiotic therapy in postoperative peritonitis

Augustin et al, Crit Care 2010:15;R20
Optimization in patients with (n=41) or without (n=66) multiple drug resistant (MDR) bacteria

Augustin et al, Crit Care 2010:15;R20
Health-care related infection

Resistant pathogens

Yes

Imipenem, meropenem, doripenem + amikacin
piperacillin/tazo + amikacin
cefepime/ceftazidime + amikacin + metronidazole

No

Yes

Imipenem, meropenem, doripenem + amikacin + vancomycin
piperacillin/tazo + amikacin + vancomycin
cefepime/ceftazidime + amikacin + metronidazole + vancomycin

Signs of severity
 Increased risk of candida infection

- APACHE II score >17
- Candida observed at direct examination of peritoneal fluid
- Acute respiratory failure
- Gastro-duodenal source of infection

<table>
<thead>
<tr>
<th>Grade</th>
<th>Se (%)</th>
<th>Sp (%)</th>
<th>PPV (%)</th>
<th>PNV (%)</th>
<th>A (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Grade A</td>
<td>3</td>
<td>100</td>
<td>40</td>
<td>100</td>
<td>40</td>
</tr>
<tr>
<td>Grade B</td>
<td>33</td>
<td>87</td>
<td>46</td>
<td>79</td>
<td>54</td>
</tr>
<tr>
<td>Grade C</td>
<td>84</td>
<td>50</td>
<td>67</td>
<td>72</td>
<td>71</td>
</tr>
<tr>
<td>Grade D</td>
<td>100</td>
<td>13</td>
<td>100</td>
<td>64</td>
<td>65</td>
</tr>
</tbody>
</table>

Se, sensitivity; Sp, specificity; PPV, Predictive positive value; PNV, negative predictive value; A, Accuracy

Dupont H. Crit Care Med 2003;31:752
Recommendations

48. Antifungal therapy for patients with severe community-acquired or health care–associated infection is recommended if *Candida* is grown from intra-abdominal cultures (B-II).

51. For the critically ill patient, initial therapy with an echinocandin instead of a triazole is recommended (B-III).

52. Because of toxicity, amphotericin B is not recommended as initial therapy (B-II).
Signs of severity
Candida infection
Community-acquired infection
Health-care related infection

- Yes
- No

fluconazole

- Yes
- Yes

echinocandins
caspofungin, micafungin, anidulafungin
In summary

• Early management with adequate dose

• Limited help of international guidelines

• Major importance of
  National or regional epidemiology for CAI
  Local ecology for HCAI

• De-escalation as soon as possible