Surgical Site Infections - a 21st Century Challenge
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Royal College of Surgeons of England, London

Intra-abdominal infections - an everyday surgical challenge
Dr Massimo Sartelli
m.sartelli@virgilio.it

Macerata Hospital (Italy)
Department of Surgery
Chief: I Patrizi
Intra-abdominal infections – an everyday surgical challenge

Classification

Diagnosis

Source control

Antimicrobial therapy
Classification
Classification

Intra-abdominal infections (IAIs) include many pathological conditions, ranging from uncomplicated appendicitis to faecal peritonitis. IAIs are classified into uncomplicated and complicated.
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.
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
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.
- **Tertiary peritonitis** is a recurrent infection of the peritoneal cavity that follows either primary or secondary peritonitis.
Secondary bacterial peritonitis

Secondary bacterial peritonitis arises as a consequence of injury to an intrabdominal viscus from intrinsic disease or extrinsic trauma.

Secondary bacterial peritonitis
<table>
<thead>
<tr>
<th>Secondary peritonitis</th>
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<tbody>
<tr>
<td><strong>Stomach</strong></td>
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<tr>
<td>Peptic ulcer perforation</td>
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<tr>
<td>Malignancy</td>
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<td>Trauma (mostly penetrating)</td>
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<td><strong>Duodenum</strong></td>
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<td>Peptic ulcer perforation</td>
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<td>Trauma (blunt and penetrating)</td>
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<tr>
<td>Iatrogenic</td>
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<tr>
<td><strong>Biliary tract</strong></td>
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<tr>
<td>Cholecystitis</td>
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<td>Stone perforation from gallbladder (ie, gallstone ileus)</td>
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<tr>
<td>or common duct</td>
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<tr>
<td>Malignancy</td>
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<td>Trauma (mostly penetrating)</td>
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<td>Iatrogenic</td>
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<tr>
<td><strong>Small bowel</strong></td>
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<td>Ischemic bowel</td>
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<td>Incarcerated hernia (internal and external)</td>
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<tr>
<td>Closed loop obstruction</td>
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<td>Crohn disease</td>
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<tr>
<td>Malignancy (rare)</td>
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<tr>
<td>Meckel diverticulum</td>
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<tr>
<td>Trauma (mostly penetrating)</td>
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</tbody>
</table>
Diagnosis
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).

SIRS manifestations
Core body temperature $> 38°$ C or $< 36°$ C, heart rate $> 90$ beats per minute, respiratory rate $> 20$ breaths per minute (not ventilated) or $\text{PaCO}_2 < 32$ mm Hg (ventilated), $\text{WBC} > 12,000$, $< 4,000$ 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.
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 infectious and help monitor adequacy of abscess drainage
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
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.

A negative CT generally indicates a very low probability of a process that can be reversed by surgical intervention, however bowel ischaemia cannot be excluded, particularly in the early stages.

If the diagnosis of peritonitis is made clinically, a CT scan is not necessary and generally delays surgical intervention without offering clinical advantage.
CT abdomen
Source control
Source control

Source control represents a key component of success in therapy of sepsis. It includes drainage of infected fluids, debridement of infected soft tissues, removal of infected devices or foreign bodies, and finally, definite measures to correct anatomic derangement resulting in ongoing microbial contamination and to restore optimal function.

Although highly logical, since source control is the best way to reduce quickly the bacterial inoculum, most recommendations have, however, low grade due to the difficulty to perform appropriate randomized clinical trials in this respect.

Source control

Source control should be obtained as early as possible after the diagnosis of intra-abdominal sepsis has been confirmed. Inability to control the septic source is associated significantly with increase in mortality.
Gastro-duodenal perforation
Gastro-duodenal perforation

In perforated peptic ulcer, surgery is the treatment of choice. In selected cases (Pts yunger than 70 ys old, no shock, no peritonitis, lack of spillage of the water-soluble contrast medium at gastroduodenogram) non operative management may be attempted. After initial non operative management, no improvement of conditions within 24 hours or rapid deterioration are indication to surgery.

Crisp E. Cases of perforation of the stomach with deductions therefrom relative to the character and treatment of that lesion. Lancet. 1843;2:639.
Gastro-duodenal perforation

Laparoscopic repair of perforated peptic ulcer is safe and effective in centers with experience. The p.o. outcome of laparoscopic approach does not significantly differ from that of open surgery, except for lower analgesic p.o. request. In all studies the patients had small ulcers (mean diameter 1 cm) and all patients received simple suture, mostly with omental patch, or suturless repair; No experience is reported with emergency laparoscopic resection or laparoscopic repair of large ulcers.

Sanabria A, Villegas MI, Morales Uribe CH. Laparoscopic repair for perforated peptic ulcer disease. Cochrane Database of Systematic Reviews 2010 (Mar), Issue 4), one meta-analysis

Appendicitis
Acute appendicitis

Acute appendicitis is the most common intra-abdominal condition requiring emergency surgery.
Uncomplicated appendicitis

Operative intervention for acute, nonperforated appendicitis performed as soon as is the gold standard.

Studies have demonstrated that antibiotics alone may be useful to treat patients with early, non-perforated appendicitis, even if there is a risk of recurrence.


Laparoscopic Vs open appendectomy

Both open and laparoscopic approaches to appendectomy are appropriate.
Use of either approach should be decided by the surgeon's expertise. The laparoscopic approach is useful for obese patients, elderly patients and patients whose diagnosis is uncertain, especially women of childbearing age.

Appendicular abscess
Appendicular abscess

Although appendix abscess occurs in 10% of patients with acute appendicitis, its surgical management is surrounded with controversy.

The traditional management of appendiceal mass has been initial conservative treatment followed by interval appendectomy. Recently interval appendectomy has been questioned, and there is much controversy whether interval appendectomy is appropriate for adults with an appendicular abscess.

Appendicular peritonitis

Patients with perforated appendicitis should undergo urgent intervention to provide adequate source control
Diverticulitis
Diverticulitis

Nonoperative treatment, with bowel rest and antibiotics, is suggested in patients with uncomplicated diverticulitis. The decision to recommend elective sigmoid colectomy after recovery from acute diverticulitis should be made on a case-by-case basis.

Diverticular abscess
Diverticular abscess

Intravenous antibiotic treatment alone is usually the most appropriate treatment for patients with a small (<4 cm in diameter) diverticular abscess and image guided percutaneous drainage is for those with a large (>4 cm in diameter) one.


Diverticular peritonitis

Urgent operation is required for patients with diffuse peritonitis or for those who fail non-operative management of acute diverticulitis

Cholecystitis
Laparoscopic cholecystectomy has been accepted as an effective treatment for acute cholecystitis


Timing of cholecystectomy

Early cholecystectomy: Surgery + antimicrobial prophylaxis

Delayed Cholecystectomy: Antimicrobial therapy + delayed surgery
Timing of cholecystectomy

Evidence suggests that early laparoscopic cholecystectomy reduces the total length of hospital stay and the risk of readmissions attributable to recurrent acute cholecystitis.


Cholecystostomy in elderly and critically ill patients

Some reports (case-series studies) have studied the effectiveness and safety of percutaneous transhepatic gallbladder drainage as the treatment of first choice for acute cholecystitis in elderly patients, particularly in those with comorbid conditions, and they indicate its usefulness.


Gallbladder perforation

Gallbladder perforation is an unusual initial presentation of gallbladder disease. Early diagnosis of gallbladder perforation and immediate surgical intervention are of prime importance in decreasing morbidity and mortality associated with this condition.

It is rarely diagnosed preoperatively. Late operative intervention is associated with increased morbidity, mortality, number of ICU admissions, and long postoperative hospital stays. An early cholecystectomy strategy may lead to improved outcomes but may be difficult to implement and may not be cost-effective.

Biliary peritonitis
Biliary peritonitis

Lavage
Biliary peritonitis

Cholecystectomy
Biliary peritonitis

Debridement
Biliary peritonitis

Drainage
Cholangitis
Biliary drainage

Biliary drainage is a radical method to relieve cholestasis, a cause of acute cholangitis, and takes a central part in the treatment of acute cholangitis. Biliary drainage can be achieved by three different procedures:

• endoscopic,
• percutaneous transhepatic,
• open drainage
Biliary drainage

It has been reported that when no appropriate biliary drainage was available 20–30 years ago, the mortality of acute cholangitis with conservative treatment was extremely high. There has been no randomized controlled trial (RCT) comparing conservative treatment and biliary drainage. However, many patients with acute cholangitis cannot be saved by conservative treatment alone.


Post-operative peritonitis
Post-operative Infections

The most common cause of postoperative peritonitis is anastomotic failure/leak.
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
Early relaparotomy in post-operative peritonitis

Delaying relaparotomy for more than 24 h and presence of organ failure result in higher mortality in postoperative intra-abdominal infections.

Early relaparotomy for post-operative peritonitis

After relaparotomy for generalized postoperative peritonitis, a relaparotomy strategy may be indicated whenever source control is uncertain.


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
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.

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.
Inappropriate choice of initial antibiotic therapy in sIAI patients leads to more clinical failure resulting in a longer hospital stay and higher costs of hospitalization compared with appropriate initial antibiotic therapy.


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<thead>
<tr>
<th></th>
<th>Inappropriate</th>
<th>Appropriate</th>
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<tbody>
<tr>
<td>Mortality and antibiotic therapy</td>
<td>23%</td>
<td>14%</td>
<td>0.15</td>
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<tr>
<td>Morbidity and antibiotic therapy</td>
<td>44%</td>
<td>30%</td>
<td>0.04</td>
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</table>
Risk stratification

The definition of "risk" in intra-abdominal infections remains vague.

“High risk” is generally intended to describe patients with a high risk for treatment failure. Effective management of high risk patients requires the early use of appropriate, broad-spectrum empirical antimicrobial therapy.
**Risk factors**

**Infection risk factors**
- Hospital acquired infections
- Recent exposure to antibiotics

**Intrinsic risk factors**
- High severity of illness (APACHE II score >15)
- Advanced age
- Comorbidity and degree of organ dysfunction
- Low albumin level
- Poor nutritional status
- Immunodepression
- Presence of malignancy

**Management risk factors**
- Delay in the initial intervention (>24 h)
- Inability to achieve adequate source control
Risk stratification

The stratification of the patient’s risk is important to optimize the antibiotic treatment plan. The increased mortality associated with inappropriate empiric antibiotic therapy cannot be reversed by subsequent modifications. Therefore knowledge of patient’s risk is essential to begin treatment as soon as possible with the most appropriate regimen.
Antimicrobial resistance
MDRO = multi-drug resistant organisms

- MRSA
- VISA
- VRSA
- VRE
- ESBL (*Enterbacteriaceae*)
- KPC (*Klebsiella pneumoniae*)
- Metallo Beta Lactamases
  - *Pseudomonas aeruginosa*
  - *Acinetobacter baumannii*
  - *Stenotrophomonas maltophilia*
  - *Klebsiella spp.*
Impact of Antimicrobial Resistance

- Increased morbidity / mortality
- Increased cost

Edwards J, ICAAC, 2003
Short communication

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

Stephen P. Hawser\textsuperscript{a,}\textsuperscript{*}, Samuel K. Bouchillon\textsuperscript{b}, Daryl J. Hoban\textsuperscript{b}, Robert E. Bada\textsuperscript{b}

\textsuperscript{a} IHMA Europe Srl, 4 Route de la Corniche, 1066 Epatinges, Switzerland
\textsuperscript{b} International Health Management Associates, Inc., Schaumburg, IL, USA
SMART study (2005-2007)

The most frequently isolated organisms were *Escherichia coli*, *Klebsiella pneumoniae*, of which 18.0% of E. coli and 26.2% of K. pneumoniae were positive for extended-spectrum beta-lactamase (ESBL). Overall, resistance among GNB increased during 2005-2007 and resistance rates in 2007 were generally higher than data from previous years.

**SMART study (2005-2007)**

In vitro susceptibility rates of the ten most commonly isolated organisms from 251 SMART centres from 38 countries in 2005–2007.

<table>
<thead>
<tr>
<th>Organism</th>
<th>No. of isolates (% of total 19 703)</th>
<th>% susceptible a</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Escherichia coli</strong></td>
<td>9486 (48.1%)</td>
<td>96.0</td>
</tr>
<tr>
<td><strong>E. coli ESBL+</strong></td>
<td>1704 (8.6%, 18.0% b)</td>
<td>70.3</td>
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<tr>
<td><strong>Klebsiella pneumoniae</strong></td>
<td>2604 (13.2%)</td>
<td>81.6</td>
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<tr>
<td><strong>K. pneumoniae ESBL+</strong></td>
<td>683 (3.5%, 26.2% b)</td>
<td>6.0</td>
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<tr>
<td><strong>Pseudomonas aeruginosa</strong></td>
<td>1745 (8.9%)</td>
<td>86.5</td>
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<tr>
<td><strong>Enterobacter cloacae</strong></td>
<td>1107 (5.9%)</td>
<td>84.4</td>
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<tr>
<td><strong>Proteus mirabilis</strong></td>
<td>703 (3.6%)</td>
<td>90.9</td>
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<tr>
<td><strong>Klebsiella oxytoca</strong></td>
<td>588 (3.0%)</td>
<td>82.8</td>
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<tr>
<td><strong>K. oxytoca ESBL+</strong></td>
<td>64 (0.4%, 14.2% b)</td>
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<tr>
<td><strong>Citrobacter freundii</strong></td>
<td>562 (2.9%)</td>
<td>62.6</td>
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<tr>
<td><strong>Enterobacter aerogenes</strong></td>
<td>358 (1.8%)</td>
<td>86.6</td>
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<tr>
<td><strong>Moraxella morganti</strong></td>
<td>344 (1.8%)</td>
<td>74.1</td>
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<td><strong>Serratia marcescens</strong></td>
<td>215 (1.1%)</td>
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<thead>
<tr>
<th>AMK</th>
<th>CPE</th>
<th>FOX</th>
<th>CAZ</th>
<th>CRO</th>
<th>CIP</th>
<th>LVX</th>
<th>Tzp</th>
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</table>

AMK, amikacin; CPE, cefoperazone; FOX, ceftazidime; CAZ, ceftazidime; CRO, ceftriaxone; CIP, ciprofloxacin; LVX, levofloxacin; Tzp, piperacillin/tazobactam; EPM, ertapenem; IPM, imipenem; ESBL+, extended spectrum β-lactamase producing isolates.

a Drug susceptibility breakpoints were as follows: AMK, ≤16 µg/mL; CPE, ≤8 µg/mL; FOX, ≤8 µg/mL; CAZ, ≤8 µg/mL; CRO, ≤8 µg/mL; CIP, ≤1 µg/mL; LVX, ≤2 µg/mL; Tzp, ≤16 µg/mL (Pseudomonas ≤64 µg/mL); EPM, ≤2 µg/mL; IPM, ≤4 µg/mL. [5]. Grey shading indicates susceptibilities that were ≥90%; NA, no breakpoint defined by the Clinical and Laboratory Standards Institute.

b Percent values for ESBL+ isolates are described as % of grand total of isolates followed by % of corresponding species.

Data from SMART (Study for Monitoring Antimicrobial Resistance Trends) in the period 2005 to 2007 no antimicrobial agent exhibited susceptibility of more than 90% against *Pseudomonas*. The most active agents were amikacin and piperacillin/tazobactam to which 86.5% of Pseudomonas were susceptible.
Incidence and Antimicrobial Susceptibility of *Escherichia coli* and *Klebsiella pneumoniae* with Extended-Spectrum β-Lactamases in Community- and Hospital-Associated Intra-Abdominal Infections in Europe: Results of the 2008 Study for Monitoring Antimicrobial Resistance Trends (SMART)"}

Stephen P. Hawser,¹,* Samuel K. Bouchillon,² Daryl J. Hoban,² Robert E. Badal,² Rafael Cantón,³,⁴ and Fernando Baquero³,⁴

IHMA Europe Sàrl, 1066 Epalinges, Switzerland¹; International Health Management Associates, Inc., Schaumburg, Illinois 60173-3817; Servicio de Microbiología, Hospital Universitario Ramón y Cajal and CIBER en Epidemiología y Salud Pública (CIBERESP), Madrid, Spain³; and Instituto Ramón y Cajal de Investigación Sanitaria (IRYCIS), Madrid, Spain⁴

Received 23 February 2010/Returned for modification 26 March 2010/Accepted 20 April 2010
From 2002 to 2008, there was a significant increase in extended-spectrum beta-lactamase (ESBL)-positive *Escherichia coli* isolates in European intra-abdominal infections, from 4.3% in 2002 to 11.8% in 2008 ($P < 0.001$), but not for ESBL-positive *Klebsiella pneumoniae* isolates (16.4% to 17.9% [$P > 0.05$]).

Hospital-associated isolates were more common than community-associated isolates, at 14.0% versus 6.5%, respectively, for *E. coli* ($P < 0.001$) and 20.9% versus 5.3%, respectively, for *K. pneumoniae* ($P < 0.01$). Carbapenems were consistently the most active drugs tested.

Antimicrobial regimen

- Source
- Patient’s clinical condition
- Risk factors for specific microorganism and/or resistance patterns
Community-acquired extra-biliary IAIs
Community acquired extrabiliary IAI
No critically ill patient
Absence of risk factors for ESBL

<table>
<thead>
<tr>
<th>AMOXICILLIN/CLAVALANATE</th>
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<tbody>
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<td>Daily schedule: 2.2 g every 6 hours (Infusion time 2 hours)</td>
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</table>

Or (Allergy to beta-lactams)

<table>
<thead>
<tr>
<th>CIPROFLOXACIN + METRONIDAZOLE</th>
</tr>
</thead>
<tbody>
<tr>
<td>Daily schedule: 400 mg every 8 hours (Infusion time 30 min)</td>
</tr>
<tr>
<td>Daily schedule: 500 mg every 6 hours (Infusion time 1 hour)</td>
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</tbody>
</table>

Community acquired extrabiliary IAI

No critically ill patient

*Presence of risk factors for ESBL*

<table>
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<th>ERTAPENEM</th>
<th>OR</th>
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<tbody>
<tr>
<td>Daily schedule: 1 g every 24 hours (Infusion time 2 hours)</td>
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<table>
<thead>
<tr>
<th>TIGECYCLINE</th>
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<tbody>
<tr>
<td>Daily schedule: 100 mg LD then 50 mg every 24 hours (Infusion time 2 hours)</td>
<td></td>
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</table>

Community acquired extrabiliary IAI
Critically ill patient

*Absence of risk factors for ESBL*

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**PIPERACILLIN/TAZOBACTAM**
Daily schedule: 16 g by continuous infusion or
4 g every 6 hours (infusion time 4 hours)

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Community acquired extrabiliary IAI
Critically ill patient
*Presence of risk factors for ESBL*

<table>
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<tbody>
<tr>
<td>Daily schedule: 500 mg every 6 hours (Infusion time 6 hours)</td>
</tr>
<tr>
<td>OR</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th><strong>IMIPENEM</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>Daily schedule: 500 mg every 4 hours (Infusion time 3 hours) (Infusion time 2 hours)</td>
</tr>
<tr>
<td>+/-</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th><strong>FLUCONAZOLE</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>Daily schedule: 600 mg LD then 400 mg every 24 hours (Infusion time 2 hours)</td>
</tr>
</tbody>
</table>

Biliary IAIs
Community acquired biliary IAI
No critically ill patient
Absence of risk factors for ESBL

<table>
<thead>
<tr>
<th>AMOXICILLIN/CLAVULANATE</th>
</tr>
</thead>
<tbody>
<tr>
<td>Daily schedule: 2.2 g every 6 hours (Infusion time 2 hours)</td>
</tr>
</tbody>
</table>

OR (Allergy to beta-lactams)

<table>
<thead>
<tr>
<th>CIPROFLOXACIN +/- METRONIDAZOLE</th>
</tr>
</thead>
<tbody>
<tr>
<td>Daily schedule: 400 mg every 8 hours (Infusion time 30 min)</td>
</tr>
<tr>
<td>Daily schedule: 500 mg every 6 hours (Infusion time 1 hour)</td>
</tr>
</tbody>
</table>

Community acquired biliary IAI
No critically ill patient
*Presence of risk factors for ESBL*

<table>
<thead>
<tr>
<th><strong>TIGECYCLINE</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>Daily schedula: 100 mg LD then 50 mg every 12 hours (Infusion time 2 hours)</td>
</tr>
</tbody>
</table>

Community acquired biliary IAI
Critically ill patient
*Absence of risk factors for ESBL*

<table>
<thead>
<tr>
<th>PIPERACILLIN/TAZOBACTAM</th>
</tr>
</thead>
<tbody>
<tr>
<td>Daily schedule: 16 g by continuous infusion or 4 g every 6 hours (Infusion time 4 hours)</td>
</tr>
</tbody>
</table>

Community acquired biliary IAI
Critically ill patient
*Presence of risk factors for ESBL*

<table>
<thead>
<tr>
<th><strong>PIPERACILLIN</strong></th>
<th>Daily schedule: 16 g by continuous infusion or 4 g every 6 hours (Infusion time 4 hours)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>+</td>
</tr>
<tr>
<td><strong>TIGECYCLINE</strong></td>
<td>Daily schedule: 100 mg LD then 50 mg every 12 hours (Infusion time 2 hours)</td>
</tr>
<tr>
<td></td>
<td>+/-</td>
</tr>
<tr>
<td><strong>FLUCONAZOLE</strong></td>
<td>Daily schedule: 600 mg LD then 400 mg every 24 hours (Infusion time 2 hours)</td>
</tr>
</tbody>
</table>

Hospital-acquired extra-biliary IAIs
Hospital acquired extrabiliary IAI
No critically ill patient

<table>
<thead>
<tr>
<th><strong>PIPERACILLIN</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>Daily schedule: 16 g  by Continuous Infusion</td>
</tr>
<tr>
<td>Or</td>
</tr>
<tr>
<td>Daily schedule: 4 g  every 6 hours by Infusion Time: 4 hours</td>
</tr>
<tr>
<td>+</td>
</tr>
<tr>
<td><strong>TIGECYCLINE</strong></td>
</tr>
<tr>
<td>Daily schedule: 100 mg LD then 50 mg every 12 h by infusion Time: 2 hours</td>
</tr>
<tr>
<td>+</td>
</tr>
<tr>
<td><strong>FLUCONAZOLE</strong></td>
</tr>
<tr>
<td>Daily Schedula: 600 mg LD then 400 mg every 24 h by infusion time: 2 hours</td>
</tr>
</tbody>
</table>

Hospital acquired extrabiliary IAI
Critically ill patient

<table>
<thead>
<tr>
<th>Antibiotic</th>
<th>Daily Schedule</th>
<th>Infusion Time</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>MEROPENEM</strong></td>
<td>500 mg every 6 h by infusion</td>
<td>6 hours</td>
</tr>
<tr>
<td>or</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>IMIPENEM</strong></td>
<td>500 mg every 4 h by Infusion</td>
<td>3 hours</td>
</tr>
<tr>
<td>or</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>DORIPENEM</strong></td>
<td>500 mg every 8 h by Infusion</td>
<td>4 hours</td>
</tr>
<tr>
<td>+</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>FLUCONAZOLE</strong></td>
<td>600 mg LD then 400 mg every 24 h by infusion</td>
<td>2 hours</td>
</tr>
<tr>
<td>+</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>TEICOPLANIN</strong></td>
<td>LD 12 mg/kg/12h for 3 doses then 6 mg/kg every 12 h</td>
<td></td>
</tr>
<tr>
<td>(with TDM corrections – PD target 20-30 mg/L)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Daily schedule:</td>
<td>16 g by continuous infusion or</td>
<td></td>
</tr>
<tr>
<td>4 g every 6 hours (infusion time 4 hours)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Thank you

m.sartelli@virgilio.it