

Review

The diversity of definitions of multidrug-resistant (MDR) and pandrug-resistant (PDR) *Acinetobacter baumannii* and *Pseudomonas aeruginosa*

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Different definitions of the terms multidrug-resistant (MDR) and pandrug-resistant (PDR) *Acinetobacter baumannii* and *Pseudomonas aeruginosa* have been used in the biomedical literature. The authors searched for relevant studies indexed in the PubMed database (01/2000–09/2005) to systematically examine the various definitions of MDR and PDR for these bacteria. Initially 107 retrieved relevant studies were reviewed. Ninety-two studies were further analysed, 50 of which focused on *A. baumannii* and 42 on *P. aeruginosa*. A considerable diversity of definitions of the terms MDR and PDR *A. baumannii* and *P. aeruginosa* was found. Of note, the term PDR was inappropriately used in all five studies that used it. The review reveals that various definitions have been used for the terms MDR and PDR *A. baumannii* and *P. aeruginosa*, a fact that causes confusion to researchers and clinicians. The authors believe that at least a widely accepted definition for PDR *A. baumannii* and *P. aeruginosa* should be uniformly used worldwide.

Background

The medical community has been witnessing a growing epidemic of infections due to Gram-negative bacteria resistant to many classes of antibiotics in most countries of the world (Sharma *et al.*, 2005; Canton *et al.*, 2003; Hsueh *et al.*, 2002; Landman *et al.*, 2002). Several investigators have studied the various aspects of these infections including mechanisms and risk factors of development of resistance as well as the effectiveness and toxicity of various therapeutic options (Harbarth & Samore, 2005; Epstein *et al.*, 2004). In addition, the prevalence and epidemiology of bacteria resistant to antimicrobial agents have become the focus of numerous single-centre and multi-centre surveillance studies (Tambic *et al.*, 2002; Jones, 2003).

We observed that different definitions regarding antimicrobial resistance are used in publications dealing with infections caused by *Acinetobacter baumannii* or *Pseudomonas aeruginosa*. In particular the terms ‘multi-drug-resistant (MDR)’ and ‘pandrug-resistant (PDR)’ have been used to characterize isolates of *A. baumannii* or *P. aeruginosa* with a variety of genotypic and phenotypic characteristics. This is a noteworthy fact that causes considerable confusion among researchers and clinicians. Thus we sought to systematically examine the various definitions of MDR and PDR *A. baumannii* and *P. aeruginosa* used in the biomedical literature during recent years.

Literature search

We searched for relevant studies indexed in the PubMed database and published in the period 01/2000–09/2005. We searched for articles that had the words ‘multidrug’, ‘multi-drug’, ‘MDR’, ‘multiresistance’, ‘multi-resistance’, ‘multiresistant’, ‘multi-resistant’, ‘pandrug’, ‘pan-drug’ or ‘PDR’ and ‘*Acinetobacter baumannii*’ or ‘*Pseudomonas aeruginosa*’ in their title.

Our search was limited to studies that were performed in humans, were written in English, and had available abstracts in PubMed, by making use of the respective ‘Limits’ functions of the PubMed search engine. The title and the abstract of studies that were retrieved from the initial search were examined for relevance. Then, the full-published papers of the relevant studies were reviewed to extract the definitions of MDR or PDR *A. baumannii* or *P. aeruginosa* used in the papers. We excluded from further analysis studies that were written by the same first author when the same definition for MDR or PDR was used.

Reviewed publications

We reviewed the title and the abstract of 107 initially retrieved studies, out of which 53 studies reported results for *A. baumannii* and 54 for *P. aeruginosa* isolates. Based on our inclusion criteria we identified 50 (Abbo *et al.*, 2005; Alarcon *et al.*, 2001; Appleman *et al.*, 2000; Blahova *et al.*, 2001; Bou *et al.*, 2000; Cawley *et al.*, 2002; Corbella *et al.*, 2000; El Shafie

et al., 2004; Gales *et al.*, 2001; Garnacho-Montero *et al.*, 2003; Giacometti *et al.*, 2000; Giamarellos-Bourboulis *et al.*, 2001; Gorman *et al.*, 2003; Higgins *et al.*, 2004; Hsueh *et al.*, 2002; Huys *et al.*, 2005; Jain & Danziger, 2004; Jiménez-Mejías *et al.*, 2002; Jones *et al.*, 2004; Joshi *et al.*, 2003; Kuo *et al.*, 2003, 2004; Landman *et al.*, 2002; Lee *et al.*, 2005; Levin *et al.*, 2001; Ling *et al.*, 2001; Maniatis *et al.*, 2003; Maragakis *et al.*, 2004; Maslow *et al.*, 2005; Michalopoulos *et al.*, 2005a; Mussi *et al.*, 2005; Oh *et al.*, 2002; Paavilainen *et al.*, 2001; Pimentel *et al.*, 2005; Podnos *et al.*, 2001; Roberts *et al.*, 2001; Ruiz *et al.*, 2003; Saugar *et al.*, 2002; Simor *et al.*, 2002; Smolyakov *et al.*, 2003; Tognim *et al.*, 2004; Turton *et al.*, 2004; Urban *et al.*, 2003; van Dessel *et al.*, 2004; Wang *et al.*, 2003; Wilson *et al.*, 2004; Wood *et al.*, 2003; Wu *et al.*, 2004; Yoon *et al.*, 2004; Zeana *et al.*, 2003) and 42 (Ahmed *et al.*, 2002; Belet *et al.*, 2004; Bratu *et al.*, 2005; Brito *et al.*, 2003; Bukholm *et al.*, 2002; Cao *et al.*, 2004; Davies *et al.*, 2003; Defez *et al.*, 2004; Domenig *et al.*, 2001; Douglas *et al.*, 2001; Dubois *et al.*, 2001; Erdem *et al.*, 2003; Fraser *et al.*, 2004; Giamarellos-Bourboulis *et al.*, 2000, 2005; Goossens, 2003; Hamer, 2000; Hsueh *et al.*, 2005; Jones *et al.*, 2001; Jones *et al.*, 2004; Jung *et al.*, 2004; Kocazeybek *et al.*, 2002; Landman *et al.*, 2002; Lang *et al.*, 2000; Lin *et al.*, 2003; Luzzaro *et al.*, 2001; Mirakhur *et al.*, 2003; Miranda *et al.*, 2001; Ohmagari *et al.*, 2005; Oie *et al.*, 2003; Ortega *et al.*, 2004; Pagani *et al.*, 2005; Paramythiotou *et al.*, 2004; Pellegrino *et al.*, 2002; Pirnay *et al.*, 2003; Pitten *et al.*, 2001; Rossolini & Mantengoli, 2005; Schelenz & French, 2000; Shahid *et al.*, 2003; Takeyama *et al.*, 2002; Tascini *et al.*, 2004; Thong *et al.*, 2004) studies that reported on MDR or PDR *A. baumannii* and *P. aeruginosa* isolates, respectively. Three studies that reported on MDR *Acinetobacter* were excluded because they referred to species other than *A. baumannii* (two studies) or had the same first author who used the same definition of MDR in another paper included in our systematic review (one study). Twelve studies that reported on MDR *Pseudomonas* were excluded because they described cellular mechanisms for multidrug resistance (five studies), had the same first author and used the same definition of MDR *P. aeruginosa* as another paper included in our review (four studies), referred to species other than *P. aeruginosa* (two studies), or reported on MDR cancer cells and not *P. aeruginosa* (one study).

MDR and PDR *A. baumannii*

In Table 1 we present the characteristics of the 50 studies that reported on MDR or PDR *A. baumannii* isolates. As shown, substantially different definitions were used in the identified studies. Four studies reported on PDR isolates (Kuo *et al.*, 2003, 2004; Lee *et al.*, 2005; Wang *et al.*, 2003). The term PDR was used inappropriately in all of these studies. Specifically, the term PDR was used despite the fact that the isolates were not tested for *in vitro* susceptibility to sulbactam in two studies (Lee *et al.*, 2005; Kuo *et al.*, 2003) and to polymyxins in three studies (Kuo *et al.*, 2003, 2004; Lee *et al.*, 2005). In one study the isolates were defined as

PDR although they were tested and found to be sensitive to colistin (Wang *et al.*, 2003).

Among the 46 other studies that examined the term MDR *A. baumannii*, there were nine studies that used the term MDR without including any definition or a sufficient description regarding the minimum resistance that an *A. baumannii* isolate needed to have in order to be considered as MDR (Landman *et al.*, 2002; Giacometti *et al.*, 2000; Higgins *et al.*, 2004; Joshi *et al.*, 2003; Ling *et al.*, 2001; Maniatis *et al.*, 2003; Maslow *et al.*, 2005; Paavilainen *et al.*, 2001; Jain & Danziger, 2004). In addition, the authors of four studies characterized as MDR *A. baumannii* isolates that were resistant to a single antibiotic or a single class of antibiotics. Specifically, in three studies (Corbella *et al.*, 2000; Gales *et al.*, 2001; Jones *et al.*, 2004), *A. baumannii* isolates were described as MDR if they exhibited resistance to carbapenems, and in one study if they were resistant to carbapenems, ceftipime or ceftazidime (Urban *et al.*, 2003).

All parts of a broad spectrum of the antimicrobial resistance profiles were used to define the term MDR *A. baumannii* in the reviewed studies. On one side of the spectrum, the minimum resistance that was required for an isolate to be described as MDR, which is resistance to representative antibiotics of at least two classes of antimicrobial agents, was used in one study (Huys *et al.*, 2005). The middle of the spectrum of the antimicrobial resistance profiles regarding the definition of the term MDR *A. baumannii* was used in a considerable proportion of papers (24 studies). Specifically, in these studies, *A. baumannii* isolates were defined as MDR if they were resistant to representative antibiotics of at least three different classes of antimicrobial agents. The most common antibiotic categories tested against *A. baumannii* in these studies were aminoglycosides, antipseudomonal penicillins, carbapenems, cephalosporins and quinolones; in addition, colistin, ampicillin/sulbactam and/or tetracyclines (doxycycline or minocycline) were agents that were tested occasionally. On the other side of the spectrum of the various definitions of MDR *A. baumannii*, there was a group of eight studies in which the term MDR described isolates that exhibited resistance to all but one of the tested agents, most commonly polymyxins [colistin in three studies (Garnacho-Montero *et al.*, 2003; Jiménez-Mejías *et al.*, 2002; Levin *et al.*, 2001) and polymyxin B in one (Podnos *et al.*, 2001)], doxycycline or minocycline (one study) (Wood *et al.*, 2003), imipenem (one study) (Gorman *et al.*, 2003), amikacin (one study) (El Shafie *et al.*, 2004), or any one of the tested antibiotic categories (one study) (Maragakis *et al.*, 2004).

MDR and PDR *P. aeruginosa*

In Table 2, we present the 42 identified studies that reported on MDR or PDR *P. aeruginosa* isolates. As shown in Table 2, the terms PDR and MDR are defined and used in various ways when referring to *P. aeruginosa* isolates also. The term PDR was used in one study and was also defined inappropriately despite the sensitivity of *P. aeruginosa* to colistin (Hsueh *et al.*, 2005).

Table 1. Definitions of multidrug-resistant (MDR) *Acinetobacter baumannii* in the reviewed studies

The definition refers to MDR unless it is specified as the definition for PDR.

Reference	Country	MDR or PDR definition/description in the study
Appleman <i>et al.</i> (2000)	USA	MDR <i>A. baumannii</i> isolates described in the study were resistant to imipenem, ceftazidime, efotaxime, gentamicin, tobramycin, piperacillin–tazobactam, ticarcillin–clavulanate, ciprofloxacin, ofloxacin and trimethoprim–sulfamethoxazole
Bou <i>et al.</i> (2000)	Spain	Described isolates resistant to semisynthetic penicillins, ceftazidime, cefepime, ceftiofime, aztreonam, gentamicin, netilmicin, amikacin, ciprofloxacin and carbapenems. Tobramycin, sulbactam and colistin showed good activity.
Corbella <i>et al.</i> (2000)	Spain	Described carbapenem-resistant isolates
Giacometti <i>et al.</i> (2000)	Italy	Not defined or specified
Alarcon <i>et al.</i> (2001)	Spain	Described a strain resistant to all tested antibiotics, including imipenem, doxycycline and colistin, and intermediate only to tobramycin
Blahova <i>et al.</i> (2001)	Slovak Republic	Described isolates resistant to kanamycin, ticarcillin, cephalothin, cefotaxime, ceftazidime and aztreonam and susceptible to carbapenems, sulbactam and ampicillin–sulbactam
Gales <i>et al.</i> (2001)	North, Central and South America (SENTRY study)	Described isolates resistant to imipenem (polymyxin 90 % sensitive when tested)
Giamarellos-Bourboulis <i>et al.</i> (2001)	Greece	Described isolates resistant to ampicillin–sulbactam, cefotaxime, ceftriaxone, ceftazidime, cefepime, amikacin and ciprofloxacin
Levin <i>et al.</i> (2001)	Brazil	Described isolates resistant to all commercially available antimicrobials except colistin
Ling <i>et al.</i> (2001)	Singapore	Not defined or specified
Paavilainen <i>et al.</i> (2001)	Finland	Not defined or specified
Podnos <i>et al.</i> (2001)	USA	Described isolates sensitive only to polymyxin B and resistant to amikacin, imipenem and sulbactam
Roberts <i>et al.</i> (2001)	New Zealand	Described a strain sensitive only to carbapenems, tobramycin and amikacin
Cawley <i>et al.</i> (2002)	USA	Described isolates resistant to piperacillin–tazobactam, tobramycin, levofloxacin, ceftazidime, aztreonam, imipenem–silastin and amikacin
Hsueh <i>et al.</i> (2002)	Taiwan	Described isolates resistant to ‘almost all commercially available antibiotics tested’ (i.e. ceftazidime, cefepime, ticarcillin–clavulanate, piperacillin–tazobactam, aztreonam, imipenem, meropenem, gentamicin, amikacin, ofloxacin and ciprofloxacin)
Jiménez-Mejías <i>et al.</i> (2002)	Spain	Described an isolate susceptible only to colistin
Landman <i>et al.</i> (2002)	USA	Not defined or specified. Overall >50 % of isolates were resistant to one or both carbapenems, 12 % were resistant to all commonly tested antibiotics, and approximately 65 % of isolates were susceptible to amikacin and sulbactam; 98 % isolates were susceptible to polymyxin B
Oh <i>et al.</i> (2002)	Korea	Defined as resistance to eight or more of the following antibiotics: ampicillin, carbenicillin, piperacillin, ticarcillin, cefotaxime, ceftiofime, ceftazidime, aztreonam, imipenem, amikacin, gentamicin, kanamycin, tobramycin, ciprofloxacin, norfloxacin, sulfamethoxazole and trimethoprim
Saugar <i>et al.</i> (2002)	Spain	Described an isolate resistant to ticarcillin, cefotaxime, imipenem, tobramycin, amikacin, ofloxacin and doxycycline, but sensitive to colistin
Simor <i>et al.</i> (2002)	Canada	Defined as resistance to penicillins, cephalosporins, piperacillin–tazobactam, trimethoprim–sulfamethoxazole, ciprofloxacin, gentamicin and tobramycin. All isolates were susceptible to imipenem and some to amikacin.
Garnacho-Montero <i>et al.</i> (2003)	Spain	Described isolates that were resistant to imipenem and sensitive only to colistin in one treatment arm, and at least carbapenem-sensitive in the other treatment arm
Gorman <i>et al.</i> (2003)	Canada	Described an isolate sensitive only to imipenem and intermediate to amikacin
Joshi <i>et al.</i> (2003)	India	Not defined or specified

Table 1. cont.

Reference	Country	MDR or PDR definition/description in the study
Kuo <i>et al.</i> (2003)	Taiwan	PDR was defined as resistance to all antibiotics commercially available (ceftazidime, ciprofloxacin, cefepime, aztreonam, ciprofloxacin, piperacillin–tazobactam, ticarcillin–clavulanate, ofloxacin, amikacin, imipenem and meropenem). Not tested for colistin or ampicillin–sulbactam.
Maniatis <i>et al.</i> (2003)	Greece	Not defined or specified. Most isolates were resistant to 8–9 out of the following 10: amikacin, ampicillin–sulbactam, aztreonam, ceftazidime, ciprofloxacin, gentamicin, netilmicin, piperacillin, ticarcillin–clavulanate and tobramycin. All were sensitive to imipenem.
Ruiz <i>et al.</i> (2003)	Spain	Described isolates resistant to at least amikacin, amoxycillin–clavulanic acid, ampicillin, ceftazidime and chloramphenicol
Smolyakov <i>et al.</i> (2003)	Israel	Described isolates resistant to all antibiotics tested routinely but susceptible only to ampicillin–sulbactam and colistin
Urban <i>et al.</i> (2003)	USA	Described isolates resistant to cefepime, ceftazidime or imipenem, or sensitive only to polymyxins and sulbactam
Wang <i>et al.</i> (2003)	Taiwan	PDR was defined as resistance to all currently available antimicrobials (including carbapenems), except colistin (polymyxin B)
Wood <i>et al.</i> (2003)	USA	Described isolates sensitive only to doxycycline or minocycline (colistin not tested)
Zeana <i>et al.</i> (2003)	USA	Defined as resistance to imipenem or meropenem plus amikacin or tobramycin plus a third-generation cephalosporin
El Shafie <i>et al.</i> (2004)	Qatar	Defined as susceptibility only to amikacin (resistant to ampicillin, third-generation cephalosporins, piperacillin–tazobactam, carbapenems, gentamicin and ciprofloxacin)
Higgins <i>et al.</i> (2004)	Germany	Not defined or specified
Jain & Danziger (2004)	USA	Not defined or specified
Jones <i>et al.</i> (2004)	USA	Described isolates resistant to a carbapenem (imipenem or meropenem)
Kuo <i>et al.</i> (2004)	Taiwan	PDR was defined as resistance to all antibiotics routinely tested (i.e. ampicillin–sulbactam, ceftazidime, piperacillin–tazobactam, cefepime, aztreonam, ciprofloxacin, trovafloxacin, moxifloxacin, garenoxacin, amikacin, imipenem and meropenem)
Maragakis <i>et al.</i> (2004)	USA	Defined as susceptibility to no more than one class of antimicrobial agents, excluding colistin
Tognim <i>et al.</i> (2004)	South America	Not defined or specified
Turton <i>et al.</i> (2004)	UK	Described isolates highly resistant to ampicillin, piperacillin, piperacillin–tazobactam, ceftazidime, cefotaxime, gentamicin and ciprofloxacin, and most isolates were carbapenem resistant. Amikacin sensitivity varied.
Van Dessel <i>et al.</i> (2004)	Belgium, France, Greece, Poland, Portugal, South Africa, Spain and Turkey	Described isolates resistant to at least five of the following antibiotics: sitafloxacin, ciprofloxacin, piperacillin–tazobactam, ceftriaxone, ceftazidime, imipenem, gentamicin, amikacin and trimethoprim–sulfamethoxazole
Wilson <i>et al.</i> (2004)	USA	Defined as resistance to all penicillins, all cephalosporins, ciprofloxacin, gentamicin and imipenem
Wu <i>et al.</i> (2004)	Taiwan	Described isolates highly resistant to ampicillin–sulbactam, carbenicillin, ceftazidime, cefoperazone, cefixime, chloramphenicol, gentamicin, ciprofloxacin, ceftriaxone, piperacillin and trimethoprim–sulfamethoxazole
Yoon <i>et al.</i> (2004)	USA	Described isolates resistant to all commonly used antibiotics, including imipenem (8/8 isolates) and colistin (1/8 isolates)
Abbo <i>et al.</i> (2005)	Israel	Defined as resistance to piperacillin–tazobactam, cefepime, ceftazidime, aztreonam, ciprofloxacin, gentamicin and tobramycin but could be susceptible to amikacin, ampicillin–sulbactam, imipenem, meropenem and minocycline
Huys <i>et al.</i> (2005)	Netherlands, UK, Czech Republic, France, Denmark and Brazil	Defined as resistance to at least two antibiotics of different classes including aminoglycosides, chloramphenicol, tetracyclines and/or erythromycin

Table 1. cont.

Reference	Country	MDR or PDR definition/description in the study
Lee <i>et al.</i> (2005)	Taiwan	PDR was defined as resistance to carbapenems, second- and third-generation cephalosporins, antipseudomonas penicillins, fluoroquinolones and aminoglycosides
Maslow <i>et al.</i> (2005)	USA	Not defined or specified. Described isolates with variable resistance to amikacin, ampicillin–sulbactam, ceftazidime, ciprofloxacin, gentamicin, imipenem–cilastatin and tobramycin.
Michalopoulos <i>et al.</i> (2005a)	Greece	Described isolates sensitive only to colistin (drugs tested not specified)
Mussi <i>et al.</i> (2005)	Argentina	Defined as simultaneous resistance to at least two β -lactams (including ampicillin–sulbactam, ceftazidime, cefotaxime, piperacillin and piperacillin–tazobactam), gentamicin or amikacin, ciprofloxacin and trimethoprim–sulfamethoxazole
Pimentel <i>et al.</i> (2005)	Australia	Defined as sensitivity only to tobramycin, amikacin and meropenem

There were 41 studies referring to *P. aeruginosa* in which the term MDR was used. There were seven studies that did not provide sufficient information on the minimum resistance that an isolate had to exhibit in order to be characterized as MDR (Landman *et al.*, 2002; Mirakhur *et al.*, 2003; Fraser *et al.*, 2004; Giamarellou-Bourboulis *et al.*, 2005; Hamer, 2000; Shahid *et al.*, 2003; Belet *et al.*, 2004). Also, in two studies (Jones *et al.*, 2004; Defez *et al.*, 2004) the term MDR was used inappropriately to describe isolates that exhibited resistance to a single antibiotic (Defez *et al.*, 2004) or a single class of antibiotics (Jones *et al.*, 2004).

The term MDR *P. aeruginosa* was used in the remaining 32 studies for isolates that had a diversity of antimicrobial susceptibility profiles, similarly to most of the studies that reported on MDR *A. baumannii*. Specifically, on one side of the spectrum of the antimicrobial resistance profiles the term MDR was used for isolates with the least resistant profile that can be appropriately characterized as MDR, which is resistance to at least two specific representatives of at least two classes of antibiotics (four studies) (Erdem *et al.*, 2003; Ortega *et al.*, 2004; Schelenz & French, 2000; Tascini *et al.*, 2004). In the great majority of the rest of the analysed articles (25 studies), the term MDR *P. aeruginosa* was used to report on isolates resistant to at least three drugs from a variety of antibiotic categories, mainly aminoglycosides, antipseudomonas penicillins, carbapenems, cephalosporins and quinolones. Finally, on the other extreme of the spectrum of the antimicrobial resistance profiles for the definition of MDR, isolates were described as MDR if they were resistant to all tested antibiotics (one study) (Giamarellou-Bourboulis *et al.*, 2000) or to all tested antibiotics except for colistin (two studies) (Dubois *et al.*, 2001; Thong *et al.*, 2004).

Evaluation of the reviewed data

The main finding of our systematic review is that the terms MDR and PDR for *A. baumannii* and *P. aeruginosa* are defined and/or used by researchers around the world in a

variety of ways. This variability may cause confusion, since there are considerable differences in the antibiotics tested *in vitro* in each of the presented studies. Specifically, the data presented in this systematic review show that investigators use different resistance profiles to various antimicrobial agents to define the term MDR or PDR *A. baumannii* or *P. aeruginosa*.

Although there have been a few attempts from some committees to establish rational and evidence-based definitions for MDR, it seems that these definitions were not widely accepted and used. Concerns may be raised about the validity and usefulness of some of the proposed definitions. For example, the definition by the French National Committee for Nosocomial Infections, which was used in the study by Defez *et al.* (2004), could be easily criticized since the finding of resistance to just one of three selected antibiotics (ticarcillin, ceftazidime and imipenem) sufficed to define an isolate as MDR. This definition contrasts with the meaning of the prefix multi (that in Latin means ‘many’) because the definition takes into account only resistance to β -lactam antibiotics. On the other hand, the definition by the American Cystic Fibrosis Foundation that was used in the study by Davies *et al.* (2003) regarding MDR *P. aeruginosa* isolates from cystic fibrosis patients was more inclusive and the term MDR was used in agreement with this definition in some relevant studies (Mirakhur *et al.*, 2003; Jones *et al.*, 2001; Lang *et al.*, 2000).

The confusion regarding the use of the term PDR is more profound than for the term MDR. This is because the prefix pan (that in Greek means ‘every’ or ‘to all’) should not be interpreted in more than one way. Thus it is rather confusing that some investigators use this term to describe isolates that are susceptible only to polymyxins (Wang *et al.*, 2003). Although such isolates exhibit resistance to many antibiotics, the existence of even one antibiotic with good activity against the microbes automatically excludes the isolates from being called PDR. In addition, an isolate should have a documented resistance to representative

Table 2. Definitions of multidrug-resistant (MDR) *Pseudomonas aeruginosa* in the reviewed studies

The definition refers to MDR unless it is specified as the definition for PDR.

Reference	Country	MDR or PDR definition/description in the study
Giamarellos-Bourboulis <i>et al.</i> (2000)	Greece	MDR for <i>P. aeruginosa</i> was defined as resistance to all potentially active antibiotics (third-generation cephalosporins, carbapenems, antipseudomonas penicillins, aminoglycosides, monobactams and quinolones). Isolates were not tested for colistin.
Hamer (2000)	USA	Not defined or specified
Lang <i>et al.</i> (2000)	USA	Defined as resistance to all antibiotics in two of the following three antibiotic classes: (1) β -lactams, including piperacillin, aztreonam and imipenem; (2) aminoglycosides, including amikacin, gentamicin and tobramycin; (3) fluoroquinolones and particularly ciprofloxacin
Schelenz & French (2000)	UK	Described isolates resistant to ceftazidime and azlocillin
Domenig <i>et al.</i> (2001)	Austria	Described an isolate susceptible only to meropenem and colistin
Douglas <i>et al.</i> (2001)	Australia	Described an isolate resistant to gentamicin, piperacillin and ciprofloxacin
Dubois <i>et al.</i> (2001)	France	Defined as resistance to all potentially active antibiotics (third- and fourth-generation cephalosporins, carbapenems, antipseudomonas penicillins, aminoglycosides, monobactams and quinolones) except colistin
Jones <i>et al.</i> (2001)	UK	Described isolates resistant to ceftazidime, piperacillin, aztreonam, imipenem, meropenem and ciprofloxacin
Luzzaro <i>et al.</i> (2001)	Italy	Described isolates resistant to piperacillin, broad-spectrum and fourth-generation cephalosporins, monobactams, aminoglycosides and fluoroquinolones
Miranda <i>et al.</i> (2001)	Mexico	Described isolates resistant to aminoglycosides (gentamicin, amikacin, netilmicin, isepamicin), third- (cefotaxime, ceftazidime, ceftizoxime) and fourth- (cefepime) generation cephalosporins, quinolones (norfloxacin, pefloxacin), carbapenems (imipenem, meropenem) and ticarcillin-clavulanate
Pitten <i>et al.</i> (2001)	Germany	Described isolates resistant to β -lactams, including carbapenems and aztreonam, to aminoglycosides and quinolones
Ahmed <i>et al.</i> (2002)	India	Described isolates that were resistant to at least five of the following antibiotics tested: carbenicillin, ciprofloxacin, gentamicin, norfloxacin, tetracycline and tobramycin
Bukholm <i>et al.</i> (2002)	Norway	Described isolates resistant to carbapenems, fluoroquinolones and azlocillin
Kocazeybek <i>et al.</i> (2002)	Turkey	Defined as resistance to three or more antipseudomonas agents
Landman <i>et al.</i> (2002)	USA	Not defined or specified. Overall >90% of isolates were susceptible to amikacin and 76% of isolates were susceptible to imipenem.
Pellegrino <i>et al.</i> (2002)	Brazil	Described isolates susceptible to at least polymyxin. One-third of isolates exhibited resistance to 8, 9 or 10 (all) of the other tested antibiotics
Brito <i>et al.</i> (2003)	Brazil	Described isolates resistant to ceftazidime and aminoglycosides
Davies <i>et al.</i> (2003)	UK	Used the definition of the American CF Foundation – resistance to all agents in at least two of the following groups of antibiotics: β -lactams, aminoglycosides and fluoroquinolones
Erdem <i>et al.</i> (2003)	Turkey	Described isolates resistant to at least two of the following: piperacillin-tazobactam, cefepime, meropenem and ciprofloxacin
Goossens (2003)	Europe	Defined as resistance to ceftazidime, ciprofloxacin and gentamicin
Lin <i>et al.</i> (2003)	Japan	Described an isolate resistant to piperacillin, ceftazidime, cefazolin, aztreonam, ciprofloxacin, gentamicin, imipenem and meropenem
Mirakhor <i>et al.</i> (2003)	UK	Not defined or specified. The strains were resistant to ceftazidime, tobramycin, meropenem, aztreonam, cotrimoxazole, imipenem, piperacillin, gentamicin and ciprofloxacin and sensitive only to colistin.
Oie <i>et al.</i> (2003)	Japan	Described isolates resistant to piperacillin, meropenem, ceftazidime, cefoperazone-sulbactam, aztreonam, amikacin and ciprofloxacin
Pirnay <i>et al.</i> (2003)	Belgium	Described isolates that were resistant to at least aztreonam, ceftriaxone, ciprofloxacin and imipenem
Shahid <i>et al.</i> (2003)	India	Not defined or specified. The majority (83.3%) of isolates were resistant to 7/11 or more antibiotics (five antibiotics were non-antipseudomonas). The most common resistance pattern was resistance to tetracycline, cotrimoxazole, amikacin, chloramphenicol, ampicillin, carbenicillin and clindamycin.

Table 2. cont.

Reference	Country	MDR or PDR definition/description in the study
Takeyama <i>et al.</i> (2002)	Japan	Described isolates resistant to ceftazidime, cefoperazone, cefepime, imipenem, piperacillin, aztreonam, amikacin, gentamicin, tobramycin, ciprofloxacin and sulfamethoxazole–trimethoprim
Belet <i>et al.</i> (2004)	Turkey	Not defined or specified. Most isolates were resistant to all aminoglycosides, third-generation cephalosporins and carbapenems, and susceptible only to ciprofloxacin.
Cao <i>et al.</i> (2004)	China	Described isolates resistant to ceftazidime, ciprofloxacin, piperacillin and imipenem
Defez <i>et al.</i> (2004)	France	Used the definition of the French National Technical Committee for Nosocomial Infections (1999) – resistance to at least one of the three following antibiotics: ticarcillin, ceftazidime and imipenem
Fraser <i>et al.</i> (2004)	USA	Not defined or specified
Jones <i>et al.</i> (2004)	USA	Described isolates resistant to a carbapenem (imipenem or meropenem)
Jung <i>et al.</i> (2004)	USA	Defined as resistance to at least three of the four drugs ceftazidime, imipenem, ciprofloxacin and tobramycin
Ortega <i>et al.</i> (2004)	Holland	Defined as resistance to at least two classes of antibiotics
Paramythiotou <i>et al.</i> (2004)	Greece	Defined as resistance to piperacillin, ceftazidime, imipenem and ciprofloxacin
Tascini <i>et al.</i> (2004)	Italy	Defined as resistance to two or more classes of antipseudomonal agents (ureidopenicillins, cephalosporins, carbapenems, quinolones and aminoglycosides)
Thong <i>et al.</i> (2004)	Japan	Described isolates resistant to all commercially available drugs except colistin
Bratu <i>et al.</i> (2005)	USA	Defined as resistance to imipenem as well as to at least two of the following antipseudomonal agents: fluoroquinolones, amikacin and other β -lactam agents (cefepime, ceftazidime, aztreonam or piperacillin–tazobactam)
Giamarellos-Bourboulis <i>et al.</i> (2005)	Greece	Not defined or specified
Hsueh <i>et al.</i> (2005)	Taiwan	PDR was defined as resistance to all cephalosporins, piperacillin–tazobactam, aztreonam, carbapenems, ciprofloxacin and aminoglycosides. All isolates had an MIC $\leq 4 \mu\text{g ml}^{-1}$ for colistin.
Ohmagari <i>et al.</i> (2005)	Japan	Defined as resistance to at least three of the four following groups: (1) imipenem or meropenem; (2) cefepime or ceftazidime; (3) piperacillin, piperacillin–tazobactam or ticarcillin–clavulanic acid; and (4) ciprofloxacin or levofloxacin
Pagani <i>et al.</i> (2005)	Italy	Described isolates resistant to carbapenems, ceftazidime, cefepime, gentamicin, tobramycin and fluoroquinolones
Rossolini & Mantengoli (2005)	Italy	Described the SENTRY surveillance program definition for MDR (resistance to piperacillin, ceftazidime, imipenem and gentamicin). Also described that, in recent years, MDR is defined as resistance to at least three of six drugs, including amikacin, gentamicin, ciprofloxacin, piperacillin, ceftazidime and imipenem.

antibiotics of specific classes of antimicrobial agents to be characterized as PDR. Thus a *P. aeruginosa* isolate should be defined as PDR only if it is resistant to agents from all seven available antipseudomonal classes of antimicrobial agents, i.e. antipseudomonal penicillins, cephalosporins, carbapenems, monobactams, quinolones, aminoglycosides and polymyxins (Falagas *et al.*, 2005). Similarly, with the current knowledge regarding antimicrobial resistance patterns worldwide, *A. baumannii* isolates should be called PDR if they are resistant to representative antibiotics from all of the above categories plus to sulbactam, to one tetracycline (minocycline or doxycycline) and tigecycline. Departure from these definitions of PDR *A. baumannii* and *P. aeruginosa* may cause confusion to clinicians because it suggests the lack of antimicrobial agents for the management of infections caused by these bacteria, while a potential salvage therapeutic option is available (Michalopoulos *et al.*, 2005b).

Limitations in the evaluation of the reviewed data

Our review is not without limitations. We restricted our search to papers published in English. However, the search and analysis of articles published in other languages would have probably revealed more confusion regarding the definition of the terms MDR and PDR *A. baumannii* and *P. aeruginosa*. Also, we limited our search to a recent period (01/2000–09/2005) because we appreciate that the definition of MDR may be evolving over time due to changes in the antimicrobial resistance patterns of bacteria. In addition, we did not extract data regarding the cut-off points used for the *in vitro* antimicrobial susceptibility testing, although such an effort would probably reveal more problems in the use of the various definitions of the terms MDR and PDR *A. baumannii* and *P. aeruginosa*. Furthermore, there is a need to mention that our review deals with resistance as

measured *in vitro*. The clinical response of a patient after the administration of an antimicrobial agent(s) does not always correlate with the laboratory findings. Finally, it should be mentioned that definitions related to antimicrobial resistance patterns of pathogens need continuous update; for example, the *in vitro* susceptibility of *Acinetobacter* isolates to tigecycline should or will need to be tested also.

Conclusion

Our review reveals that various definitions have been used for the term MDR and even more importantly for the term PDR *A. baumannii* or *P. aeruginosa* isolates in the relevant publications during recent years. We believe that the relevant professional societies and authorities responsible for the surveillance and prevention of bacterial resistance to antimicrobial agents should try to formulate definitions for both terms, in order to enhance the communication between researchers and clinicians around the world. We acknowledge that it is probably difficult to establish a definition for MDR *A. baumannii* and *P. aeruginosa* that would be widely accepted by investigators and clinicians worldwide. However, we believe that a widely accepted definition for PDR *A. baumannii* and *P. aeruginosa* should be uniformly used.

References

- Abbo, A., Navon-Venezia, S., Hammer-Muntz, O., Krichali, T., Siegman-Igra, Y. & Carmeli, Y. (2005). Multidrug-resistant *Acinetobacter baumannii*. *Emerg Infect Dis* **11**, 22–29.
- Ahmed, N., Bal, A., Khan, A. A. & 9 other authors (2002). Whole genome fingerprinting and genotyping of multiple drug resistant (MDR) isolates of *Pseudomonas aeruginosa* from endophthalmitis patients in India. *Infect Genet Evol* **1**, 237–242.
- Alarcon, T., Lopez-Hernandez, S., Andreu, D., Saugar, J. M., Rivas, L. & Lopez-Brea, M. (2001). In vitro activity of CA(1-8)M(1-18), a synthetic cecropin A-melittin hybrid peptide, against multiresistant *Acinetobacter baumannii* strains. *Rev Esp Quimioter* **14**, 184–190.
- Appleman, M. D., Belzberg, H., Citron, D. M., Heseltine, P. N., Yellin, A. E., Murray, J. & Berne, T. V. (2000). In vitro activities of nontraditional antimicrobials against multiresistant *Acinetobacter baumannii* strains isolated in an intensive care unit outbreak. *Antimicrob Agents Chemother* **44**, 1035–1040.
- Belet, N., Hacıomeroglu, P. & Kucukoduk, S. (2004). Ciprofloxacin treatment in newborns with multi-drug-resistant nosocomial *Pseudomonas* infections. *Biol Neonate* **85**, 263–268.
- Blahova, J., Kralikova, K., Krcmery, V., Sr, Kubonova, K., Vaculikova, A., Mikovicova, A., Klokocnikova, L., Hanzen, J. & Jezek, P. (2001). Transferable antibiotic resistance in multiresistant nosocomial *Acinetobacter baumannii* strains from seven clinics in the Slovak and Czech Republics. *J Chemother* **13**, 143–147.
- Bou, G., Cervero, G., Dominguez, M. A., Quereda, C. & Martinez-Beltran, J. (2000). Characterization of a nosocomial outbreak caused by a multiresistant *Acinetobacter baumannii* strain with a carbapenem-hydrolyzing enzyme: high-level carbapenem resistance in *A. baumannii* is not due solely to the presence of beta-lactamases. *J Clin Microbiol* **38**, 3299–3305.
- Bratu, S., Quale, J., Cebular, S., Heddurshetti, R. & Landman, D. (2005). Multidrug-resistant *Pseudomonas aeruginosa* in Brooklyn, New York: molecular epidemiology and in vitro activity of polymyxin B. *Eur J Clin Microbiol Infect Dis* **24**, 196–201.
- Brito, D. V., Oliveira, E. J., Matos, C., Abdallah, V. O. & Gontijo Filho, P. P. (2003). An outbreak of conjunctivitis caused by multiresistant *Pseudomonas aeruginosa* in a Brazilian newborn intensive care unit. *Braz J Infect Dis* **7**, 234–235.
- Bukholm, G., Tannaes, T., Kjelsberg, A. B. & Smith-Erichsen, N. (2002). An outbreak of multidrug-resistant *Pseudomonas aeruginosa* associated with increased risk of patient death in an intensive care unit. *Infect Control Hosp Epidemiol* **23**, 441–446.
- Canton, R., Coque, T. M. & Baquero, F. (2003). Multi-resistant Gram-negative bacilli: from epidemics to endemics. *Curr Opin Infect Dis* **16**, 315–325.
- Cao, B., Wang, H., Sun, H., Zhu, Y. & Chen, M. (2004). Risk factors and clinical outcomes of nosocomial multi-drug resistant *Pseudomonas aeruginosa* infections. *J Hosp Infect* **57**, 112–118.
- Cawley, M. J., Suh, C., Lee, S. & Ackerman, B. H. (2002). Nontraditional dosing of ampicillin-sulbactam for multidrug-resistant *Acinetobacter baumannii* meningitis. *Pharmacotherapy* **22**, 527–532.
- Corbella, X., Montero, A., Pujol, M., Dominguez, M. A., Ayats, J., Argerich, M. J., Garrigosa, F., Ariza, J. & Gudiol, F. (2000). Emergence and rapid spread of carbapenem resistance during a large and sustained hospital outbreak of multiresistant *Acinetobacter baumannii*. *J Clin Microbiol* **38**, 4086–4095.
- Davies, G., McShane, D., Davies, J. C. & Bush, A. (2003). Multiresistant *Pseudomonas aeruginosa* in a pediatric cystic fibrosis center: natural history and implications for segregation. *Pediatr Pulmonol* **35**, 253–256.
- Defez, C., Fabbro-Peray, P., Bouziges, N., Gouby, A., Mahamat, A., Daures, J. P. & Sotto, A. (2004). Risk factors for multidrug-resistant *Pseudomonas aeruginosa* nosocomial infection. *J Hosp Infect* **57**, 209–216.
- Domenig, C., Traunmuller, F., Kozek, S., Wisser, W., Klepetko, W., Steininger, R., Spiss, C. & Thalhammer, F. (2001). Continuous beta-lactam antibiotic therapy in a double-lung transplanted patient with a multidrug-resistant *Pseudomonas aeruginosa* infection. *Transplantation* **71**, 744–745.
- Douglas, M. W., Mulholland, K., Denyer, V. & Gottlieb, T. (2001). Multi-drug resistant *Pseudomonas aeruginosa* outbreak in a burns unit – an infection control study. *Burns* **27**, 131–135.
- Dubois, V., Arpin, C., Melon, M., Melon, B., Andre, C., Frigo, C. & Quentin, C. (2001). Nosocomial outbreak due to a multiresistant strain of *Pseudomonas aeruginosa* P12: efficacy of cefepime-amikacin therapy and analysis of beta-lactam resistance. *J Clin Microbiol* **39**, 2072–2078.
- El Shafie, S. S., Alishaq, M. & Leni, G. M. (2004). Investigation of an outbreak of multidrug-resistant *Acinetobacter baumannii* in trauma intensive care unit. *J Hosp Infect* **56**, 101–105.
- Epstein, B. J., Gums, J. G. & Drlica, K. (2004). The changing face of antibiotic prescribing: the mutant selection window. *Ann Pharmacother* **38**, 1675–1682.
- Erdem, I., Kucukercan, M. & Ceran, N. (2003). In vitro activity of combination therapy with cefepime, piperacillin-tazobactam, or meropenem with ciprofloxacin against multidrug-resistant *Pseudomonas aeruginosa* strains. *Chemotherapy* **49**, 294–297.
- Falagas, M. E., Bliiziotis, I. A., Kasiakou, S. K., Samonis, G., Athanassopoulou, P. & Michalopoulos, A. (2005). Outcome of infections due to pandrug-resistant (PDR) Gram-negative bacteria. *BMC Infect Dis* **5**, 24.
- Fraser, T. G., Reiner, S., Malczynski, M., Yarnold, P. R., Warren, J. & Noskin, G. A. (2004). Multidrug-resistant *Pseudomonas aeruginosa*

- cholangitis after endoscopic retrograde cholangiopancreatography: failure of routine endoscope cultures to prevent an outbreak. *Infect Control Hosp Epidemiol* 25, 856–859.
- Gales, A. C., Jones, R. N., Forward, K. R., Linares, J., Sader, H. S. & Verhoef, J. (2001).** Emerging importance of multidrug-resistant *Acinetobacter* species and *Stenotrophomonas maltophilia* as pathogens in seriously ill patients: geographic patterns, epidemiological features, and trends in the SENTRY Antimicrobial Surveillance Program (1997–1999). *Clin Infect Dis* 32, S104–S113.
- Garnacho-Montero, J., Ortiz-Leyba, C., Jimenez-Jimenez, F. J., Barrero-Almodovar, A. E., Garcia-Garmendia, J. L., Bernabeu-Wittell, M., Gallego-Lara, S. L. & Madrazo-Osuna, J. (2003).** Treatment of multidrug-resistant *Acinetobacter baumannii* ventilator-associated pneumonia (VAP) with intravenous colistin: a comparison with imipenem-susceptible VAP. *Clin Infect Dis* 36, 1111–1118.
- Giacometti, A., Cirioni, O., Del Prete, M. S., Barchiesi, F., Paggi, A. M., Petrelli, E. & Scalise, G. (2000).** Comparative activities of polycationic peptides and clinically used antimicrobial agents against multidrug-resistant nosocomial isolates of *Acinetobacter baumannii*. *J Antimicrob Chemother* 46, 807–810.
- Giamarellos-Bourboulis, E. J., Grecka, P., Dionyssiou-Asteriou, A. & Giamarellou, H. (2000).** Impact of n-6 polyunsaturated fatty acids on growth of multidrug-resistant *Pseudomonas aeruginosa*: interactions with amikacin and ceftazidime. *Antimicrob Agents Chemother* 44, 2187–2189.
- Giamarellos-Bourboulis, E. J., Xirouchaki, E. & Giamarellou, H. (2001).** Interactions of colistin and rifampin on multidrug-resistant *Acinetobacter baumannii*. *Diagn Microbiol Infect Dis* 40, 117–120.
- Giamarellos-Bourboulis, E. J., Kentepozidis, N., Antonopoulou, A., Plachouras, D., Tsaganos, T. & Giamarellou, H. (2005).** Postantibiotic effect of antimicrobial combinations on multidrug-resistant *Pseudomonas aeruginosa*. *Diagn Microbiol Infect Dis* 51, 113–117.
- Goossens, H. (2003).** Susceptibility of multi-drug-resistant *Pseudomonas aeruginosa* in intensive care units: results from the European MYSTIC study group. *Clin Microbiol Infect* 9, 980–983.
- Gorman, S. K., Zed, P. J., Dhingra, V. K. & Ronco, J. J. (2003).** Rapid imipenem/cilastatin desensitization for multidrug-resistant *Acinetobacter* pneumonia. *Ann Pharmacother* 37, 513–516.
- Hamer, D. H. (2000).** Treatment of nosocomial pneumonia and tracheobronchitis caused by multidrug-resistant *Pseudomonas aeruginosa* with aerosolized colistin. *Am J Respir Crit Care Med* 162, 328–330.
- Harbarth, S. & Samore, M. H. (2005).** Antimicrobial resistance determinants and future control. *Emerg Infect Dis* 11, 794–801.
- Higgins, P. G., Wisplinghoff, H., Stefanik, D. & Seifert, H. (2004).** In vitro activities of the beta-lactamase inhibitors clavulanic acid, sulbactam, and tazobactam alone or in combination with beta-lactams against epidemiologically characterized multidrug-resistant *Acinetobacter baumannii* strains. *Antimicrob Agents Chemother* 48, 1586–1592.
- Hsueh, P. R., Liu, C. Y. & Luh, K. T. (2002).** Current status of antimicrobial resistance in Taiwan. *Emerg Infect Dis* 8, 132–137.
- Hsueh, P. R., Tseng, S. P., Teng, L. J. & Ho, S. W. (2005).** Pan-drug-resistant *Pseudomonas aeruginosa* causing nosocomial infection at a university hospital in Taiwan. *Clin Microbiol Infect* 11, 670–673.
- Huys, G., Cnockaert, M., Vanechoutte, M., Woodford, N., Nemeč, A., Dijkshoorn, L. & Swings, J. (2005).** Distribution of tetracycline resistance genes in genotypically related and unrelated multiresistant *Acinetobacter baumannii* strains from different European hospitals. *Res Microbiol* 156, 348–355.
- Jain, R. & Danziger, L. H. (2004).** Multidrug-resistant *Acinetobacter* infections: an emerging challenge to clinicians. *Ann Pharmacother* 38, 1449–1459.
- Jiménez-Mejías, M. E., Pichardo-Guerrero, C., Márquez-Rivas, F. J., Martín-Lozano, D., Prados, T. & Pachón, J. (2002).** Cerebrospinal fluid penetration and pharmacokinetic/pharmacodynamic parameters of intravenously administered colistin in a case of multidrug-resistant *Acinetobacter baumannii* meningitis. *Eur J Clin Microbiol Infect Dis* 21, 212–214.
- Jones, A. M., Govan, J. R., Doherty, C. J., Dodd, M. E., Isalska, B. J., Stanbridge, T. N. & Webb, A. K. (2001).** Spread of a multiresistant strain of *Pseudomonas aeruginosa* in an adult cystic fibrosis clinic. *Lancet* 358, 557–558.
- Jones, R. N. (2003).** Global epidemiology of antimicrobial resistance among community-acquired and nosocomial pathogens: a five-year summary from the SENTRY Antimicrobial Surveillance Program (1997–2001). *Semin Respir Crit Care Med* 24, 121–134.
- Jones, R. N., Deshpande, L., Fritsche, T. R. & Sader, H. S. (2004).** Determination of epidemic clonality among multidrug-resistant strains of *Acinetobacter* spp. and *Pseudomonas aeruginosa* in the MYSTIC Programme (USA, 1999–2003). *Diagn Microbiol Infect Dis* 49, 211–216.
- Joshi, S. G., Litake, G. M., Niphadkar, K. B. & Ghole, V. S. (2003).** Multidrug resistant *Acinetobacter baumannii* isolates from a teaching hospital. *J Infect Chemother* 9, 187–190.
- Jung, R., Fish, D. N., Obritsch, M. D. & MacLaren, R. (2004).** Surveillance of multi-drug resistant *Pseudomonas aeruginosa* in an urban tertiary-care teaching hospital. *J Hosp Infect* 57, 105–111.
- Kocazeybek, B., Arabaci, U., Erenturk, S. & Akdur, H. (2002).** Investigation of various antibiotic combinations using the E-Test method in multiresistant *Pseudomonas aeruginosa* strains. *Chemotherapy* 48, 31–35.
- Kuo, L. C., Yu, C. J., Lee, L. N., Wang, J. L., Wang, H. C., Hsueh, P. R. & Yang, P. C. (2003).** Clinical features of pandrug-resistant *Acinetobacter baumannii* bacteremia at a university hospital in Taiwan. *J Formos Med Assoc* 102, 601–606.
- Kuo, L. C., Teng, L. J., Yu, C. J., Ho, S. W. & Hsueh, P. R. (2004).** Dissemination of a clone of unusual phenotype of pandrug-resistant *Acinetobacter baumannii* at a university hospital in Taiwan. *J Clin Microbiol* 42, 1759–1763.
- Landman, D., Quale, J. M., Mayorga, D., Adedeji, A., Vangala, K., Ravishankar, J., Flores, C. & Brooks, S. (2002).** Citywide clonal outbreak of multiresistant *Acinetobacter baumannii* and *Pseudomonas aeruginosa* in Brooklyn, NY: the preantibiotic era has returned. *Arch Intern Med* 162, 1515–1520.
- Lang, B. J., Aaron, S. D., Ferris, W., Hebert, P. C. & MacDonald, N. E. (2000).** Multiple combination bactericidal antibiotic testing for patients with cystic fibrosis infected with multiresistant strains of *Pseudomonas aeruginosa*. *Am J Respir Crit Care Med* 162, 2241–2245.
- Lee, C. M., Lim, H. K., Liu, C. P. & Tseng, H. K. (2005).** Treatment of pandrug resistant *Acinetobacter baumannii*. *Scand J Infect Dis* 37, 195–199.
- Levin, A. S., Gobara, S., Mendes, C. M., Cursino, M. R. & Sinto, S. (2001).** Environmental contamination by multidrug-resistant *Acinetobacter baumannii* in an intensive care unit. *Infect Control Hosp Epidemiol* 22, 717–720.
- Lin, Y. W., Adachi, S., Watanabe, K., Umeda, K. & Nakahata, T. (2003).** Serial granulocyte transfusions as a treatment for sepsis due to multidrug-resistant *Pseudomonas aeruginosa* in a neutropenic patient. *J Clin Microbiol* 41, 4892–4893.
- Ling, M. L., Ang, A., Wee, M. & Wang, G. C. (2001).** A nosocomial outbreak of multiresistant *Acinetobacter baumannii* originating from an intensive care unit. *Infect Control Hosp Epidemiol* 22, 48–49.

- Luzzaro, F., Mantengoli, E., Perilli, M., Lombardi, G., Orlandi, V., Orsatti, A., Amicosante, G., Rossolini, G. M. & Toniolo, A. (2001). Dynamics of a nosocomial outbreak of multidrug-resistant *Pseudomonas aeruginosa* producing the PER-1 extended-spectrum beta-lactamase. *J Clin Microbiol* **39**, 1865–1870.
- Maniatis, A. N., Pournaras, S., Orkopoulou, S., Tassios, P. T. & Legakis, N. J. (2003). Multiresistant *Acinetobacter baumannii* isolates in intensive care units in Greece. *Clin Microbiol Infect* **9**, 547–553.
- Maragakis, L. L., Cosgrove, S. E., Song, X. & 7 other authors (2004). An outbreak of multidrug-resistant *Acinetobacter baumannii* associated with pulsatile lavage wound treatment. *JAMA* **292**, 3006–3011.
- Maslow, J. N., Glaze, T., Adams, P. & Lataillade, M. (2005). Concurrent outbreak of multidrug-resistant and susceptible sub-clones of *Acinetobacter baumannii* affecting different wards of a single hospital. *Infect Control Hosp Epidemiol* **26**, 69–75.
- Michalopoulos, A., Kasiakou, S. K., Rosmarakis, E. S. & Falagas, M. E. (2005a). Cure of multidrug-resistant *Acinetobacter baumannii* bacteraemia with continuous intravenous infusion of colistin. *Scand J Infect Dis* **37**, 142–145.
- Michalopoulos, A. S., Tsiodras, S., Rellos, K., Mentzelopoulos, S. & Falagas, M. E. (2005b). Colistin treatment in patients with ICU-acquired infections caused by multiresistant Gram-negative bacteria: the renaissance of an old antibiotic. *Clin Microbiol Infect* **11**, 115–121.
- Mirakhor, A., Gallagher, M. J., Ledson, M. J., Hart, C. A. & Walshaw, M. J. (2003). Fosfomycin therapy for multiresistant *Pseudomonas aeruginosa* in cystic fibrosis. *J Cyst Fibros* **2**, 19–24.
- Miranda, G., Leanos, B., Marquez, L., Valenzuela, A., Silva, J., Carrillo, B., Munoz, O. & Solorzano, F. (2001). Molecular epidemiology of a multiresistant *Pseudomonas aeruginosa* outbreak in a paediatric intensive care unit. *Scand J Infect Dis* **33**, 738–743.
- Mussi, M. A., Limansky, A. S. & Viale, A. M. (2005). Acquisition of resistance to carbapenems in multidrug-resistant clinical strains of *Acinetobacter baumannii*: natural insertional inactivation of a gene encoding a member of a novel family of beta-barrel outer membrane proteins. *Antimicrob Agents Chemother* **49**, 1432–1440.
- Oh, J. Y., Kim, K. S., Jeong, Y. W., Cho, J. W., Park, J. C. & Lee, J. C. (2002). Epidemiological typing and prevalence of integrons in multiresistant *Acinetobacter* strains. *APMIS* **110**, 247–252.
- Ohmagari, N., Hanna, H., Graviss, L. & 8 other authors (2005). Risk factors for infections with multidrug-resistant *Pseudomonas aeruginosa* in patients with cancer. *Cancer* **104**, 205–212.
- Oie, S., Uematsu, T., Sawa, A., Mizuno, H., Tomita, M., Ishida, S., Okano, Y. & Kamiya, A. (2003). In vitro effects of combinations of antipseudomonal agents against seven strains of multidrug-resistant *Pseudomonas aeruginosa*. *J Antimicrob Chemother* **52**, 911–914.
- Ortega, B., Groeneveld, A. B. & Schultsz, C. (2004). Endemic multidrug-resistant *Pseudomonas aeruginosa* in critically ill patients. *Infect Control Hosp Epidemiol* **25**, 825–831.
- Paavilainen, T., Alanen, M., Makela, M., Routamaa, M., Jarvinen, H., Huovinen, P. & Kotilainen, P. (2001). Infrequent isolation of multiresistant *Acinetobacter baumannii* from the staff tending a colonized patient with severe burns. *Infect Control Hosp Epidemiol* **22**, 388–391.
- Pagani, L., Colinson, C., Migliavacca, R., Labonia, M., Docquier, J. D., Nucleo, E., Spalla, M., Li Bergoli, M. & Rossolini, G. M. (2005). Nosocomial outbreak caused by multidrug-resistant *Pseudomonas aeruginosa* producing IMP-13 metallo-beta-lactamase. *J Clin Microbiol* **43**, 3824–3828.
- Paramythiotou, E., Lucet, J. C., Timsit, J. F. & 7 other authors (2004). Acquisition of multidrug-resistant *Pseudomonas aeruginosa* in patients in intensive care units: role of antibiotics with antipseudomonal activity. *Clin Infect Dis* **38**, 670–677.
- Pellegrino, F. L., Teixeira, L. M., Carvalho, Md. Mda. G. & 8 other authors (2002). Occurrence of a multidrug-resistant *Pseudomonas aeruginosa* clone in different hospitals in Rio de Janeiro, Brazil. *J Clin Microbiol* **40**, 2420–2424.
- Pimentel, J. D., Low, J., Styles, K., Harris, O. C., Hughes, A. & Athan, E. (2005). Control of an outbreak of multi-drug-resistant *Acinetobacter baumannii* in an intensive care unit and a surgical ward. *J Hosp Infect* **59**, 249–253.
- Pirnay, J. P., De Vos, D., Cochez, C. & 7 other authors (2003). Molecular epidemiology of *Pseudomonas aeruginosa* colonization in a burn unit: persistence of a multidrug-resistant clone and a silver sulfadiazine-resistant clone. *J Clin Microbiol* **41**, 1192–1202.
- Pitten, F. A., Panzig, B., Schroder, G., Tietze, K. & Kramer, A. (2001). Transmission of a multiresistant *Pseudomonas aeruginosa* strain at a German University Hospital. *J Hosp Infect* **47**, 125–130.
- Podnos, Y. D., Cinat, M. E., Wilson, S. E., Cooke, J., Gornick, W. & Thrupp, L. D. (2001). Eradication of multi-drug resistant *Acinetobacter* from an intensive care unit. *Surg Infect (Larchmt)* **2**, 297–301.
- Roberts, S. A., Findlay, R. & Lang, S. D. (2001). Investigation of an outbreak of multi-drug resistant *Acinetobacter baumannii* in an intensive care burns unit. *J Hosp Infect* **48**, 228–232.
- Rossolini, G. M. & Mantengoli, E. (2005). Treatment and control of severe infections caused by multiresistant *Pseudomonas aeruginosa*. *Clin Microbiol Infect* **11**, 17–32.
- Ruiz, J., Navia, M. M., Casals, C., Sierra, J. M., Jimenez De Anta, M. T. & Vila, J. (2003). Integron-mediated antibiotic multiresistance in *Acinetobacter baumannii* clinical isolates from Spain. *Clin Microbiol Infect* **9**, 907–911.
- Saugar, J. M., Alarcon, T., Lopez-Hernandez, S., Lopez-Brea, M., Andreu, D. & Rivas, L. (2002). Activities of polymyxin B and cecropin A-melittin peptide CA(1-8)M(1-18) against a multi-resistant strain of *Acinetobacter baumannii*. *Antimicrob Agents Chemother* **46**, 875–878.
- Schelenz, S. & French, G. (2000). An outbreak of multidrug-resistant *Pseudomonas aeruginosa* infection associated with contamination of bronchoscopes and an endoscope washer-disinfector. *J Hosp Infect* **46**, 23–30.
- Shahid, M., Malik, A. & Sheeba (2003). Multidrug-resistant *Pseudomonas aeruginosa* strains harbouring R-plasmids and AmpC beta-lactamases isolated from hospitalised burn patients in a tertiary care hospital of North India. *FEMS Microbiol Lett* **228**, 181–186.
- Sharma, R., Sharma, C. L. & Kapoor, B. (2005). Antibacterial resistance: current problems and possible solutions. *Indian J Med Sci* **59**, 120–129.
- Simor, A. E., Lee, M., Vearncombe, M. & 7 other authors (2002). An outbreak due to multiresistant *Acinetobacter baumannii* in a burn unit: risk factors for acquisition and management. *Infect Control Hosp Epidemiol* **23**, 261–267.
- Smolyakov, R., Borer, A., Riesenber, K., Schlaeffer, F., Alkan, M., Porath, A., Rimar, D., Almog, Y. & Gilad, J. (2003). Nosocomial multi-drug resistant *Acinetobacter baumannii* bloodstream infection: risk factors and outcome with ampicillin-sulbactam treatment. *J Hosp Infect* **54**, 32–38.
- Takeyama, K., Kunishima, Y., Matsukawa, M., Takahashi, S., Hirose, T., Kobayashi, N., Kobayashi, I. & Tsukamoto, T. (2002). Multidrug-resistant *Pseudomonas aeruginosa* isolated from the urine of patients with urinary tract infection. *J Infect Chemother* **8**, 59–63.
- Tambic, A. A., Tambic, T., Kalenic, S. & Jankovic, V. (2002). Surveillance for antimicrobial resistance in Croatia. *Emerg Infect Dis* **8**, 14–18.

- Tascini, C., Gemignani, G., Ferranti, S., Tagliaferri, E., Leonildi, A., Lucarini, A. & Menichetti, F. (2004).** Microbiological activity and clinical efficacy of a colistin and rifampin combination in multidrug-resistant *Pseudomonas aeruginosa* infections. *J Chemother* **16**, 282–287.
- Thong, K. L., Lai, K. S., Ganeswrie, R. & Puthuchear, S. D. (2004).** Pulsed-field gel electrophoresis of multidrug-resistant and -sensitive strains of *Pseudomonas aeruginosa* from a Malaysian hospital. *Jpn J Infect Dis* **57**, 206–209.
- Tognim, M. C., Andrade, S. S., Silbert, S., Gales, A. C., Jones, R. N. & Sader, H. S. (2004).** Resistance trends of *Acinetobacter* spp. in Latin America and characterization of international dissemination of multi-drug resistant strains: five-year report of the SENTRY Antimicrobial Surveillance Program. *Int J Infect Dis* **8**, 284–291.
- Turton, J. F., Kaufmann, M. E., Warner, M., Coelho, J., Dijkshoorn, L., van der Reijden, T. & Pitt, T. L. (2004).** A prevalent, multiresistant clone of *Acinetobacter baumannii* in Southeast England. *J Hosp Infect* **58**, 170–179.
- Urban, C., Segal-Maurer, S. & Rahal, J. J. (2003).** Considerations in control and treatment of nosocomial infections due to multidrug-resistant *Acinetobacter baumannii*. *Clin Infect Dis* **36**, 1268–1274.
- van Dessel, H., Dijkshoorn, L., van der Reijden, T., Bakker, N., Paauw, A., van den Broek, P., Verhoef, J. & Brisse, S. (2004).** Identification of a new geographically widespread multiresistant *Acinetobacter baumannii* clone from European hospitals. *Res Microbiol* **155**, 105–112.
- Wang, S. H., Sheng, W. H., Chang, Y. Y. & 7 other authors (2003).** Healthcare-associated outbreak due to pan-drug resistant *Acinetobacter baumannii* in a surgical intensive care unit. *J Hosp Infect* **53**, 97–102.
- Wilson, S. J., Knipe, C. J., Zieger, M. J., Gabehart, K. M., Goodman, J. E., Volk, H. M. & Sood, R. (2004).** Direct costs of multidrug-resistant *Acinetobacter baumannii* in the burn unit of a public teaching hospital. *Am J Infect Control* **32**, 342–344.
- Wood, G. C., Hanes, S. D., Boucher, B. A., Croce, M. A. & Fabian, T. C. (2003).** Tetracyclines for treating multidrug-resistant *Acinetobacter baumannii* ventilator-associated pneumonia. *Intensive Care Med* **29**, 2072–2076.
- Wu, T. L., Ma, L., Chang, J. C., Su, L. H., Chu, C., Leu, H. S. & Siu, L. K. (2004).** Variable resistance patterns of integron-associated multidrug-resistant *Acinetobacter baumannii* isolates in a surgical intensive care unit. *Microb Drug Resist* **10**, 292–299.
- Yoon, J., Urban, C., Terzian, C., Mariano, N. & Rahal, J. J. (2004).** In vitro double and triple synergistic activities of Polymyxin B, imipenem, and rifampin against multidrug-resistant *Acinetobacter baumannii*. *Antimicrob Agents Chemother* **48**, 753–757.
- Zeana, C., Larson, E., Sahni, J., Bayuga, S. J., Wu, F. & Della-Latta, P. (2003).** The epidemiology of multidrug-resistant *Acinetobacter baumannii*: does the community represent a reservoir? *Infect Control Hosp Epidemiol* **24**, 275–279.