Outbreaks of Infection in the ICU: What's up at the Beginning of the Twenty-First Century?

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12.1 Introduction

Two recent sets of publications were taken into consideration when preparing our analysis of infectious outbreaks in the intensive care unit (ICU). The first concerns the emergence of severe acute respiratory syndrome (SARS) and avian flu in 2003, and a spread across the world of a novel influenza caused by SwH1N1 in 2009. These viral infections had a major impact on intensive care and are described in Chap. 20. This chapter is dedicated to describing outbreaks caused by bacteria and fungi, with references to secondary infections associated with flu and SARS [1, 2]. The second publication concerns the "International Study of the Prevalence and Outcomes of Infection in Intensive Care Units" published in December 2009 [3]. Although this is a point-prevalence study, it provides information about the global epidemiology of Infection in ICUs. Unfortunately, it could not give insight into outbreaks of infection in ICUs, so we searched for specific publications describing such outbreaks.

In the second (2005) edition of this book, we analysed the usefulness of molecular techniques in selected outbreaks [4]. The majority of outbreaks occurred in the last decade of the twentieth century. However, reports were usually published several years later. A similar pattern was observed when we analysed outbreaks published in the first decade of the twenty-first century: the actual outbreaks occurred a few years earlier. Indeed, the above-mentioned point-prevalence study was conducted on 8 May 2007 but published in December 2009 [3]. Therefore, for accuracy, this analysis indicates when outbreaks actually happened and when they were subsequently published. *Acinetobacter* outbreaks were selected to illustrate

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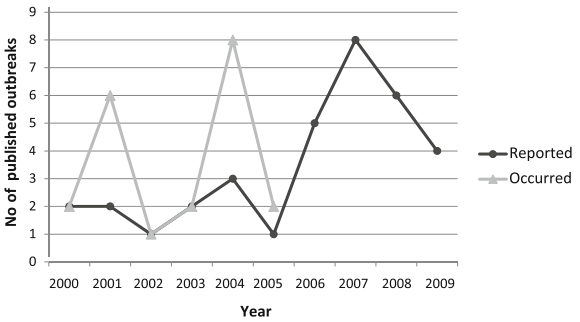

Fig. 12.1 *Acinetobacter* outbreaks published in 2000–2003 actually occurred in 1996–1999

this point (Fig. 12.1). In addition to the reported outbreaks, a number of publications considered many relevant aspects of infection and outbreaks in ICU. Some of these are included in this chapter. We analysed 97 publications, the majority of which met the definition of an outbreak in neonatal (NICU), paediatric (PICU) and adult (AICU) ICUs and reported since 2000. The main objective of this analysis was to find out whether there were any new features in the outbreaks of infection in ICU at the beginning of the new century, including those influenced by new viruses.

12.2 Methods of Analysis

12.2.1 Search Strategy

We searched MEDLINE for outbreaks published between January 2000 and September 2009. The search terms used were intensive care unit, adult ICU, paediatric ICU, neonatal ICU and outbreaks.

12.2.2 Framework of Analysis

We used the same framework as in the second edition of this book; however, outbreaks were not presented separately per ICU type but according to causative organisms, in the following order: methicillin-resistant *Staphylococcus aureus* (MRSA), vancomycin-resistant enterococci (VRE), aerobic Gram-negative bacilli (AGNB), *Pseudomonas* spp., *Acinetobacter* spp. and fungi, together with the selected features searched (Table 12.1). The number of analysed outbreaks is stated, but only selected outbreaks are shown and listed in the references.

Table 12.1 Outbreak microorganisms and features searched

Causative microorganisms	Features				
	Emerging threats	Methods used	Pathogenesis	Prevention and control	Endpoint
MRSA, VRE, AGNB, *Pseudomonas* spp., *Acinetobacter* spp., fungi	New antibiotic resistance, SARS, H1N1	Surveillance cultures, molecular techniques, statistics	Exogenous versus endogenous, endemic infection versus outbreak	Hygiene, anti-sepsis, SDD	Morbidity and mortality associated with outbreak

SDD selective digestive decontamination

12.3 MRSA Outbreaks

We retrieved reports on six outbreaks [5–10] published since 2000; five occurred in AICUs and one in an animal ICU. Reports of two outbreaks were published in 2002 and three in 2004, all occurring between 1997 and 2000. One report published in 2007 did not report the actual time of the outbreak. These outbreaks are summarised briefly according to their countries of origin. A paper from Italy published in 2002 reported a unique experience of controlling a MRSA outbreak of 8 months' duration in a medical/surgical AICU in 1998 using enterally administered vancomycin in mechanically ventilated patients [5]. Another report from Italy, published in 2004, described the identification of a variant of the "Rome clone" of MRSA responsible for an outbreak in a cardiac surgery ICU, which occurred in 1999 in a hospital in Rome. This strain had decreased sensitivity to vancomycin and was resistant to many antibiotics [6]. A study from Germany published in 2002 described the occurrence of MRSA in ICU in terms of endemic and epidemic infections followed from January 1997 to June 2000.This study involved 139 ICUs, 51 of which (37%) had MRSA infections. Outbreaks (three or more MRSA infections within 3 months) were registered in 13 ICUs, clusters (two MRSA infections within 3 months) in further 12 units and single events in 26 [7]. A publication from Spain showed that enterally administered vancomycin can control endemic MRSA in ICUs without promoting VRE. This study was carried out over a 49-month period from July 1996 to 2000 and published in 2004 [8]. In 2007, a report from Canada presented a recent outbreak of MRSA carriage in an animal ICU. This finding appears important, as the strain responsible for the animal outbreak was indistinguishable from a strain in humans commonly isolated in Canada and the USA. Infection control measures, including active surveillance of all animals in the ICU, were used to control the outbreak. As transmission of MRSA within the unit occurred without infections and did not persist for a prolonged period of time, staff screening was surprisingly not initiated [9]. A paper from China published in 2004 described an MRSA outbreak due to an increased

acquisition rate in ICU associated with an outbreak of SARS, which occurred in 2003. From 12 March to 31 May, only patients with SARS were admitted to the 22-bed unit. During this period, infection control precautions were upgraded, which included wearing gloves and gowns at all times. However, data suggested that MRSA transmission might be unexpectedly increased if gloves and gowns were worn all the time [10].

12.4 Enterococcal Outbreaks

There have been ten outbreaks in AICUs published since 2000: eight were caused by VRE, one was sensitive to vancomycin and one was sensitive to vancomycin but resistant to linezolid. We selected seven reports and summarised them according to the countries of origin and time of events and publishing.

A paper from Pakistan published in 2002 was the country's first experience with a vancomycin resistant *Enterococcus faecium* outbreak in the ICU and NICU. The outbreak occurred in 2002, lasted 1 month and all but one isolate was of a single clone [11]. All isolates were resistant to gentamicin, ampicillin and tetracycline but sensitive to chloramphenicol. Six patients were colonised and four infected, with positive blood cultures; two of each died before specific therapy could be started (50% mortality rate). In 2005, a report from Italy described an outbreak of VRE colonisation and infection in an ICU that lasted 16 months (2001–2002) [12]. Fifty-six patients were colonised by *E. faecium*, and *E. faecalis* was detected in only two cases. Because of the low pathogenicity of VRE, the authors questioned whether it was worthwhile to have a specific VRE surveillance programme. For the 2004 Lowbury lecture, Pearman reported the Australian experience with VRE, which he described as "from disaster to ongoing control". This was the first outbreak of VRE, which was caused by *E. faecium* in an ICU and hospital wards and lasted 5 months in 2001. A vigilant VRE control programme prevented the epidemic strain from becoming endemic in the hospital [13]. An outbreak due to glycopeptide-resistant enterococci (GRE) in an ICU with simultaneous circulation of two different clones was reported from France in 2008. The outbreak lasted several months in 2003 without infections, but the significant colonisation caused organisational problems in the ICU [14]. An outbreak of VRE in an ICU was reported from China in 2009. The outbreak was caused by *E. faecium* and lasted 11 months (2006–2007). A detailed molecular analysis showed that genetically unrelated isolates had transferred vancomycin resistance by conjugation [15]. A paper from Korea reported an outbreak of VRE in a neurological ICU. VRE was mainly isolated from urine specimens associated with the presence of a Foley catheter. Of 52 patients colonised with VRE, only two had active infection [16]. In 2009, a report from Spain presented an outbreak of linezolid-resistant *E. faecalis* in an ICU and reanimation unit [17]. This was the first report of a clonal outbreak of linezolid-resistant *E. faecalis* in Spain. The strain was sensitive to imipenem, vancomycin, teicoplanin and rifampicin. Most patients were exposed to linezolid within a year (2005–2006). The use of linezolid began in

2002. The increase in its use continued until 2005 when a mutant was identified by molecular analysis.

12.5 AGNB Outbreaks

Fourteen reports on outbreaks were retrieved since 2000. Eight were caused by *Klebsiella pneumoniae*, four by *Serratia marcescens*, one by *Enterobacter cloacae* and one by simultaneous infection of *E. cloacae* and *S. marcescens*. Three *Klebsiella*, three *Serratia* and the remaining two were selected for analysis. We discuss *Pseudomonas* and *Acinetobacter* outbreaks separately.

12.5.1 *Klebsiella* Outbreaks

An outbreak of *Klebsiella* infection in NICU and PICU was published from Spain in 2004; this outbreak occurred in 2002–2003 and lasted 1 year [18]. The outbreak was polyclonal. Two predominant clones of *Klebsiella* harboured a special gene (SHV5) for the beta-lactamase enzyme responsible for multi-drug-resistant *Klebsiella*. According to the authors, this type of *Klebsiella* was not reported previously in Spain. Another clone harbouring two different genes responsible for multidrug resistance but dissimilar from the above was reported. A report from The Netherlands published in 2001 described an outbreak of infections with a multi-drug-resistant *Klebsiella* strain [19] associated with contaminated roll boards in operating rooms. This outbreak in 2000 showed how an unusual source of the outbreak can be revealed by systematic surveillance. In 2008, a polyclonal outbreak of extended spectrum beta-lactamase (ESBL)-producing *K. pneumoniae* in an ICU of a university hospital in Belgium was reported [20]. This was a 2-month outbreak that occurred in 2005 with 18 isolates. There was one predominant clone, two clones with several isolates and four with unique isolates. The cause of the outbreak was not clear but was associated with a dramatic increase in the number of imported carriers during the previous weeks.

12.5.2 *Enterobacter cloacae* Outbreaks

An outbreak caused by ESBL-producing *E. cloacae* in a cardiothoracic ICU was reported from Spain in 2007 [21]. The outbreak occurred in 2005, lasted 3 months, and involved seven patients. Molecular analysis revealed two clones responsible for the outbreak: one carried a single ESBL; the other carried two ESBLs. Both clones showed resistance to quinolones and aminoglycosides. The outbreak was brought under control by the implementation of barrier measures and cephalosporin restrictions.

12.5.3 *Serratia marcescens* Outbreaks

An outbreak was reported from Germany in 2002 [22] in both the NICU and PICU, lasted from September to November 1998 and involved 15 patients. Two epidemic strains were associated with cross-infection in groups of five and ten patients, respectively. Two epidemic clones were detected from the surfaces of an ICU room, but an original source was not identified. The outbreak was stopped by routine infection-control measures. A report from Malaysia in 2004 described an outbreak of *Serratia* infections that lasted 10 days in an AICU [23]. The single outbreak strain was found in insulin and sedative solutions administered to patients. An outbreak of *S. marcescens* colonisation and infection in a neurological ICU that occurred from May 2002 to March 2003 was reported from a Dutch university medical centre in 2006 [24]. The outbreak strain was traced to a healthcare worker (HCW) with long-term carriage on the hands. The skin of the HCW's hands was psoriatic. The epidemic ended after the colonised HCW went on leave, with subsequent eradication treatment. A heterogeneous outbreak of *E. cloacae* and *S. marcescens* infections in a surgical ICU was published by a group of authors from San Francisco, USA [25]. The outbreak lasted from December 1997 through January 1998. Molecular techniques ruled out a point source or significant cross-contamination as modes of transmission. The authors concluded that patient-related factors, such as respiratory tract colonisation and duration of central line placement might have played a role in this outbreak.

12.5.4 *Pseudomonas* Outbreaks

Several reports have been published on infections caused by multi-drug-resistant *Pseudomonas* spp. in ICUs since 2000. We retrieved 19 reports; not all were outbreaks, as some were described as endemic infections. In addition, one outbreak was caused by *Burkholderia cepacia*. We selected a few outbreaks that we believed would represent the main problems occurring in ICUs, such as multidrug resistance, clonality, transmission source and mode and infection severity.

In 2000, a publication from Norway reported an outbreak of multi-drug-resistant *P. aeruginosa* associated with increased risk of death [26]. The outbreak occurred from December 1999 to September 2000, was monoclonal and the strain was introduced into the ICU early in 1998 and was maintained thereafter. All patients were ventilated. The strain was resistant to carbapenems, quinolones and azlocillin. In 13 infected patients, ten of whom died, *Pseudomonas* was found in one or all specimens, such as respiratory secretions, ventilator tubes, connection tubes and the water catcher of the ventilator system. The bacterium was also isolated from water taps. In addition to enhanced control of infection measures, complete elimination of the outbreak was achieved after water taps were pasteurised and sterile water was used when a solvent was needed. In 2003, French authors published a report on the epidemiology of *P. aeruginosa* in an ICU [27]. Although between 1996 and 1997 the prevalence of *P. aeruginosa* infections reached 30% of all hospital-acquired infections, the authors did not call this an outbreak, despite the fact that this was

twice the national prevalence of 15% observed in ICUs. However, this high prevalence prompted the authors to conduct a prospective epidemiological study from July 1997 to February 1998. We selected this study as a good example of activities necessary to prevent a major outbreak. The authors described how systematic surveillance was carried out (oropharyngeal and rectal swabs on admission and twice weekly afterwards). This practice revealed that during the study period, the overall incidence of *P. aeruginosa* carriage was 43%: 17% on admission and 26% acquired in the ICU. In addition 16/191 (8%) patients developed the infection. The authors also pointed out that intestinal carriage was a prerequisite for colonisation or infection. Genotyping analysis of 81 isolates indicated that 70% belonged to genotype 1, 4% to genotype 2 and that remaining isolates were not genetically related. It has also been shown that mechanical ventilation was associated with *P. aeruginosa* carriage and ineffective antibiotics significantly increased the risk of colonisation and infection in ICU. The authors concluded that not only do endogenous sources account for the majority of colonisation or infection due to *P. aeruginosa* but that exogenous sources may be involved in some instances. In an epidemic setting, the authors' stance was to reinforce standard barrier precautions. However, the main message of this study is the necessity to adopt and pursue preventive measures.

In 2008, an outbreak of severe *B. cepacia* infections in an ICU was reported from Spain [28]. The outbreak occurred over a period of 18 days in August 2006 when *B. cepacia* were recovered from different clinical samples associated with bacteraemia in three cases, lower respiratory tract infection in one and urinary tract infection in one. Samples of antiseptics, eau de cologne and moisturising milk available on treatment carts were collected and cultured. *B. cepacia* was isolated not only from three samples of the moisturising body milk that had been applied to the patients but also from two new hermetically closed units. All strains recovered from environmental and clinical samples belonged to the same clone. The cream was withdrawn from all hospital units, and no new cases of *B. cepacia* developed. The authors concluded that the presence of bacteria in cosmetic products, even within accepted limits, may lead to severe life-threatening infections in severely ill patients.

12.5.5 *Acinetobacter* Outbreaks

We retrieved 34 publications on *Acinetobacter* outbreaks, 11 of which were not strictly outbreaks, and actually not reported as such, but rather described general epidemiology, antibiotic resistance, infection control or treatment options. Most of these problems are dealt with in relevant chapters of this edition. Following our approach, we summarise only a few outbreaks, which appeared to offer some new findings or insights.

A 2000 report from Italy described an outbreak of infusion-related *A. baumannii* bacteraemia in an eight-bed ICU [29]. From 6 June to 15 July 2000, six cases were identified. All patients received parenterally administered solutions prepared by ICU nurses, which was subsequently proven to be the source of infection. Three patients

died from sepsis despite treatment with a combination of meropenem and amikacin, which were shown by laboratory tests to be synergistic. This high mortality rate (50%) was explained by the authors as being due to persistent bacteraemia related to the repeated infusions of contaminated solutions. Once aseptic preparation was carried out in the hospital pharmacy, this outbreak was controlled, and further infusion-related nosocomial bacteraemia was prevented. From the USA, a publication in 2001 reported an outbreak of multiresistant *Acinetobacter* colonisation and infection in an ICU [30]. The strain was sensitive only to polymyxin. The outbreak lasted an entire year between 1996 and 1997 and involved 57 patients, 27 of whom were infected and 25 colonised. The arrival of a colonised burn patient (>50% total body surface area) from an outside hospital was responsible for the outbreak. Although on typing two strains were found, the only identified primary source was the original burn patient. Ten deaths resulted from infections (37% of infected patients). The authors claimed that this outbreak served as a model of eradication of multi-drug-resistant organisms, as the *Acinetobacter* was eliminated from all ICU patients by multidisciplinary measures that included the following: cohort and contact isolation of all colonised and infected patients; introduction of strict aseptic measures such as hand washing, barrier isolation, equipment and room cleaning; sterilisation of ventilator equipment; and individual dedication of medical equipment to each patient. A paper was published from Australia in 2007 regarding carbapenem-resistant *A. baumannii* [31]. We selected this publication as an illustration of an extensive molecular analysis rather than for a critical review of the outbreak, which occurred in an ICU between 1999 and 2000. Based on their findings, the authors claim that antibiotic-resistant genes are readily exchanged between co-circulating strains in epidemics of phenotypically indistinguishable organisms. In conclusion, they recommend that epidemiological investigation of major outbreaks should include whole-genome typing as well as analysis of potentially transmissible genes and their vehicles. Finally, we found a paper in a journal from Kuwait not found by our Internet research [32]. The authors reported three different outbreaks of multi-drug-resistant *A. baumannii* infections involving 24 patients aged 16–75 years that occurred in an ICU in the course of 1 year between 2006 and 2007. The outbreak was polyclonal and successfully controlled with tigecycline, to which two causative clones were sensitive. Three additional distinct clones were isolated from the environment. Due to lack of appropriate surveillance cultures, no explanation was offered for the origin of epidemic clones. Subsequently, in a letter to the editor, our interpretation that "…microbial gut overgrowth increased spontaneous mutation, which led to polyclonality and antibiotic resistance in the critically ill" was accepted by the authors [33, 34].

12.6 Fungal Outbreaks

Thirteen publications were retrieved from MEDLINE, five of which described outbreaks of remarkable findings. The remaining papers reported some important aspects of fungal species, colonisation, infection and treatments, predominantly as surveys, and as such were not included in our analysis.

Outbreaks presented here were caused by uncommon opportunistic fungi. Two reports described ICU outbreaks caused by *Hansenula anomala*, an opportunistic yeast first reported from a Liverpool, UK, NICU in 1986 [35]. In 2001, a report from Croatia described an outbreak in a surgical ICU [36]. *H. anomala* was isolated from blood taken from eight patients between 23 August and 6 December 1993. All patients were treated with antifungal therapy; three died from complications of underlying disease. The introduction of strict hygienic measures stopped the spread of infection, but the outbreak ceased with the introduction of a new batch of cotton from another manufacturer, which was used for venipuncture-site disinfection. However, the authors could not find evidence for infection source and transmission route. The second report, from Brazil (2005), describes an outbreak in a PICU [37]. The authors reported their finding as an outbreak of *Pichia anomala*, a newly introduced name for *H. anomala*. From October 2002 to January 2004, 17 children developed *P. anomala* fungemia. The median age was 1.1 year, and the main underlying conditions were congenital malformations and neoplastic disease. The overall mortality rate was 41.2% despite treatment with amphotericin B. During a 2-week period in April 2003, when new cases occurred, surveillance cultures revealed that 67.9% of patients were colonised with yeasts, but no single patient was found to be colonised with *P. anomala*. Thus, no source was found at that time. The outbreak was not controlled until orally administered prophylaxis with nystatin and topical application of an iodoform to venipuncture sites were started.

An extraordinary outbreak of invasive gastritis caused by *Rhizopus microsporus* in an adult ICU was reported from Spain in 2004 [38]. Over a 14-week period (between November 1995 and March 1996), gastric mucormycosis was diagnosed in five patients, four of whom were admitted to ICU with severe community-acquired pneumonia and one with multiple trauma. The main symptom was upper gastrointestinal haemorrhage. Isolated filamentous fungi were identified as *R. microsporus* var. *rhizopodiformis* and were detected in gastric aspiration samples and traced to wooden tongue depressors used to prepare medication for oral administration (and given to patients through a nasogastric catheter) and in some tongue depressors stored in unopened boxes unexposed to the ICU environment. The outbreak was terminated when contaminated tongue depressors were withdrawn from use. This outbreak was attributable to the 40% mortality rate; wooden material should not be used in the hospital setting.

In 2004, an outbreak of three cases of *Dipodascus capitatus* infection in an ICU was reported from Japan [39]. The index case was pulmonary infection with a fulminant course of fungal infection, which resulted in death, in a patient with acute myelocytic leukaemia who shared a room for at least 1 week with the two other patients, suggesting the possibility of transmission. One of the other two patients died from multiple organ dysfunction. The presence of *D. capitatus* might have been due to contamination in the respiratory ICU. In all cases, *D. capitatus* was identified in sputum, deep tracheal aspiration samples, blood and urine samples. The authors concluded that *D. capitatus* should be added to the lengthening list of opportunistic fungal pathogens that

can cause infection in immune-compromised patients, with the danger of transmission and potential outbreak.

An outbreak of *Saccharomyces cerevisiae* fungemia in an ICU was reported from Spain in 2005 [40]. During the period from 15 to 30 April, three patients with *S. cerevisiae* fungemia were identified. The only identified risk factor was treatment with a probiotic containing this yeast. The three patients received the product via nasogastric tube for a mean of 8.5 days before the culture was positive. Surveillance cultures for the control patients admitted at the same time did not reveal any carriers. All three patients died from causes unrelated to *S. cerevisiae*. Discontinuation of use of the product for treatment or prevention of *Clostridium difficile*-associated diarrhoea in the unit stopped the outbreak of infection. In conclusion, the authors warned that the use of *S. cerevisiae* should be carefully reassessed in immune-compromised or critically ill patients.

12.7 Discussion

An outbreak is defined as an event where two or more patients in a defined location are infected by identical, often multi-drug-resistant, microorganisms transmitted via the hands of HCW, usually within an arbitrary time period of 2 weeks. There are two different types of infection involved in outbreaks: secondary endogenous and exogenous. Outbreaks of secondary endogenous infections are invariably preceded by outbreaks of carriage of abnormal flora, whereas outbreaks of exogenous infections are not preceded by outbreaks of abnormal carriage. These two types of outbreaks each require a different type of management: enterally and topically administered antimicrobials for secondary endogenous and exogenous outbreaks, respectively. Ongoing surveillance efforts, i.e. throat and rectal swabs on admission and twice weekly thereafter, to monitor the efficacy of systematic decontamination of the digestive tract (SDD) and to identify the emergence of antimicrobial resistant threats, is an intrinsic component of any decontamination programme. In this sense, a well-designed programme contains an intrinsic degree of protection against antibiotic-resistant organism emergence. Surveillance cultures of throat and rectum are more sensitive in detecting resistance than are diagnostic samples [41]. Additionally, there is a close relationship between surveillance and diagnostic samples. Once a resistant microorganism reaches overgrowth concentrations, i.e. $\geq 10^5$/ml saliva and/or gram of faeces, diagnostic samples become positive [8].

In our review, 28 outbreaks were selected to illustrate the situation at the beginning of this century. As a matter of fact, the majority of the outbreaks was related to the previous decade. However, biased or not, our analysis described 19 outbreaks that occurred after 2000 and nine from last century, although the outbreaks were published in this century (Fig. 12.1). This suggests that some new problems indeed emerged in this century.

It is important to record the number of papers retrieved according the causative organisms: MRSA six, VRE ten, AGNB 14, *Pseudomonas* spp. 19, *Acinetobacter* spp. 23 and fungi 13. Perhaps, against our expectation, AGNB organisms—in

Table 12.2 New and older trends at the beginning of the twenty-first century

New trends	Older trends
Emerging viral infections may increase bacterial and fungal outbreaks	Surveillance cultures mostly used after outbreaks occurred
Extensive use of molecular techniques proved that many outbreaks are polyclonal and detected new genes responsible for antibiotic resistance	Pathogenesis of outbreaks rarely clarified due to lack of surveillance cultures SDD still rarely used for control of outbreaks In general, endemic infections more common than outbreaks
Emergence of new resistant clones	Infection control measures usually enhanced after outbreak occurred
The principle of SDD extended to other antibiotics, e.g. vancomycin to prevent MRSA outbreaks	Mortality primarily attributed to underlying disease, with exception of NICU and direct injection of pathogen

SDD selective decontamination of the digestive tract; *MRSA* methicillin-resistant *Staphylococcus aureus*; *NICU* neonatal intensive care unit

particular, opportunists such as *Pseudomonas* and *Acinetobacter*—prevailed significantly, for which there must be a reason. If we take MRSA as an example, all around the world, this drug-resistant pathogen has been a primary focus for nosocomial infection control and treatment for years. Thus, there are fewer outbreaks. An extensive study from Germany that involved 139 ICUs showed that cluster and single MRSA infections were significantly more common than actual outbreaks (38 ICUs compared with 12, respectively) [7]. To our knowledge, there were no similar studies for VRE and AGNB, but one would anticipate similar findings and interpretation.

On the other hand, opportunistic pathogens such as *Pseudomonas* spp., *Acinetobacter* spp. and fungi often caused unexpected outbreaks, particularly in immunocompromised patients. They originated from external sources and were difficult to treat because of their resistance to multiple antibiotics.

Our search for specific features relevant to published outbreaks revealed some new, and confirmed some older, trends (Table 12.2). Probably the best example of how new viral infections—such as SARS—can change the rate of bacterial and fungal infections in ICUs came from the experience in China [10]. There was a significant increase in the rate of MRSA and *Candida* spp. acquisition in an ICU during the SARS period. It may be anticipated, therefore, that in the future, SARS and influenza viral infections would lead to complex ICU outbreaks.

We pointed out earlier how using molecular techniques revealed that many outbreaks were due to more than one clone [4]. Our analysis confirms this, although the origin of different clones remained obscure in all reports in which polyclonality was detected. However, we recently put forward a hypothesis that microbial gut overgrowth is responsible for increased spontaneous mutation leading to polyclonality and antibiotic resistance [42]. Furthermore, extensive use

of molecular techniques not only revealed a number of new genes responsible for antibiotic resistance [18] but showed that genetically unrelated organisms readily exchange antibiotic resistance genes [15, 31]. Yet further, a new trend is related to the SDD concept. Two studies, one from Italy and one from Spain, reported the use of enterally administered vancomycin to control and prevent, respectively, MRSA outbreaks [5, 8]. This is further evidence that the principle of SDD can be used with antimicrobials directed specifically to the causative organism. As early as 1993 we reported how selective decontamination with nystatin successfully controlled a *Candida* outbreak in an NICU [43].

Among older trends, surveillance cultures, or lack of them, are still prominent. Even in 2009 there were authors responsible for infection control in hospitals and ICUs who claimed that "…surveillance cultures of all patients with potential to develop infection are difficult and very costly…" [44]. Some time ago (1994), we expressed an alternative view in response to an identical attitude [45]. Needless to say, lack of surveillance cultures not only delays the recognition of an outbreak and its control but also precludes the understanding of the pathogenesis of the majority of outbreaks. Surveillance cultures are also crucial for detecting outbreaks of exogenous pathogenesis, i.e. without carriage. On the other hand, the source of an exogenous outbreak is readily identified with molecular techniques. Some of these outbreaks are striking, such as one from this analysis in which *Acinetobacter*-contaminated parentally administered solutions were repeatedly infused to patients, leading to a very high mortality rate of 50% [29].

In conclusion, new trends as well as old confirm what we indicated in the previous edition of this book, which is that to control and prevent ICU outbreaks, surveillance cultures and SDD should be integrated in routine infection-control measures.

References

1. El-Masri MM, Williams KM, Fox-Wasylyshyn SM (2004) Severe acute respiratory syndrome: another challenge for critical care nurses. AACN Clin Issues 15:150–159
2. Burns SM (2009) H1N1 influenza is here. J Hosp Infect 73:200–202
3. Vincent JL, Rello J, Marshall J et al (2009) International study of the prevalence and outcome of infection in intensive care units. JAMA 302:2323–2329
4. Damjanovic V, Corbella X, van der Spoel JI, van Saene HKF (2005) Outbreaks of infection in intensive care units—usefulness of molecular techniques for outbreak analysis. In: van Saene HKF, Silvestri L, de la Cal MA (eds) Infection control in the intensive care unit, 2nd edn. Springer, Milan, pp 247–296
5. Silvestri L, Milanese M, Oblach L et al (2002) Enteral vancomycin to control methicillin-resistant *Staphylococcus aureus* outbreak in mechanically ventilated patients. Am J Infect Control 30:391–399
6. Cassone M, Campanile F, Pantosti A et al (2004) Identification of a variant 'Rome clone' of methicillin-resistant *Staphylococcus aureus* with decreased susceptibility to vancomycin, responsible for an outbreak in an intensive care unit. Microb Drug Res 10:43–49
7. Gastmeier P, Sohr D, Geffers C et al (2002) Occurrence of methicillin-resistant *Staphylococcus aureus* infections in German intensive care units. Infection 4:198–202

8. de la Cal MA, Cerda E, van Saene HKF et al (2004) Effectiveness and safety of enteral vancomycin to control endemicity of methicillin-resistant *Staphylococcus aureus* in a medical/surgical intensive care unit. J Hosp Infect 56:175–183
9. Weese JS, Faires M, Rousseau J et al (2007) Cluster of methicillin-resistant *Staphylococcus aureus* colonisation in a small animal intensive care unit. JAMA 231:1361–1364
10. Yap FH, Gomersall CD, Fung KS et al (2004) Increase in methicillin-resistant *Staphylococcus aureus* acquisition rate and change in pathogen pattern associated with an outbreak of severe acute respiratory syndrome. Clin Infect Dis 39:511–516
11. Khan E, Sarwari A, Hasan R et al (2002) Emergence of vancomycin-resistant *Enterococcus faecium* at a tertiary care hospital in Karachi, Pakistan. J Hosp Infect 52:292–296
12. Peta M, Carretto E, Bdbarini D et al (2006) Outbreak of vancomycin-resistant *Enterococcus* spp. on an Italian general intensive care unit. Clin Microbiol Infect 12:163–169
13. Pearman JW (2006) 2004 Lowbury lecture: the Western Australian experience with vancomycin-resistant enterococci—from disaster to ongoing control. J Hosp Infect 63:14–26
14. Delamare C, Lameloise V, Lozniewski A et al (2008) Glycopeptide-resistant *Enterococcus* outbreak in an ICU with simultaneous circulation of two different clones. Pathol Biol 56:454–460
15. Zhu X, Zeng B, Wang S et al (2009) Molecular characterization of outbreak-related strains of vancomycin-resistant *Enterococcus faecium* from an intensive care unit in Beijing, China. J Hosp Infect 72:147–154
16. Se BY, Chun HJ, Yi HJ et al (2009) Incidence and risk factors of infections caused by vancomycin-resistant *Enterococcus* colonization in neurosurgical intensive care unit patients. J Korean Neurosurg Soc 46:123–129
17. Gomez-Gil R, Romero-Gomez MP, Garcia-Arias A et al (2009) Nosocomial outbreak of linezolid-resistant *Enterococcus faecalis* infection in a tertiary care hospital. Diag Microb Infect Dis 65:175–179
18. Brinas L, Lantero M, Zarazaga M et al (2004) Outbreak of SHV-5 beta-lactamase-producing *Klebsiella pneumoniae* in a neonatal–pediatric intensive care unit in Spain. Microb Drug Res 10:354–358
19. van't Veen A, van der Zee A, Nelson J et al (2005) Outbreak of infection with a multiresistant *Klebsiella pneumoniae* strain associated with contaminated roll boards in operating rooms. J Clin Microbiol 43:4961–4967
20. Laurent C, Rodriguez-Villalobos H, Rost F et al (2008) Intensive care unit outbreak of extended-spectrum beta-lactamase-producing *Klebsiella pneumoniae* controlled by cohorting patients and reinforcing infection control measures. Infect Control Hosp Epidemiol 29: 517–524
21. Manzur A, Tubau F, Pujol M et al (2007) Nosocomial outbreak due to extended-spectrum-beta-lactamase-producing *Enterobacter cloacae* in a cardiothoracic intensive care unit. J Clin Microbiol 45:2365–2369
22. Steppberger K, Walter S, Claros MC et al (2002) Nosocomial neonatal outbreak of Serratia marcescens–analysis of pathogens by pulsed field gel electrophoresis and polymerase chain reaction. Infection 30:277–281
23. Alfizah H, Nordiah AJ, Rozaidi WS (2004) Using pulsed-field gel electrophoresis in the molecular investigation of an outbreak of *Serratia marcescens* infection in an intensive care unit. Singap Med J 45:214–218
24. de Vries JJ, Bass WH, van der Ploeg K et al (2006) Outbreak of *Serratia marcescens* colonization and infection traced to a healthcare worker with long-term carriage on the hands. Infect Control Hosp Epidemiol 27:1153–1158
25. Dorsey G, Borneo HT, Sun SJ et al (2000) A heterogeneous outbreak of *Enterobacter cloacae* and *Serratia marcescens* infections in a surgical intensive care unit. Infect Control Hosp Epidemiol 21:465–469
26. Bukholm G, Tannaes T, Kjelsberg AB et al (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

27. Thuong M, Arvaniti K, Ruimy R et al (2003) Epidemiology of *Pseudomonas aeruginosa* and risk factors for carriage acquisition in an intensive care unit. J Hosp Infect 53:274–282
28. Alvarez-Lerma F, Maull E, Terradas R et al (2008) Mosturizing body milk as a reservoir of *Burkholderia cepacia*: outbreak of nosocomial infection in a multidisciplinary intensive care unit. Crit Care 12:R10
29. Menichetti F, Tascini C, Ferranti S et al (2000) Clinical and molecular epidemiology of an outbreak of infusion-related *Acinetobacter baumannii* bacteremia in an intensive care unit. Le Infezioni Medicina 1:24–29
30. Podnos YD, Cinat ME, Wilson SE et al (2001) Eradication of multi-drug resistant *Acinetobacter* from an intensive care unit. Surg Infect 2:297–301
31. Valenzuela JK, Thomas L, Partridge SR et al (2007) Hospital gene transfer in a polyclonal outbreak of carbapenem-resistant *Acinetobacter baumannii*. J Clin Microbiol 45:453–460
32. Jamal W, Salama M, Dehrab N et al (2009) Role of tigecycline in the control of carbapenem-resistant *Acinetobacter baumannii* outbreak in an intensive care unit. J Hosp Infect 72: 234–242
33. Damjanovic V, Taylor N, van Saene HKF (2009) Origin of epidemic clones of *Acinetobacter* in the critically ill. J Hosp Infect 73:285–286
34. Rotimi VO, Jamal W, Salama M (2009) Control of *Acinetobacter* outbreaks in the intensive care unit. J Hosp Infect 73:286–287
35. Murphy N, Damjanovic V, Hart CA et al (1986) Infection and colonisation of neonates by *Hansenula anomala*. Lancet 1:291–293
36. Kalenic S, Jandrlic M, Vegar V et al (2001) *Hansenula anomala* outbreak at a surgical intensive care unit: a search for risk factors. Eur J Epidemiol 17:491–496
37. Pasqualotto AC, Sukiennik TC, Severo LC et al (2005) An outbreak of *Pichia anomala* fungaemia in a Brazilian pediatric intensive care unit. Infect Control Hosp Epidemiol 26:553–558
38. Maravi-Poma E, Rodriguez-Tudela JL, de Jalon JG et al (2004) Outbreak of gastric mucormycosis associated with the use of wooden tongue depressors in critically ill patients. Intensive Care Med 30:724–728
39. Eroz G, Otag F, Erturan Z et al (2004) An outbreak of *Dipodascus capitatus* infection in the ICU: three case reports and review of the literature. Jpn J Infect Dis 57:248–252
40. Munoz P, Bouza E, Cuenca-Estrella M et al (2005) *Saccharomyces cerevisiae* fungemia: an emerging infectious disease. Clin Infect Dis 40:1625–1634
41. D'Agata EMC, Venkataraman L, De Girolami P et al (1999) Colonization with broad-spectrum cephalosporin-resistant Gram-negative bacilli in intensive care units during a nonoutbreak period: prevalence, risk factors, and rate of infection. Crit Care Med 27: 1090–1095
42. van Saene HK, Taylor N, Damjanovic V et al (2008) Microbial gut overgrowth guarantees increased spontaneous mutation leading to polyclonality and antibiotic resistance in the critically ill. Curr Drug Targets 9:419–421
43. Damjanovic V, Connolly CM, van Saene HKF et al (1993) Selective decontamination with nystatin for control of a *Candida* outbreak in a neonatal intensive care unit. J Hosp Infect 24:245–259
44. Miranda LN, van der Heijden IM, Costa SF et al (2009) Candida colonisation as a source of candaemia. J Hosp Infect 72:9–16
45. Damjanovic V, van Saene HKF, Weindling AM et al (1994) The multiple value of surveillance cultures: an alternative view. J Hosp Infect 28:71–75