OPEN ACCESS

Review Article

Where is the difference between an epidemic and a high endemic level with respect to nosocomial infection control measures? An analysis based on the example of vancomycin-resistant Enterococcus faecium in hematology and oncology departments

Wo ist der Unterschied zwischen epidemischen und hoch endemischen Niveaus bezüglich nosokomialer Infektionskontrollmaßnahmen? Eine Analyse an dem Beispiel von Vancomycin-resistentem Enterococcus faecium auf hämatologischen und onkologischen Stationen

Nikos Ulrich[1]
Petra Gastmeier[1]

1 Institute for Hygiene and Environmental Medicine, Charité – University Medicine, Berlin, Germany

Abstract

Some infection control recommendations distinguish epidemic and endemic levels for infection control. However, it is often difficult to separate long lasting outbreaks from high endemic levels and it remains open, if this distinction is really useful.

Aim: To compare infection control measures in endemic and epidemic outbreaks.

Methods: The example of vancomycin-resistant *Enterococcus faecium* outbreaks in haematology or oncology departments was used to analyse differences in infection control measures between outbreaks and high endemic levels. The outbreak database and PubMed, including long lasting outbreaks, were used for this analysis. Two time limits were used for separation: 6 and 12 months. In addition, monoclonal and polyclonal outbreaks were distinguished.

Findings: A total of 36 outbreaks were included. 13 outbreaks lasted 6 months or less, 9 outbreaks more than 6 months but at maximum 12 months and 9 more than 12 months. For the remaining outbreaks, no information about their duration was available. Altogether, 11 outbreaks were monoclonal and 20 polyclonal. Considering infection control measures, there were almost no differences between the different groups compared. Patient screening was given up in 37.5% of long lasting outbreaks (>12 months) and hand hygiene not reported in the majority of polyclonal outbreaks (77.8%).

Conclusion: Despite many institutions trying to add further infection control measures in case of an outbreak, evidence based infection control measures should be implemented in endemic and epidemic situations. The crucial aspect is probably the degree of implementation and its control in both situations.

Keywords: outbreaks, endemic, vancomycin-resistant enterococci, haematology, oncology

Zusammenfassung

Einige Krankenhaus-Hygieneempfehlungen unterscheiden zwischen epidemischen und endemischen Niveaus bei Infektionskontrollmaßnahmen. Oft ist es schwer, zwischen lang andauernden Ausbrüchen und einem hohen endemischen Niveau zu unterscheiden und es bleibt unklar, ob diese Unterscheidung sinnvoll ist.

Ziel: Vergleich von Infektionskontrollmaßnahmen bei endemischen und epidemischen Ausbrüchen.
Methoden: Das Beispiel von Vancomycin-resistentem *Enterococcus faecium* auf hämatologischen und onkologischen Stationen wurde verwendet, um die unterschiedlichen Infektionskontrollmaßnahmen bei Ausbrüchen und bei hohen endemischen Niveaus zu vergleichen. Für die Analyse wurden die Outbreak-Datenbank sowie PubMed verwendet. Es wurden zwei zeitliche Grenzen zur Unterscheidung von epidemischen und endemischen Situationen gesetzt: 6 und 12 Monate. Zusätzlich wurden monoklonale und polyklonale Ausbrüche unterschieden.
Ergebnis: Insgesamt wurden 36 Artikel in die Analyse aufgenommen. 13 Ausbrüche hatten eine maximale Dauer von 6 Monaten, 9 Ausbrüche dauerten länger als 6 Monate, aber nicht länger als 12 Monate und 9 Ausbrüche dauerten länger als 12 Monate. In den verbliebenden Ausbrüchen wurde keine Angabe zur Dauer gemacht. Insgesamt waren 11 Ausbrüche monoklonal und 20 polyklonal. Bezüglich der Infektionskontrollmaßnahmen gab es nahezu keinen Unterschied zwischen den beiden Gruppen. Patientenscreening wurde in 37,5% der langen Ausbrüche (>12 Monate) nicht durchgeführt und über verstärkte Händehygiene wurde in der Mehrheit der polyklonalen Ausbrüche (77,8%) nicht berichtet.
Schlussfolgerung: Obwohl viele Institutionen versuchen, weitere Infektionskontrollmaßnahmen im Fall eines Ausbruchs hinzuzufügen, sollten Evidenz basierte Maßnahmen in epidemischen und endemischen Situationen eingesetzt werden. Offensichtlich ist der entscheidende Punkt, in welchem Maß die Infektionskontrollmaßnahmen umgesetzt werden und wie die Umsetzung kontrolliert wird.

Schlüsselwörter: Ausbruch, endemisch, Vancomycin-resistente Enterococci, Hämatologie, Onkologie

Introduction

Some infection control guidelines distinguish control measures in endemic and epidemic conditions [1], [2], [3]. In addition, some authors require that future studies have to differentiate between epidemic and endemic situations in order to adjust prevention strategies for the individual settings [4]. However, often it is not clear, if an outbreak is continuing or if it should be categorized a high endemic level. In the literature, one can sometimes find terms such as “sustainable endemic outbreak” or “prolonged outbreak” [5], [6], [7], [8]. It is also difficult to understand, why different infection control measures are recommended for both outbreak situations and endemic conditions. If a measure has shown to be effective in decreasing the risk of transmission or the risk of infection based on scientific literature, it should be applied.
Difficulties in distinguishing outbreaks and high endemic levels of nosocomial pathogens occur very often for example in the case of vancomycin-resistant *Enterococcus faecium* (VRE) in haematology and oncology departments. In this patient group asymptomatic colonization of the gastrointestinal tract is more common than clinically recognized infection by a ratio of 10:1 [9]. As a consequence, situations with a large number of VRE colonizations are often not recognized as a problem and not considered a real outbreak. However, in particular bloodstream infections due to VRE are associated with substantial morbidity and mortality. Even under the conditions of modern VRE therapies, mortality is almost twice as high when the pathogen causing blood stream infection is a VRE compared with Vancomycin susceptible *E. faecium* [10], [11]. That means outbreaks in this patient group are a serious problem. Therefore we want to use this example to answer the question whether a distinction between epidemic and endemic conditions for infection control measures is really useful.

Methods

Primarily, we used the outbreak database to investigate this question. It contains not only many outbreaks but also many sustained and prolonged outbreaks (often over 2 years) which normally should be regarded as a high endemic level.
The Outbreak Database (http://www.outbreakdatabase.com) is a database containing nosocomial outbreaks worldwide and is currently the largest collection of nosocomial outbreaks [12]. The database contains information from nosocomial outbreaks in a standardized format. Parameters on several levels can be set in order to obtain more specific search results. In this case, parameters have been set to only include articles that contain ‘vancomycin-resistant *Enterococcus faecium*’ as the microorganism and ‘haematology/oncology’ as the location. The

articles found in the outbreak database in February 2017 were then reviewed and a manual search of reference lists of these articles was conducted and, if appropriate, included in our study. To identify additional articles which are not yet filed in the outbreak database, but also relevant to the topic of interest, two additional searches of PubMed were performed on the same day using the following combination of MeSH terms:

- [hematology] AND [vancomycin-resistant *Enterococcus faecium*]
- [oncology] AND [vancomycin-resistant *Enterococcus faecium*]

When available the following items were extracted from each VRE outbreak: duration of the outbreak, if typing was performed and the infection control measures applied.

To distinguish short and long outbreaks (high endemic levels), two different definitions for the duration of a short outbreak were used: at maximum 6 months and 12 months. Due to monoclonal clusters sometimes being considered as an outbreak and polyclonal clusters as a high endemic level, we also used the typing information of the outbreaks as a distinction. Most of the outbreaks we found were not really monoclonal. Often, in addition to a dominating strain, one or two other strains were found. Therefore, we considered an outbreak as mainly monoclonal if more than 75% of strains were indistinguishable.

The statistical analyses to compare the two groups were performed with 'open epiInfo' using Fisher's exact test.

Results

Our search yielded 36 outbreaks appropriate for this study [13], [14], [15], [16], [17], [18], [19], [20], [21], [22], [23], [24], [25], [26], [27], [28], [29], [30], [31], [32], [33], [34], [35], [36], [37], [38], [39], [40], [41], [42], [43], [44], [45], [46], [47], [48], [49]. The mean duration of 31 outbreaks with information about its duration was 11 months (range 1 to 36 months). Molecular typing was performed in 31 articles mainly using pulse field gel electrophoresis (PFGE).

On average 4.5 infection control measures per outbreak were employed (range 1 to 9). The most frequent measure adopted was patient screening in 28 outbreaks, followed by isolation/cohorting in 21 outbreaks. 14 outbreaks involved environmental screening and in 15 outbreaks intensified cleaning and disinfection of the environment was reported. Six outbreaks reported the closure of the affected location. A full overview of the extracted data is given in Table 1.

Table 1: Overview of all extracted data from 36 outbreaks

Article	Country	Duration (in months)	Source	Typing method	Measures	Risk factors	Type of study	Transmission	Deaths
Nolan et al., 2009 [32]	USA	18	patient	* PFGE	* isolation * personnel training * disinfection/sterilization * modification of care/ equipment	* devices (enteral feeding tube, gastrostomy tube, nasogastric tube) * lack of empirical contact precautions	case-control study		
Marcade et al., 2014 [29]	France			* PCR * PFGE	* patient screening * isolation/cohorting * hand disinfection * closure of affected location				0
Valdezate et al., 2012 [44]	Spain	9	patient	* PFGE * multiple-locus variable-number tandem-repeat analysis (MLVA) * multilocus sequence typing (MLST)	* patient screening * isolation/cohorting * hand hygiene * disinfection/sterilization				7
Pendle et al., 2008 [37]	Australia	6		* PCR * PFGE	* patient screening		case report		2

(Continued)

Table 1: Overview of all extracted data from 36 outbreaks

Article	Country	Duration (in months)	Source	Typing method	Measures	Risk factors	Type of study	Transmission	Deaths
Chlebicki et al., 2006 [16]	Singapore		patient	* PCR * PFGE	* closure of affected location * patient screening * isolation/cohorting * protective clothing * disinfection/sterilization * personnel training * personnel surveillance * environmental screening		case report		2
Böröcz et al., 2005 [13]	Hungary	6		* PFGE	* environmental screening * patient screening * isolation/cohorting * restriction of workload * hand hygiene		case report		
Kawalec et al., 2007 [24]	Poland			* PFGE * MLSA	* patient screening		case report		
Lesens et al., 2006 [27]	France	7	patient	* PFGE	* patient screening	* urinary catheter use * prior exposure to a third-generation cephalosporin * prior exposure to antianaerobials	case-control study	patient-to-patient transmission	2
Worth et al., 2007 [46]	Australia	22		* PFGE	* patient screening * closure of affected location * disinfection/sterilization	* AML * vancomycin therapy during the previous 30 d	case-control study		3
Gambarotto et al., 2000 [19]	France	7		* PCR * PFGE	* isolation/cohorting * patient surveillance				
Burnie et al, 2002 [14]	UK			* PFGE					6
Timmers et al., 2002 [57]	Netherlands	11		* AFLP (amplified fragment length polymorphism)	* isolation/cohorting * reinforcement of hand hygiene * restriction of workload * patient surveillance * protective clothing * personnel training * disinfection/sterilization * modification of care/ equipment	* antibiotic use within 1 month before admission * low albumin levels at baseline	case-control study	personnel	5
Deplano et al., 2007 [17]	Belgium	27		* PCR * PFGE	* patient surveillance * protective clothing * disinfection/sterilization				

(Continued)

Table 1: Overview of all extracted data from 36 outbreaks

Article	Country	Duration (in months)	Source	Typing method	Measures	Risk factors	Type of study	Transmission	Deaths
Knoll et al., 2005 [25]		15		* PCR * PFGE	* environmental screening * patient screening * personnel screening (hands of staff) * isolation/cohorting * hand hygiene * protective clothing * change of antibiotic use			* personnel * environment	
Yoo et al., 2005 [47]	Korea	24		* PFGE		no risk factors found	case-control study	patient-to-patient transmission	15
Oh et al., 2004 [34]	Korea	4	patient	* PCR * PFGE	* personnel screening * patient screening * environmental screening * isolation/cohorting * hand hygiene	* prolonged hospital stay * male gender * care in a 6-bed room * more surgical, vancomycin or ceftizoxime and less Metronidazole therapy	case-control study	* patient-to-patient transmission * personnel	
Sample et al., 2002 [40]	Canada	6	patient	* PFGE	* closure of affected location * isolation/cohorting * sterilization/disinfection * patient screening * environmental screening * modification of equipment/care * protective clothing			environment	3
Hanna et al., 2001 [20]	USA	4	patient	* PFGE	* isolation/cohorting * patient screening * closure of affected location * disinfection/sterilization * protective clothing * personnel training * personnel surveillance		case report		
Kawalec et al., 2001 [23]	Poland	8		* PCR * PFGE * restriction fragment length polymorphism (RFLP) * restriction endonuclease analysis of plasmids (REAP)			case report		
Kawalec et al., 2000 [22]	Poland	36		* PCR * PFGE * RFLP	* environmental screening		case report		

(Continued)

Table 1: Overview of all extracted data from 36 outbreaks

Article	Country	Duration (in months)	Source	Typing method	Measures	Risk factors	Type of study	Transmission	Deaths
McCarthy et al., 2000 [30]	South Africa			* PCR * PFGE	* patient screening * personnel training * isolation/cohorting * hand hygiene * protective clothing * disinfection/sterilization * environmental screening		case report		
Loeb et al., 1999 [28]	Canada	2			* isolation/cohorting * environmental cleaning * patient screening	* Cephalosporin use	case-control study		
Nourse et al., 1998 [33]	Republic of Ireland	3		* PCR * PFGE	* patient screening * isolation/cohorting * protective clothing * environmental screening * disinfection/sterilization * educational training for patients and staff	* duration of neutropenia * antibiotic therapy * the number of antibiotic agents received * duration of therapy with amikacin, ceftazidime or Teicoplanin	case-control study	*environmental spread * patient-to-patient transmission	2
Schuster et al., 1999 [42]	Germany	15		* PCR * PFGE	* patient screening * change of antibiotic use * isolation/cohorting * protective clothing * hand disinfection/ sterilization				5
Lavery et al., 1997 [26]	Ireland	6	patient	* PFGE	* patient screening * personnel surveillance * environmental screening			environment	
Rizkalla et al., 1997 [38]	Ireland	1	more than one source	* random amplification of polymorphic DNA (RAPD)	* patient screening * personnel screening * environmental screening * change of antibiotic use				
Chadwick et al., 1996 [15]	UK	30	patient	* PCR * PFGE	* modification of antibiotic use * improved environmental cleaning * environmental screening * personnel training * modification of care/ equipment * change of antibiotic use				4
Edmond et al., 1995 [18]	USA	9		* contour-clamped homogeneous electric field (CHEF) electrophoresis	* patient screening * environmental screening * isolation/cohorting * modification of care/equipment * personnel training * hand disinfection * change of antibiotic use	reported risk factors for the development of VRE baecteremia, not for contracting VRE in general. Therefore not considered.	case-control study	personnel	8

(Continued)

Table 1: Overview of all extracted data from 36 outbreaks

Article	Country	Duration (in months)	Source	Typing method	Measures	Risk factors	Type of study	Transmission	Deaths
Montecalvo et al., 1994 [31]	USA	12		* PCR * PFGE	* patient screening * isolation/cohorting				4
Singh-Naz et al., 1999 [43]		3		* PFGE	* patient screening * environmental screening	* young age * use of invasive devices * administration of antimicrobial therapy * immunosuppression * underlying diagnosis of malignancy or sickle cell disease	cohort study	patient-to-patient transmission	
Wardal et al., 2014 [45]	Poland	5		* PFGE * multilocus variable-number tandem repeat (VNTR) analysis (MLVA)					
Ozorowski et al., 2009 [35]	Poland	10		* PCR * PFGE	* patient screening * isolation/cohorting * hand disinfection * disinfection/sterilization * protective clothing * education program for doctors on rational antibiotic therapy * change of antibiotic use				
Iosifidis et al., 2012 [21]	Greece	6		* PCR * PFGE	* patient screening * isolation/cohorting * protective clothing * disinfection/sterilization * closure of affected location * personnel training * change of antibiotic use	* A case-control study did not show any particular risk factors for colonization.	case-control study		2
Schmidt-Hieber et al., 2007 [41]	Germany	6		* PCR	* isolation/cohorting * patient screening * personnel screening/surveillance * environmental screening * protective clothing * hand disinfection * personnel training			patient-to-patient transmission	5
Rubin et al., 1992 [39]		12			* patient screening * isolation/cohorting * modification of antibiotic use	* administration of antibiotics, administration of vancomycin in particular * length of hospitalization	case-control study	personnel	
Park et al., 2011 [36]	South Korea	72	environ-ment	* PFGE * MLST	* patient screening * protective clothing		case report	through contact with contaminated environment	

Table 2: Comparison of long and short outbreaks according to two thresholds (maximum duration of a short outbreaks ≤6 months and ≤12 months)

	Long outbreaks/ high endemic level (>6 months)	Short outbreaks (≤6 months)	P value	Long outbreaks/ high endemic level (>12 months)	Short outbreaks ≤12 months)	P value
Number of outbreaks with information about duration#	18	13		9	22	
Control measures						
Outbreaks with information about control measures	16	12		8	20	
Closure of department/unit	1 (6.2%)	3 (25.0%)	n.s.	1 (12.5%)	3 (15.0%)	n.s.
Enforcement of hand hygiene	6 (37.5%)	3 (25.0%)	n.s.	2 (25.0%)	7 (35.0%)	n.s.
Protective clothing	6 (37.5)	5 (41.7%)	n.s.	4 (50.0%)	7 (35.0%)	n.s.
Isolation/cohorting	10 (62.5%)	9 (75.0%)	n.s.	4 (50.0%)	15 (75.0%)	n.s.
Patient screening	13 (81.2%)	12 (100.0%)	n.s.	5 (62.5%)	20 (100.0%)	0,02
Environmental screening	4 (25.0%)	7 (58.3%)	n.s.	3 (37.5%)	8 (40.0%)	n.s.
Education/training	5 (31.2%)	4 (33.3%)	n.s.	2 (25.0%)	7 (35.0%)	n.s.
Environmental cleaning/disinfection	7 /43.8%)	4 (33.3%)	n.s.	4 (50.0%)	7 (35.0%)	n.s.
Antibiotic stewardship/restriction	6 (37.5%)	2 (17.6%)	n.s.	3 (37.5%)	5 (25.0%)	n.s.

Remaining 5 outbreaks: no information about duration)

Table 3: Comparison of polyclonal and monoclonal outbreaks

	Monoclonal#	Polyclonal	P value
Total number of outbreaks with typing information	**11**	**20**	
Among them outbreaks with duration of outbreak	**9**	**18**	
Short outbreaks ≤6 months	3 (33.3%)	9 (50.0%)	n.s.
Long outbreaks >6 months	6 (66.7%)	9 (50.0%)	n.s.
Short outbreaks ≤12 months	8 (88.9%)	12 (66.7%)	n.s.
Long outbreaks >12 months	1 (11.1%)	6 (33.3%)	n.s.
Outbreaks with no information about duration*	2 (22.2%)	2 (11.1%)	
Control measures			
Outbreaks with information about control measures	10	18	
Closure of department/unit	1 (10.0%)	4 (22.2%)	n.s.
Enforcement of hand hygiene	6 (60.0%)	4 (22.2%)	0.046
Protective clothing	4 (40.0%)	9 (50.0%)	n.s.
Isolation/cohorting	8 (80.0%)	10 (55.6%)	n.s.
Patient screening	10 (100.0%)	14 (77.8%)	n.s.
Environmental screening	4 (40.0%)	10 (55.6%)	n.s.
Education/training	3 (30.0%)	7 (38.9%)	n.s.
Environmental cleaning/disinfection	5 (50.0%)	5 (27.8%)	n.s.
Antibiotic stewardship/restriction	1 (10.0%)	5 (27.8%)	n.s.

monoclonal = at least 75% of strains not distinguishable,
* one outbreak with no information about typing and duration

Table 2 provides the infection control measures according to the duration of the outbreaks. Whereas patient screening is performed in all short outbreaks, it was not always performed in long lasting outbreaks (37.5%). This difference is significant when the limit of up to a maximum of 12 months was used. For all other infection control measures, no difference between both groups was found.

Table 3 shows the distribution according to mainly monoclonal and polyclonal outbreaks. There is no association between clonality and outbreak duration and also almost no influence on infection control measures. There is only one exception: Hand hygiene played a greater role in monoclonal outbreaks and was not reported in 77.8% of polyclonal outbreaks.

Discussion

Normally, during an outbreak, all relevant infection control measures should be applied to end the outbreak as soon as possible. However, if the implementation of infection control measures is insufficient, the same measures have to be used over a long period. In the case of a monoclonal outbreak, one might argue that the implementation of infection control measures is better in order to eliminate this specific strain as quickly as possible. On the other hand, polyclonal outbreaks provide evidence that not a specific strain with a high potential for transmission is available, but rather that a general infection control problem may exist on this ward or department.

The implementation of infection control measures also depends on the scientific evidence for these measures. In general, there is only little evidence for effective infection control measures to decrease VRE transmission and the quality of the available studies is rather low. In a meta-analysis, only hand hygiene was associated with a 47% decrease in the VRE acquisition rate while contact precautions did not significantly reduce the VRE acquisition rate [48]. Therefore, the infection control measures found in the included outbreaks represent the infection control measures normally recommended in situations with a high number of patients with multiresistant organisms and in an immunocompromised patient group [1], [9], [49], [50].

Patient screening was the most common infection control measure. It is important to detect patients with VRE early on to be able to prevent it spreading among patients. Our data for long lasting outbreaks (>12 months) show, that patient screening was given up on or not introduced at all in 37.5% of these outbreaks. The reason may be the lacking possibility to isolate and cohort all identified patients. Interestingly, hand hygiene was not reported in the majority of polyclonal outbreaks, despite being the single most important measure to stop transmission. In general hand hygiene has been emphasized in 11 articles of our review only, which is fewer than expected. This might be due to a general underreporting of enforced hand hygiene as an infection control measure, despite its use during an outbreak. Another measure that was surprisingly seldom mentioned was antibiotic stewardship. At least in longer lasting outbreaks and in polyclonal outbreaks this seems to be one of the most important interventions, but was only reported in 37.5% and 27.8% of cases respectively [51], [52], [53].

The review has a number of limitations. First, perhaps the example VRE may not be representative for other outbreaks, but it is very often associated with longer duration and was therefore selected.

Second, the two definitions to distinguish short and long outbreaks and the definition of mainly monoclonal outbreaks were mainly chosen to create groups with a similar number of outbreaks in both groups to be used for comparison. However, the tables show that the infection control measures are almost the same in the various groups.

Third, the majority of articles used PFGE or PCR as the microbiological tool to assess strain relatedness. Many of the outbreaks are from the 1990s, where whole genome sequencing (WGS) was not yet available. While PFGE is a reliable method for the detection of strain relatedness during nosocomial outbreaks, WGS offers an even more precise strain differentiation and is meanwhile often used in VRE outbreak investigations [54], [55].

Fourth, the number of VRE outbreaks considered in our review may be too small to identify further relevant differences between the different groups investigated.

Finally, there is still no uniform reporting of outbreaks as required by the ORION statement [56]. Therefore, it may be the case, that some infection control measures were used but not mentioned.

In addition and probably most important, the degree of implementation of infection control measures is a key aspect and it is impossible to derive from the outbreak description how rigorously the measures were implemented and if implementation was controlled.

In conclusion, according to our example with a relatively large number of short and long lasting outbreaks, it was impossible to identify relevant differences among infection control measures between short outbreaks and high endemic levels as well as between monoclonal and polyclonal outbreaks. Therefore, we believe the distinction of the two groups in infection control guidelines does not reflect the current situation in hospitals and may not be very helpful.

Notes

Competing interests

On behalf of all authors, the corresponding author states that there is no conflict of interest.

Funding source

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

References

1. Tacconelli E, Cataldo MA, Dancer SJ, De Angelis G, Falcone M, Frank U, Kahlmeter G, Pan A, Petrosillo N, Rodríguez-Baño J, Singh N, Venditti M, Yokoe DS, Cookson B; European Society of Clinical Microbiology. ESCMID guidelines for the management of the infection control measures to reduce transmission of multidrug-resistant Gram-negative bacteria in hospitalized patients. Clin Microbiol Infect. 2014 Jan;20 Suppl 1:1-55. DOI: 10.1111/1469-0691.12427

2. Vonberg RP, Kuijper EJ, Wilcox MH, Barbut F, Tüll P, Gastmeier P; European C difficile-Infection Control Group; European Centre for Disease Prevention and Control (ECDC)van den Broek PJ, Colville A, Coignard B, Daha T, Debast S, Duerden BI, van den Hof S, van der Kooi T, Maarleveld HJ, Nagy E, Notermans DW, O'Driscoll J, Patel B, Stone S, Wiuff C. Infection control measures to limit the spread of Clostridium difficile. Clin Microbiol Infect. 2008 May;14 Suppl 5:2-20. DOI: 10.1111/j.1469-0691.2008.01992.x
3. Morgan DJ, Kaye KS, Diekema DJ. Reconsidering isolation precautions for endemic methicillin-resistant Staphylococcus aureus and vancomycin-resistant Enterococcus. JAMA. 2014 Oct;312(14):1395-6. DOI: 10.1001/jama.2014.10142
4. Worth LJ. Vancomycin-resistant enterococci in patients with hematological malignancy: curbing an endemic pathogen. Leuk Lymphoma. 2014 Jun;55(6):1225-6. DOI: 10.3109/10428194.2013.845887
5. Suarez C, Peña C, Arch O, Dominguez MA, Tubau F, Juan C, Gavaldá L, Sora M, Oliver A, Pujol M, Ariza J. A large sustained endemic outbreak of multiresistant Pseudomonas aeruginosa: a new epidemiological scenario for nosocomial acquisition. BMC Infect Dis. 2011 Oct;11:272. DOI: 10.1186/1471-2334-11-272
6. Campos PA, Batistão DW, Gontijo-Filho PP, Ribas RM. A sustained endemic outbreak of vancomycin-resistant Enterococcus faecium: A 30-month surveillance study. Scand J Infect Dis. 2014 Aug;46(8):547-54. DOI: 10.3109/00365548.2014.912348
7. Tissot F, Blanc DS, Basset P, Zanetti G, Berger MM, Que YA, Eggimann P, Senn L. New genotyping method discovers sustained nosocomial Pseudomonas aeruginosa outbreak in an intensive care burn unit. J Hosp Infect. 2016 Sep;94(1):2-7. DOI: 10.1016/j.jhin.2016.05.011
8. Kanamori H, Parobek CM, Juliano JJ, van Duin D, Cairns BA, Weber DJ, Rutala WA. A Prolonged Outbreak of KPC-3-Producing Enterobacter cloacae and Klebsiella pneumoniae Driven by Multiple Mechanisms of Resistance Transmission at a Large Academic Burn Center. Antimicrob Agents Chemother. 2017 Jan 24;61(2). pii:e01516-16. DOI: 10.1128/AAC.01516-16
9. Reyes K, Bardossy AC, Zervos M. Vancomycin-Resistant Enterococci: Epidemiology, Infection Prevention, and Control. Infect Dis Clin North Am. 2016 Dec;30(4):953-965. DOI: 10.1016/j.idc.2016.07.009
10. Prematunge C, MacDougall C, Johnstone J, Adomako K, Lam F, Robertson J, Garber G. VRE and VSE Bacteremia Outcomes in the Era of Effective VRE Therapy: A Systematic Review and Meta-analysis. Infect Control Hosp Epidemiol. 2016 Jan;37(1):26-35. DOI: 10.1017/ice.2015.228
11. Ong DS, Bonten MJ, Safdari K, Spitoni C, Frencken JF, Witteveen E, Horn J, Klein Klouwenberg PM, Cremer OL; MARS consortium. Epidemiology, Management, and Risk-Adjusted Mortality of ICU-Acquired Enterococcal Bacteremia. Clin Infect Dis. 2015 Nov;61(9):1413-20. DOI: 10.1093/cid/civ560
12. Vonberg RP, Weitzel-Kage D, Behnke M, Gastmeier P. Worldwide Outbreak Database: the largest collection of nosocomial outbreaks. Infection. 2011 Feb;39(1):29-34. DOI: 10.1007/s15010-010-0064-6
13. Böröcz K, Szilágyi E, Kurcz A, Libisch B, Glatz K, Gacs M. First vancomycin-resistant Enterococcus faecium outbreak reported in Hungary. Euro Surveill. 2005 Jan 27;10(1):E050127.1.
14. Burnie J, Carter T, Rigg G, Hodgetts S, Donohoe M, Matthews R. Identification of ABC transporters in vancomycin-resistant Enterococcus faecium as potential targets for antibody therapy. FEMS Immunol Med Microbiol. 2002 Jul 12;33(3):179-89. DOI: 10.1111/j.1574-695X.2002.tb00589.x
15. Chadwick PR, Oppenheim BA, Fox A, Woodford N, Morgenstern GR, Scarffe JH. Epidemiology of an outbreak due to glycopeptide-resistant Enterococcus faecium on a leukaemia unit. J Hosp Infect. 1996 Nov;34(3):171-82. DOI: 10.1016/S0195-6701(96)90063-8
16. Chlebicki MP, Ling ML, Koh TH, Hsu LY, Tan BH, How KB, Sng LH, Wang GC, Kurup A, Kang ML, Low JG. First outbreak of colonization and infection with vancomycin-resistant Enterococcus faecium in a tertiary care hospital in Singapore. Infect Control Hosp Epidemiol. 2006 Sep;27(9):991-3. DOI: 10.1086/507289
17. Deplano A, Denis O, Nonhoff C, Rost F, Byl B, Jacobs F, Vankerckhoven V, Goossens H, Struelens MJ. Outbreak of hospital-adapted clonal complex-17 vancomycin-resistant Enterococcus faecium strain in a haematology unit: role of rapid typing for early control. J Antimicrob Chemother. 2007 Oct;60(4):849-54. DOI: 10.1093/jac/dkm270
18. Edmond MB, Ober JF, Weinbaum DL, Pfaller MA, Hwang T, Sanford MD, Wenzel RP. Vancomycin-resistant Enterococcus faecium bacteremia: risk factors for infection. Clin Infect Dis. 1995 May;20(5):1126-33. DOI: 10.1093/clinids/20.5.1126
19. Gambarotto K, Ploy MC, Turlure P, Grélaud C, Martin C, Bordessoule D, Denis F. Prevalence of vancomycin-resistant enterococci in fecal samples from hospitalized patients and nonhospitalized controls in a cattle-rearing area of France. J Clin Microbiol. 2000 Feb;38(2):620-4.
20. Hanna H, Umphrey J, Tarrand J, Mendoza M, Raad I. Management of an outbreak of vancomycin-resistant enterococci in the medical intensive care unit of a cancer center. Infect Control Hosp Epidemiol. 2001 Apr;22(4):217-9. DOI: 10.1086/501892
21. Iosifidis E, Karakoula K, Protonotariou E, Kaperoni M, Matapa E, Pournaras S, Koliouskas D, Sofianou D, Roilides E. Polyclonal outbreak of vancomycin-resistant Enterococcus faecium in a pediatric oncology department. J Pediatr Hematol Oncol. 2012 Oct;34(7):511-6. DOI: 10.1097/MPH.0b013e318257a5d3
22. Kawalec M, Gniadkowski M, Hryniewicz W. Outbreak of vancomycin-resistant enterococci in a hospital in Gdask, Poland, due to horizontal transfer of different Tn1546-like transposon variants and clonal spread of several strains. J Clin Microbiol. 2000 Sep;38(9):3317-22.
23. Kawalec M, Gniadkowski M, Zaleska M, Ozorowski T, Konopka L, Hryniewicz W. Outbreak of vancomycin-resistant Enterococcus faecium of the phenotype VanB in a hospital in Warsaw, Poland: probable transmission of the resistance determinants into an endemic vancomycin-susceptible strain. J Clin Microbiol. 2001 May;39(5):1781-7. DOI: 10.1128/JCM.39.5.1781-1787.2001
24. Kawalec M, Kedzierska J, Gajda A, Sadowy E, Wegrzyn J, Naser S, Skotnicki AB, Gniadkowski M, Hryniewicz W. Hospital outbreak of vancomycin-resistant enterococci caused by a single clone of Enterococcus raffinosus and several clones of Enterococcus faecium. Clin Microbiol Infect. 2007 Sep;13(9):893-901. DOI: 10.1111/j.1469-0691.2007.01774.x
25. Knoll M, Daeschlein G, Okpara-Hofmann J, Klare I, Wilhelms D, Wolf HH, Borneff-Lipp M. Outbreak of vancomycin-resistant enterococci (VRE) in a hematological oncology ward and hygienic preventive measures. A long-term study. Onkologie. 2005 Apr;28(4):187-92. DOI: 10.1159/000084061
26. Lavery A, Rossney AS, Morrison D, Power A, Keane CT. Incidence and detection of multi-drug-resistant enterococci in Dublin hospitals. J Med Microbiol. 1997 Feb;46(2):150-6. DOI: 10.1099/00222615-46-2-150
27. Lesens O, Mihaila L, Robin F, Baud O, Romaszko JP, Tourniac O, Constantin JM, Souweine B, Bonnet R, Bouvet A, Beytout J, Traore O, Laurichesse H. Outbreak of colonization and infection with vancomycin-resistant Enterococcus faecium in a French university hospital. Infect Control Hosp Epidemiol. 2006 Sep;27(9):984-6. DOI: 10.1086/504932

28. Loeb M, Salama S, Armstrong-Evans M, Capretta G, Olde J. A case-control study to detect modifiable risk factors for colonization with vancomycin-resistant enterococci. Infect Control Hosp Epidemiol. 1999 Nov;20(11):760-3. DOI: 10.1086/501580

29. Marcadé G, Micol JB, Jacquier H, Raskine L, Donay JL, Nicolas-Viaud S, Rouveau M, Ribaud P, Dombret H, Leclercq R, Cambau E. Outbreak in a haematology unit involving an unusual strain of glycopeptide-resistant Enterococcus faecium carrying both vanA and vanB genes. J Antimicrob Chemother. 2014 Feb;69(2):500-5. DOI: 10.1093/jac/dkt376

30. McCarthy KM, Van Nierop W, Duse A, Von Gottberg A, Kassel M, Perovic O, Smego R. Control of an outbreak of vancomycin-resistant Enterococcus faecium in an oncology ward in South Africa: effective use of limited resources. J Hosp Infect. 2000 Apr;44(4):294-300. DOI: 10.1053/jhin.1999.0696

31. Montecalvo MA, Horowitz H, Gedris C, Carbonaro C, Tenover FC, Issah A, Cook P, Wormser GP. Outbreak of vancomycin-, ampicillin-, and aminoglycoside-resistant Enterococcus faecium bacteremia in an adult oncology unit. Antimicrob Agents Chemother. 1994 Jun;38(6):1363-7. DOI: 10.1128/AAC.38.6.1363

32. Nolan SM, Gerber JS, Zaoutis T, Prasad P, Rettig S, Gross K, McGowan KL, Reilly AF, Coffin SE. Outbreak of vancomycin-resistant enterococcus colonization among pediatric oncology patients. Infect Control Hosp Epidemiol. 2009 Apr;30(4):338-45. DOI: 10.1086/596202

33. Nourse C, Murphy H, Byrne C, O'Meara A, Breatnach F, Kaufmann M, Clarke A, Butler K. Control of a nosocomial outbreak of vancomycin resistant Enterococcus faecium in a paediatric oncology unit: risk factors for colonisation. Eur J Pediatr. 1998 Jan;157(1):20-7.

34. Oh HS, Kim EC, Oh MD, Choe KW. Outbreak of vancomycin resistant enterococcus in a hematology/oncology unit in a Korean University Hospital, and risk factors related to patients, staff, hospital care and facilities. Scand J Infect Dis. 2004;36(11-12):790-4. DOI: 10.1080/00365540410021117

35. Ozorowski T, Kawalec M, Zaleska M, Konopka L, Hryniewicz W. The effect of an antibiotic policy on the control of vancomycin-resistant enterococci outbreak and on the resistance patterns of bacteria isolated from the blood of patients in a hematology unit. Pol Arch Med Wewn. 2009 Nov;119(11):712-8.

36. Park SH, Park C, Choi SM, Lee DG, Kim SH, Kwon JC, Byun JH, Choi JH, Yoo JH. Molecular epidemiology of vancomycin-resistant Enterococcus faecium bloodstream infections among patients with neutropenia over a 6-year period in South Korea. Microb Drug Resist. 2011 Mar;17(1):59-65. DOI: 10.1089/mdr.2010.0091

37. Pendle S, Jelfs P, Olma T, Su Y, Gilroy N, Gilbert GL. Difficulties in detection and identification of Enterococcus faecium with low-level inducible resistance to vancomycin, during a hospital outbreak. Clin Microbiol Infect. 2008 Sep;14(9):853-7. DOI: 10.1111/j.1469-0691.2008.02052.x

38. Rizkalla EA, Moore JE, Marshall SA, Murphy PG. Glycopeptide-resistant enterococci in Northern Ireland: first reported outbreak. J Antimicrob Chemother. 1997 Oct;40(4):607-8. DOI: 10.1093/jac/40.4.607

39. Rubin LG, Tucci V, Cercenado E, Eliopoulos G, Isenberg HD. Vancomycin-resistant Enterococcus faecium in hospitalized children. Infect Control Hosp Epidemiol. 1992 Dec;13(12):700-5. DOI: 10.2307/30146486

40. Sample ML, Gravel D, Oxley C, Toye B, Garber G, Ramotar K. An outbreak of vancomycin-resistant enterococci in a hematology-oncology unit: control by patient cohorting and terminal cleaning of the environment. Infect Control Hosp Epidemiol. 2002 Aug;23(8):468-70. DOI: 10.1086/502088

41. Schmidt-Hieber M, Blau IW, Schwartz S, Uharek L, Weist K, Eckmanns T, Jonas D, Rüden H, Thiel E, Brandt C. Intensified strategies to control vancomycin-resistant enterococci in immunocompromised patients. Int J Hematol. 2007 Aug;86(2):158-62. DOI: 10.1532/IJH97.E0632

42. Schuster F, Graubner UB, Schmid I, Weiss M, Belohradsky BH. Vancomycin-resistant-enterococci--colonization of 24 patients on a pediatric oncology unit. Klin Padiatr. 1998 Jul-Aug;210(4):261-3. DOI: 10.1055/s-2008-1043889

43. Singh-Naz N, Sleemi A, Pikis A, Patel KM, Campos JM. Vancomycin-resistant Enterococcus faecium colonization in children. J Clin Microbiol. 1999 Feb;37(2):413-6.

44. Valdezate S, Miranda C, Navarro A, Freitas AR, Cabrera JJ, Carrasco G, Coque TM, Jiménez-Romano E, Saéz-Nieto JA. Clonal outbreak of ST17 multidrug-resistant Enterococcus faecium harbouring an Inc18-like::Tn1546 plasmid in a haemo-oncology ward of a Spanish hospital. J Antimicrob Chemother. 2012 Apr;67(4):832-6. DOI: 10.1093/jac/dkr545

45. Wardal E, Markowska K, Zabicka D, Wróblewska M, Giemza M, Mik E, Połowniak-Pracka H, Woźniak A, Hryniewicz W, Sadowy E. Molecular analysis of vanA outbreak of Enterococcus faecium in two Warsaw hospitals: the importance of mobile genetic elements. Biomed Res Int. 2014;2014:575367. DOI: 10.1155/2014/575367

46. Worth LJ, Thursky KA, Seymour JF, Slavin MA. Vancomycin-resistant Enterococcus faecium infection in patients with hematologic malignancy: patients with acute myeloid leukemia are at high-risk. Eur J Haematol. 2007 Sep;79(3):226-33. DOI: 10.1111/j.1600-0609.2007.00911.x

47. Yoo JH, Lee DG, Choi SM, Choi JH, Shin WS, Kim M, Yong D, Lee K, Min WS, Kim CC. Vancomycin-resistant enterococcal bacteremia in a hematology unit: molecular epidemiology and analysis of clinical course. J Korean Med Sci. 2005 Apr;20(2):169-76. DOI: 10.3346/jkms.2005.20.2.169

48. De Angelis G, Cataldo MA, De Waure C, Venturiello S, La Torre G, Cauda R, Carmeli Y, Tacconelli E. Infection control and prevention measures to reduce the spread of vancomycin-resistant enterococci in hospitalized patients: a systematic review and meta-analysis. J Antimicrob Chemother. 2014 May;69(5):1185-92. DOI: 10.1093/jac/dkt525

49. Siegel JD, Rhinehart E, Jackson M, Chiarello L; Healthcare Infection Control Practices Advisory Committee. Management of multidrug-resistant organisms in health care settings, 2006. Am J Infect Control. 2007 Dec;35(10 Suppl 2):S165-93. DOI: 10.1016/j.ajic.2007.10.006

50. Ruhnke M, Arnold R, Gastmeier P. Infection control issues in patients with haematological malignancies in the era of multidrug-resistant bacteria. Lancet Oncol. 2014 Dec;15(13):e606-19. DOI: 10.1016/S1470-2045(14)70344-4

51. Donskey CJ, Chowdhry TK, Hecker MT, Hoyen CK, Hanrahan JA, Hujer AM, Hutton-Thomas RA, Whalen CC, Bonomo RA, Rice LB. Effect of antibiotic therapy on the density of vancomycin-resistant enterococci in the stool of colonized patients. N Engl J Med. 2000 Dec;343(26):1925-32. DOI: 10.1056/NEJM200012283432604

52. Kaki R, Yu Y, O'Neill C, Lee C, Mertz D; Hamilton Health Sciences Infection Prevention and Control Team. Vancomycin-resistant enterococcus (VRE) transmission and risk factors in contacts of VRE carriers. Infect Control Hosp Epidemiol. 2014 Jul;35(7):876-9. DOI: 10.1086/676864

53. McKinnel JA, Kunz DF, Moser SA, Vangala S, Tseng CH, Shapiro M, Miller LG. Patient-level analysis of incident vancomycin-resistant enterococci colonization and antibiotic days of therapy. Epidemiol Infect. 2016 Jun;144(8):1748-55. DOI: 10.1017/S0950268815003118

54. Higgins PG, Koehler D, Chan JZ, Cornely OA, Fätkenheuer G, Gillis M, Pallen MJ, Tien J, Seifert H, Vehreschild MJ, Millard AD. Draft Genome Sequences of Nine Clinical Isolates of Vancomycin-Resistant Enterococci. Genome Announc. 2016 Aug 18;4(4). pii: e00803-16. DOI: 10.1128/genomeA.00803-16

55. Raven KE, Reuter S, Reynolds R, Brodrick HJ, Russell JE, Török ME, Parkhill J, Peacock SJ. A decade of genomic history for healthcare-associated Enterococcus faecium in the United Kingdom and Ireland. Genome Res. 2016 Oct;26(10):1388-1396. DOI: 10.1101/gr.204024.116

56. Stone SP, Cooper BS, Kibbler CC, Cookson BD, Roberts JA, Medley GF, Duckworth G, Lai R, Ebrahim S, Brown EM, Wiffen PJ, Davey PG. The ORION statement: guidelines for transparent reporting of outbreak reports and intervention studies of nosocomial infection. Lancet Infect Dis. 2007 Apr;7(4):282-8. DOI: 10.1016/S1473-3099(07)70082-8

57. Timmers GJ, van der Zwet WC, Simoons-Smit IM, Savelkoul PH, Meester HH, Vandenbroucke-Grauls CM, Huijgens PC. Outbreak of vancomycin-resistant Enterococcus faecium in a haematology unit: risk factor assessment and successful control of the epidemic. Br J Haematol. 2002 Mar;116(4):826-33. DOI: 10.1046/j.0007-1048.2002.03339.x

Corresponding author:
Nikos Ulrich
Institute for Hygiene and Environmental Medicine, Charité – University Medicine Berlin, Hindenburgdamm 27, 12203 Berlin, Germany, Phone: +49 30 450 577 612
nikos-konstantin.ulrich@charite.de

Please cite as
Ulrich N, Gastmeier P. Where is the difference between an epidemic and a high endemic level with respect to nosocomial infection control measures? An analysis based on the example of vancomycin-resistant Enterococcus faecium in hematology and oncology departments. GMS Hyg Infect Control. 2017;12:Doc14.
DOI: 10.3205/dgkh000299, URN: urn:nbn:de:0183-dgkh0002993

This article is freely available from
http://www.egms.de/en/journals/dgkh/2017-12/dgkh000299.shtml

Published: *2017-08-28*