

## Rapid communications

# EXPERIENCE OF EUROPEAN INTENSIVE CARE PHYSICIANS WITH INFECTIONS DUE TO ANTIBIOTIC-RESISTANT BACTERIA, 2009

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A survey was performed among European intensive care physicians to obtain information about their perception and experience with selected antibiotic-resistant bacteria. Seventy-eight out of 95 (82%) participants considered having to deal with infections due to antibiotic-resistant bacteria in the intensive care unit where they work as a major or significant problem. Methicillin-resistant *Staphylococcus aureus* (MRSA) and third-generation cephalosporin-resistant *Enterobacteriaceae* were the most frequently reported antibiotic-resistant bacteria with 69 (73%) and 67 (71%) participants reporting having treated at least one patient with such an infection during the preceding six months, respectively. Antibiotic-resistant Gram-negative bacteria, including carbapenem-resistant *Enterobacteriaceae*, were more frequently reported than any selected antibiotic-resistant Gram-positive bacteria, with the exception of MRSA. Fifty (53%) participants declared having treated at least one patient infected with a bacterium totally or almost totally resistant to available antibiotics during the past six months, with 8 participants having treated more than 10 such patients and 13 having treated from 3 to 10 such patients.

### Introduction

Antibiotic resistance is a threat to public health and compromises appropriate therapy of infected patients, in particular for infections in the most severely ill in hospitals [1,2]. Increasingly, intensive care physicians in Europe and elsewhere are confronted with patients infected by bacteria for which limited or no adequate therapeutic options are available [2-4]. Data on the situation of antibiotic resistance in Europe are provided by the European Antimicrobial Resistance Surveillance System (EARSS) [5], however these data are not specific for patients in intensive care units (ICUs). There are studies on antibiotic resistance in European intensive care patients, but these are limited to only a few ICUs and countries [1,6-7]. Additionally, there is little data on infections with bacteria that are totally or almost totally resistant to antibiotics that are currently emerging in Europe [8]. In an attempt to obtain information on the perception and experience of European intensive care physicians on infections caused by antibiotic-resistant bacteria, a survey was conducted through the European Society of Intensive Care Medicine (ESICM) among its members in 2009. We report here the first results of this survey.

### Methods

The survey was designed by the European Centre for Disease Prevention and Control (ECDC) with input from an ECDC/European Medicines Agency (EMA) Joint Working Group [9] and then proposed to the Scientific Committee of ESICM. The survey included questions about the experience of the respondent with intensive care medicine and antibiotic prescribing, as well as about the ICU in which they work. It also included questions about perception of the respondent of the problem of antibiotic resistance and the number of patients that were treated, during the preceding six months in the ICU where they work, for infections caused by each of the antibiotic-resistant bacteria listed in the table. These antibiotic-resistant bacteria were selected because they are, in most cases, multidrug-resistant.

Participants gave answers on their experience during the past six months following a semi-quantitative scale: "often" (> 10 patients), "sometimes" (3-10 patients), "rarely" (1-2 patients) and never. The survey was endorsed by ESICM through its European Critical Care Network in March 2009. It was then posted on the ESICM website in its section "Survey of the month" in the beginning of April 2009 and was closed on 8 June 2009.

### Results

#### Characteristics of participants

After excluding responses issued from participants from non-European countries or non-ESICM members, 95 responses were analysed. Responses were obtained from European ESICM members from 24 countries: Austria (2 participants), Belgium (5), Croatia (2), Denmark (2), France (4), Germany (8), Greece (3), Hungary (1), Ireland (1), Israel (1, ESICM includes this country among European countries), Italy (14), Lithuania (1), Luxembourg (1), Montenegro (1), Netherlands (1), Portugal (12), Romania (5), Serbia (1), Slovakia (1), Spain (12), Sweden (2), Switzerland (1) and United Kingdom (14).

Among the participants, the median time since graduation as MD was 20 years (25th-75th percentiles: 13-27 years). Seventy-nine (83%) participants were intensive care medicine specialists with a median time since specialisation of 11 years (25th-75th percentiles: 4-18 years). Eleven participants were still in training and five had a different specialty than intensive care medicine. Seventy-five (79%) ICUs were medico-surgical ICUs with a median

size of 10 beds (25th-75th percentiles: 7-16 beds) and a median of 510 admissions per year (25th-75th percentiles: 350-850). To the question “How often do you personally prescribe antibiotic therapy to ICU patients?”, 88 (93 %) responded “commonly (> 10 patients per week)” or “often ( $\geq 3$  patients per week)”.

#### Perception of and experience with antibiotic-resistant bacteria

Having to deal with infections due to antibiotic-resistant bacteria in the ICU where they work was considered as a major or significant problem by 78 (82%) participants. The experience

of the participants of treating patients with infections due to the selected antibiotic-resistant bacteria is summarised in the Figure. Among Gram-positive bacteria, methicillin-resistant *Staphylococcus aureus* (MRSA) was the most frequently reported with 69 (73%) participants reporting having treated at least one patient with an MRSA infection during the preceding six months. Vancomycin-resistant *Enterococcus* spp. (VRE) and penicillin-resistant *Streptococcus pneumoniae* were much less frequently reported, and vancomycin-resistant or -intermediate *S. aureus* (VRSA/VISA) was the least frequently reported antibiotic-resistant

TABLE

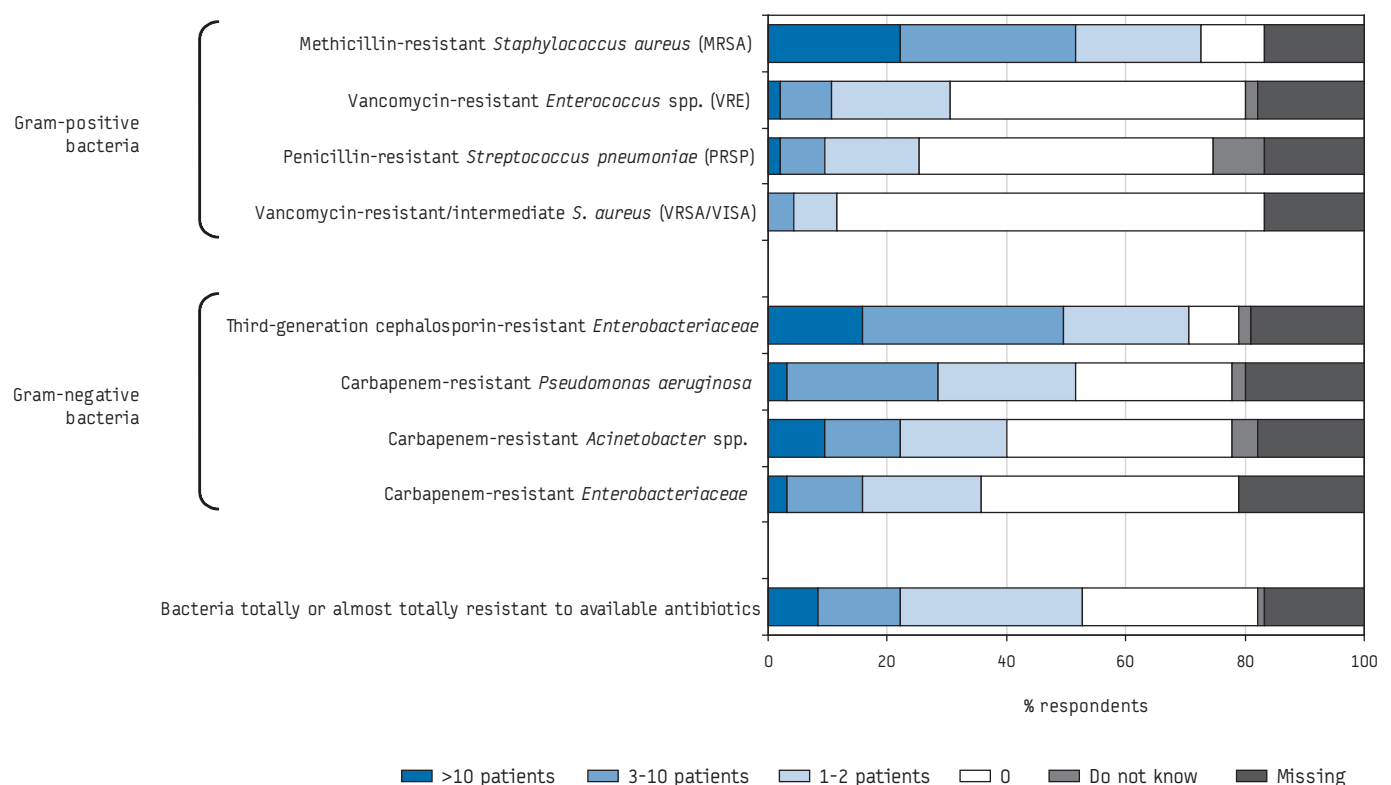
Antibiotic-resistant bacteria selected for the European intensive care physicians survey, 2009

Gram-positive bacteria	Methicillin-resistant <i>Staphylococcus aureus</i> (MRSA)
	Vancomycin-resistant/intermediate <i>S. aureus</i> (VRSA/VISA)
	Vancomycin-resistant <i>Enterococcus</i> spp. (VRE)
	Penicillin-resistant <i>Streptococcus pneumoniae</i>
Gram-negative bacteria	Third-generation cephalosporin (cefotaxime or ceftazidime or ceftriaxone)-resistant <i>Enterobacteriaceae</i> (e.g. <i>Escherichia coli</i> , <i>Klebsiella</i> spp., <i>Enterobacter</i> spp.)
	Carbapenem (imipenem or meropenem)-resistant <i>Enterobacteriaceae</i>
	Carbapenem-resistant <i>Pseudomonas aeruginosa</i>
	Carbapenem-resistant <i>Acinetobacter</i> spp.
Bacteria totally or almost totally resistant to available antibiotics*	

\*Any Gram-positive or Gram-negative bacteria considered as totally or almost totally resistant to available antibiotics based upon the appreciation of the participant. In addition, the participant was asked to specify the name of these bacteria.

FIGURE

Percentage of participants who reported having treated patients with infections due to selected antibiotic-resistant bacteria during the past six months, 2009 (n=95 participants)



Gram-positive bacteria with only 11 (12%) participants reported having treated such patients during the preceding six months. Among Gram-negative bacteria, third-generation cephalosporin-resistant *Enterobacteriaceae* were the most frequently reported with 67 (71%) participants reporting having treated at least one patient with such an infection during the preceding six months. Other selected antibiotic-resistant Gram-negative bacteria were less frequently reported. The least reported antibiotic-resistant Gram-negative bacterium, i.e. carbapenem-resistant *Enterobacteriaceae*, was more frequently reported than any selected antibiotic-resistant Gram-positive bacteria with the exception of MRSA (Figure). Forty-eight (51%) participants reported having treated at least three patients in two or more of the selected categories of antibiotic-resistant bacteria during the preceding six months, thus showing that antibiotic resistance problems faced by the participants in the unit where they work are often not limited to one single antibiotic-resistant bacterium.

Finally, 50 participants declared having treated at least one patient infected with a bacterium totally or almost totally resistant to available antibiotics during the past six months. Moreover, 8 participants declared having treated more than 10 such patients and 13 participants declared having treated from 3 to 10 such patients during the past six months (Figure). Forty-two participants mentioned the names of these bacteria totally or almost totally resistant to available antibiotics or the names of any other antibiotic-resistant bacteria that posed a problem when considering patient therapy in the ICU where they work. Among the 55 bacteria mentioned, most were Gram-negative bacteria: *Pseudomonas* spp. (mentioned 23 times, mostly *P. aeruginosa*), *Acinetobacter* spp. (17 times), *Stenotrophomonas maltophilia* (9 times) and *Enterobacteriaceae* (5 times). *Enterococcus* spp. was only cited once.

### Discussion

In hospitals, intensive care units are considered as areas where antibiotic resistance problems are the largest due to the combination of multiple factors. These factors include the concentration of severely ill patients requiring specialised care, the high frequency of use of medical devices and the high frequency of antibiotic treatment [1]. Not surprisingly, most intensive care physicians that participated in the survey felt that antibiotic resistance was a major or significant problem in their practice.

Overall, the picture of antibiotic resistance in Europe provided by this study is similar to that provided by EARSS [5], with MRSA and third-generation cephalosporin-resistant *Enterobacteriaceae* being the most frequently antibiotic-resistant bacteria encountered by European intensive care physicians. The survey also confirmed the observation of a recent joint technical report of ECDC and EMEA which showed that, with the exception of MRSA, the burden of antibiotic resistance in Europe was now mostly due to antibiotic-resistant Gram-negative bacteria [9]. In addition, it showed that many European intensive care physicians are facing patients with infections due to bacteria, mostly Gram-negative, totally or almost totally resistant to available antibiotics. The ECDC/EMEA joint technical report showed that there were very few new antibiotics with a novel mechanism of action in development to meet the challenge of multidrug-resistant bacteria, in particular to treat infections due to Gram-negative bacteria [9]. Patients with infections due to carbapenem-resistant Gram-negative bacteria often require the use of old and toxic antibiotics such as colistin [3, 8].

This study has several limitations. Firstly, it is based on the voluntary declaration of a small fraction of the more than 5,000 ESICM members. This is likely to have resulted in selection bias towards the more concerned ESICM members, in particular from southern Europe. Although the survey instructions explicitly mentioned that only one intensive care physician per ICU should participate in the survey, we cannot exclude duplicate participation from the same ICU. Finally, participants had to answer retrospectively on their experience during the preceding six months, which may have resulted in recall bias and may be the reason for approximately 20 % of missing information. The data presented here, however, are likely to be an underestimate of the situation in the included ICUs since most participants with missing information on specific antibiotic-resistant bacteria considered infections with antibiotic-resistant bacteria in the ICU where they work as a major or significant problem. Despite these limitations, the study provides a first snapshot, based on recalled recent experience, of the current antibiotic resistance problems faced by European intensive care physicians when treating patients. It also highlighted the problem of infections due to totally or almost totally resistant bacteria, which are not covered by existing surveillance systems. More comprehensive studies are now needed to assess the extent of the prevalence of such infections with totally or almost totally resistant bacteria as well as to determine the risk factors for colonization and infection with these bacteria. In the meantime, intensive care and other physicians should be made aware of their current emergence in Europe.

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