

Control of emerging extensively drug-resistant organisms (eXDRO) in France: a survey among infection preventionists from 286 healthcare facilities

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Abstract We performed a multicenter survey in May–June 2012 to assess strategies in preventing the spread of emerging extensively drug-resistant organisms (eXDRO), including glycopeptide-resistant enterococci and carbapenemase-producing Enterobacteriaceae, in a convenient sample of French healthcare facilities (HCFs). The collected data included organization and measures to: (1) identify patients at risk for carrying eXDRO, (2) investigate and control sporadic cases or outbreaks, and (3) describe prior 2010–2012 episodes with one or more colonized patients. Of the 286 participating HCFs, 163 (57 %) and 134 (47 %) reported having a specific procedure to detect repatriates or patients hospitalized in foreign countries within the last year, respectively. Among the 97 HCFs with prior at-risk patient management experience, contact precautions, hospitalization in a

single room, and screening for eXDRO carriage were quasi-systematically performed ($n=92/97$, 95 %). The alleged time between admission and alert ranged from 24 to 48 h after the patient's admission; 203 (71 %) HCFs recommended obtaining three successive negative screening samples to declare a patient free of eXDRO colonization. During the last two years, 64 HCFs (23 %) had to manage at least one eXDRO case, with a total of 20 outbreaks with more than one secondary case. This first national survey shows that French HCFs were not totally ready to control eXDRO spread in 2012. Their previous experiences and capacities in controlling eXDRO outbreaks are quite heterogeneous from one hospital to another. Further researches are needed in order to understand the constraints in applying national guidance.

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Introduction

The emergence of antibiotic resistance is a worldwide major public health challenge. The control of antibiotic-resistant bacteria spread includes strategies able to reduce the antibiotic exposure and to prevent cross-transmission between patients [1–3]. As many countries in Europe [4–6], France is affected by sporadic cases or limited outbreaks of emerging extensively drug-resistant organisms (eXDRO) [7]. In France, these eXDRO include glycopeptide-resistant enterococci (GRE) [8–11] and carbapenemase-producing Enterobacteriaceae (CPE) [12–15]. These two eXDRO were selected because they are (1) commensal bacteria of the digestive flora and (2) multidrug-resistant, with possible transfer of the resistance mechanism between bacterial species through mobile genetic elements. Those eXDRO have the potentiality to spread in the community, but, at the present time, cases remain

sporadic or are responsible for small outbreaks in French healthcare facilities (HCFs).

Currently, most eXDRO cases are associated with a history of recent stay in foreign hospitals, especially in countries with a high prevalence of eXDRO [16]. In France, the first national guidelines to limit the spread of GRE and CPE imported from repatriates and travelers hospitalized in foreign countries were published in 2010 [17]. These guidelines recommend to hospitalize at-risk patients under contact isolation precautions at hospital admission and to perform a systematic rectal swab for CPE or VRE colonization. If the rectal swab is positive, contact patients must also be screened weekly. If secondary cases are detected, eXDRO carriers, contact patients, and patients newly admitted must be separated in three distinct areas with dedicated staff, respectively. Transfer must be limited until outbreak control. If a contact patient needs to be transferred to another ward or hospital for medical reasons, isolation precaution must be maintained until three negative rectal swabs for CPE and GRE colonization are obtained. Since this publication, a national legislation was published using the mandatory early warning reporting system which has been developed by the French Institute for Public Health Surveillance (InVS) [18]. Data from this surveillance system showed a steady increase in the number of reported cases of CPE, from ten episodes in 2009 to 102 in 2014 (March), with a total number of 1,644 patients (infection 26 %); 12 % of episodes have generated secondary cases. Sixty-six percent of the episodes were caused by *Klebsiella pneumoniae* and the most frequent carbapenemase enzyme was OXA-48 (74 %) [19]. From 2003 to 2011, 888 episodes of GRE were declared by the national mandatory system, with 2,078 patients (infection 23 %); 25 % of episodes have generated secondary cases. Since 2011, the French GRE incidence has reached a plateau [19].

During the period 2010–2012, no assessment of the implementation of the French guidelines has been done across HCFs. Thus, in 2012, the French Society for Hospital Hygiene (SF2H) performed a national questionnaire survey to assess strategies for managing the risk of eXDRO spread in French HCFs.

Methods

Study period and participants

The study was performed in May and June 2012. The review board of the SF2H approved the survey and study design. Infection control practitioners were invited via e-mail to participate in an anonymous, voluntary survey, accessed through an Internet link, that took <15 min to complete. We used an e-mail database of infection control practitioners who were currently members of the SF2H on the date of the study. Non-

randomized selection was performed and the invitation was sent to almost 600 French infection control teams (ICTs).

Data collection

Collected data included variables related to: (1) organization and measures to identify at-risk patients for eXDRO colonization (i.e., repatriates or patients with recent hospitalization <1 year in a foreign country and patients who have been previously in contact with an eXDRO carrier or patients previously defined as eXDRO carriers, when they are rehospitalized, respectively); 2) existing local procedures to control eXDRO spread and to investigate sporadic cases: screening strategies for eXDRO colonization, surveillance of contact patients (i.e., patients exposed to an eXDRO carrier and cared by the same healthcare workers), hospital re-admission or cohorting, and additional control measures in outbreak situations. We also aimed to describe prior episodes with one or more patients colonized with eXDRO and control measures that have been performed.

Statistics

Data were described using the mean and standard deviation (SD) for continuous variables and proportions for qualitative variables. Continuous variables were compared using the Kruskal–Wallis test, qualitative variables using the χ^2 test, or Fisher's exact test. Results were stratified by the size of the healthcare setting, according to their bed number: 500 beds or more, between 301 and 500 beds, between 100 and 300 beds, and less than 100 beds. Statistical analysis was performed using Epi Info 6.04d software (CDC, Atlanta, GA, USA).

Results

Participants

A total of 286 HCFs participated in the survey (11 % of French hospitals), with 24 university hospitals (77 % of French university hospitals); 156 (54 %) and 130 (46 %) HCFs were public or private centers, respectively; 235 HCFs provided acute healthcare (82 %) and 51 (18 %) were rehabilitation or long-term facilities. The 286 HCFs were located in the national territory as follows: North (16 %), North-East (11 %), North-West (28 %), South-West (7 %), and South-East (38 %). Of the HCFs, 134 (47 %) had a microbiology laboratory located in the hospital, but its capacity to diagnose eXDRO was not assessed; 226 HCFs (79 %) had defined a list of prioritized eXDRO requiring specific control measures. Most HCFs ($n=214$) included GRE and CPE in their list (Table 1). HCFs included saprophytic multidrug-resistant bacteria, such as imipenem-resistant *Acinetobacter baumannii*

Table 1 Strategies to control the spread of emerging extensively drug-resistant organisms (eXDRO) from repatriates or patients with recent hospitalization in foreign hospitals among 286 French hospitals in 2012

Categories	Hospitals, n (%)	eXDRO including GRE and CPE, n (%) ^a	Reported detecting procedures		Detection and systematic alert to ICT <24 h, n (%) ^c	Operational procedure, n (%) ^d
			Repatriates, n (%) ^b	Patients with recent hospitalization in foreign hospitals, n (%) ^b		
>500 beds	55 (19.4)	53 (96.4)	42 (77.8)	37 (67.3)	28 (50.9)	5 (9.1)
301–500 beds	54 (18.9)	46 (85.2)	33 (63.5)	29 (54.7)	27 (50.9)	13 (24.1)
101–300 beds	98 (34.3)	69 (70.4)	43 (47.8)	42 (45.7)	37 (40.2)	39 (39.8)
<100 beds	76 (26.6)	44 (57.9)	35 (46.7)	28 (37.8)	24 (32.4)	39 (51.3)
Total	283*	212 (74.1)	153(56.5)	136 (49.6)	116 (42.3)	96 (33.6)

GRE glycopeptide-resistant enterococci; CPE carbapenemase-producing Enterobacteriaceae; ICT infection control team

*The numbers of beds was not available for three healthcare settings

^a $p < 10^{-6}$

^b $p < 10^{-3}$

^c $p = 0.01$

^d $p < 10^{-6}$

($n = 180$, 63 %) or multidrug-resistant *Pseudomonas aeruginosa* ($n = 57$, 20 %), in their list. Of the 286 participating HCFs, 163 (57 %) and 134 (47 %) reported having a specific procedure to early detect at hospital admission repatriates or patients recently hospitalized abroad, respectively (Table 1). And 22 % of HCFs had a global and comprehensive strategy, including early detective and active surveillance by the systematic screening of contact patients.

Management and organization to control the spread of eXDRO in French HCFs

Procedures for the management of patients colonized with eXDRO

One hundred and eighty (63 %) HCFs reported separate eXDRO-positive patients and contact patients in two or three distinct areas and dedicated specific healthcare workers (HCWs). When the first eXDRO-positive case is detected, 177 HCFs (62 %) reported also stopping new admissions until all the contact patients have been screened for eXDRO colonization. In situations with secondary cases (outbreak), 149 HCFs (52 %) reported separate patients in three distinct areas: (1) one area for eXDRO-positive patients, (2) a second area for contact patients, and (3) a third area for newly admitted patients. The cohorting of patients was completed with additional HCWs in 132 HCFs (46 %).

Two hundred and three (71 %) HCFs reported performing a monthly rectal screening for three months to assess the infectious status of eXDRO carriers and the risk of cross-transmission. Moreover, 134 HCFs (47 %) reported systematically screening patients that have been previously colonized by eXDRO when they are rehospitalized.

Procedures for the management of contact patients

Contact patients are patients who have been in contact with an eXDRO carrier. They have been cared by the same staff (nurses and medical staff). The procedures to assess the infectious status of contact patients included systematic rectal screening of all patients in contact with an eXDRO patient, either weekly ($n = 226$, 79 %) and/or at discharge ($n = 114$, 40 %). The indications to repeat rectal screening in repatriates who were negative for eXDRO colonization at admission were new antibiotic exposure during hospital stay ($n = 83$, 29 %) or transfer to a high-risk ward ($n = 60$, 21 %). Eighty-three (29 %) HCFs reported having an automatic alert system to detect contact patients at hospital readmission.

French hospitals' experiences through eXDRO episodes between 2010 and 2012

Of the 286 participating HCFs, 97 (34 %) reported having managed at-risk patients at hospital admission. When at-risk patients were hospitalized in a French hospital, the ICTs reported to be early alerted in 71 % of repatriates' hospitalizations and in 54 % of hospitalizations of patients recently hospitalized abroad. Contact precautions, hospitalization in a single room, and screening for eXDRO carriage were quasi-systematically performed ($n = 92/97$, 95 %). Between 2010 and 2012, 64 HCFs (23 %) detected GRE or CPE cases by rectal swab, but only 52 of them were able to describe their episodes (Table 2): 32 episodes were sporadic situations without secondary cases and 20 were outbreak with at least one secondary case, for a total of 101 secondary cases. Among French hospitals with outbreak situations, ten HCFs (50 %) have managed more than five eXDRO-colonized patients and

Table 2 Management of repatriates or patients with recent hospitalization abroad and patients colonized by emerging extensively drug-resistant organisms (eXDRO) in 286 French hospitals in 2012

Categories	Hospitals, <i>n</i> (%)	Previous management of patients at risk for eXDRO, <i>n</i> (%) ^a	Alert to ICT <24 h, <i>n</i> (%) ^a	Patient screening ^b , <i>n</i> (%) ^a	Previous management of eXDRO episodes, <i>n</i> (%) ^a	Situation ^b		Additional specific precautions ^b , <i>n</i> (%)
						Sporadic, <i>n</i> (%)	Epidemic	
>500 beds	55 (19.2)	37 (67.3)	29 (78.4)	29 (78.4)	31 (56.4)	13 (54.2)	11 (45.8)	22 (75.9)
301–500 beds	54 (18.9)	21 (38.9)	17 (81.0)	13 (61.9)	14 (25.9)	9 (69.2)	4 (30.8)	7 (53.8)
101–300 beds	98 (34.3)	32 (32.7)	18 (34.6)	17 (53.1)	17 (17.3)	9 (64.3)	5 (35.7)	13 (86.7)
≤100 beds	76 (26.6)	7 (9.2)	4 (57.1)	3 (42.9)	2 (2.6)	1 (100)	0 (0)	1 (50.0)
Total	283 ^b	97 (34.3)	69 (70.4)	63 (64.3)	64 (22.6)	32 (61.5)	20 (38.5)	43 (72.9)

ICT infection control team

^a $p < 0.05$

^b The numbers of beds, additional specific precautions, and epidemic or sporadic cases was not available for 3, 5, and 12 healthcare settings, respectively

five hospitals (23 %) more than ten. Among the 52 first episodes in each HCF, eXDRO detection was obtained at hospital admission ($n=26$, 50 %) or later during hospital stay ($n=26$, 50 %); 27 (52 %) eXDRO-positive index patients were repatriates and 25 (48 %) were patients with recent hospitalization abroad. Specific measures to control the eXDRO spread were added in 34 (65 %) episodes, including environmental cleaning and focus on gloves and gowns. Training of nurses and medical staff was reported in 36 (70 %) of the 52 episodes.

Discussion

This declarative survey was performed to describe the management of at-risk patients or eXDRO carriers two years after the first publication of the French guidance in 2010 [17]. It was performed among 286 voluntary HCFs located in all French regions and representing all hospital categories, with a high proportion of teaching hospitals. This survey highlights the difficulties encountered for the management (detection, screening and surveillance, healthcare organization, transfer, communication) of these patients, emphasizing the challenge of the transition from the theory to the practice for effective intervention [20, 21].

A procedure for detecting at-risk patients existed in the majority of French HCFs but was currently operational in only a third of them. The procedure to detect at-risk patients at hospital admission is essential. The results of this study suggest that a large proportion of HCFs did not systematically develop a strategy to detect eXDRO carriers at different steps of the control, such as early detection, communication to the ICT, screening, surveillance, and monitoring of the carriage in colonized or in contact patients. As previously published, early detection and active surveillance are key factors for successful control of outbreaks [7, 22–24]. In this study, 22 % of HCFs had a global and comprehensive strategy, including

early detective and active surveillance. This proportion reached 58 % in the 24 large university hospitals. However, efforts should be made to increase the capacity of hospitals to implement specific measures to avoid the risk of regional spread through transfers or absence of active surveillance of colonized patients or contact patients [10, 25, 26]. To increase the efficacy of the contact measures, two-thirds of hospitals reported performing additional measures (“enhanced” measures) related to environmental cleaning and HCW clothing protection when an at-risk patient is detected positive for eXDRO.

The data published by the EARS-Net European network indicate that the two targeted eXDRO, GRE and CPE, are still rare in France, with resistance rates of less than 1 %, while other nearby European countries have alarmingly increasing rates or endemic situations, but higher prevalence rates have been observed in other European countries (Romania 13.7 %, Italy 28.8 %, and Greece 60.5 %) [27, 28]. GRE emerged in France since 2004 with sporadic cases and also outbreaks [9, 10]. The implementation of these global strategies appeared effective in preventing epidemic situations [10], unlike other countries with endemic situations [29]. In France, the same strategies were performed to control CPE outbreaks since 2010 [30]. Even if the number of CPE episodes increased, the number of outbreaks and the number of secondary cases per episode seem to decrease significantly [30].

The difficult-to-control eXDRO are related to the worldwide diffusion and the capacity of each HCF to detect early carbapenemase producers, at least in hospital settings [31]. This first French evaluation highlights the difficulties of many institutions to implement the specific measures. Only half of HCFs have published local guidelines to detect at-risk patients, patients in contact with eXDRO carriers, and eXDRO carriers, and few of them are really functional. In sporadic situations, the strategies are heterogeneous and all the specific measures to control eXDRO spread are rarely implemented.

Several findings may explain the difficulties of French HCFs to implement or respect guidelines. Isolation measures are a common approach to prevent the spread of multidrug-resistant organisms or eXDRO. Some HCFs interpret “isolation” as a “quarantine type” separation of the patient, who is not allowed to leave the isolation room. Other HCFs isolate patients within a multibed room, and others will designate a single room for the patient, but allow him or her to move around the hospital freely, with only HCWs encouraged to wear gloves and gowns during patient care. There are also substantial differences with respect to the staffing levels available to manage isolated patients between different HCFs. For instance, if a patient is in a single room for isolation purposes, the staff-to-patient ratio may not necessarily be increased and, therefore, less time is available for patient care activities. Some of the recommendations about patient isolation are likely to be impracticable in many French HCFs because of constraints on resources and due to economic burden (availability of single rooms, bringing in extra staff, use of dedicated staff for isolated patients, weekly screening for contact patients, and laboratory eXDRO detection), and there is no advice as to how to prioritize the various demands on resources. Many HCFs rely on administration staff to maintain safe staff levels. Such staff may not be appropriate for the care of eXDRO patients, because they may be less likely to comply with the procedures set out in the guidance. Moreover, they may be a possible vector of spread of these bacteria if they are also working in other healthcare settings.

Many HCFs do not yet have the capacity to automatically detect at-risk patients at hospital admission and to survey and screen contact patients during the current hospitalization, but also when they are rehospitalized many times after being discharged. Moreover, the French law forbids establishing a nominative list of eXDRO carriers between HCFs.

Finally, some eXDRO carriers remain hospitalized unnecessarily for long periods without being transferred to a downstream facility with suitable suites care, closer to home. These situations affect the care of these patients’ quality and security and expose services to epidemic risk.

To make the implementation of such specific measures easier, the French guidelines have been recently actualized [32, 33], taking into account European reports [34, 35], but the economic burden still persists. These guidelines provide flowcharts taking into account eight different situations when an at-risk patient is detected positive for eXDRO in acute-care or in long-term care facilities. Important standard measures need to be prioritized, such as collection and elimination of feces and urines, and hand hygiene [36]. The turn-around time from admission and eXDRO detection, the types of wards, the local healthcare organization, the architectural conditions, and the level of expertise of the ICT are major factors to consider in the decision to implement a specific and feasible control strategy. The strategy needs to be adapted and discussed

through a multidisciplinary approach and to be validated by the local and regional health authority committees, particularly in epidemic situations [37]. Such specific measures should not adversely affect patient health and should not limit the patient transfer to another hospital if necessary.

This survey has several limits and our results should be interpreted with caution. The selection of the hospitals was linked to the current SF2H membership of their infection control practitioner and the selection was non-randomized. Then, hospital participation may be likely related to hospitals with previous experience in the management of at-risk patients and eXDRO carriers in sporadic or epidemic situations.

In summary, this first national survey shows that French HCFs were not totally ready to control eXDRO spread in 2012. Their previous experiences and their capacities in controlling eXDRO outbreaks are quite heterogeneous from one hospital to another. Further researches are needed in order to understand the constraints in applying national guidance.

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