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Major article

Duration of carriage of carbapenem-resistant Enterobacteriaceae following hospital discharge

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Key Words:
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Background: Hospitalized carriers of carbapenem-resistant Enterobacteriaceae (CRE) are cohorted under contact precautions, including in the days between rehospitalization and surveillance culture results. This study investigates duration of CRE carriage to define populations requiring precautions upon readmission.
Methods: Patients with CRE-positive culture during 2009-2010 were followed up by rectal swab cultures taken retrospectively and prospectively for the study or as part of clinical follow-up.
Results: One hundred thirty-seven patients met the inclusion criteria, with follow-up cultures obtained from 97. Mean time to CRE negativity was 387 days (95% confidence interval: 312-463). Seventy-eight percent of patients (64/82) had positive culture at 3 months, 65% (38/58) at 6 months, and 39% (12/30) at 1 year. Duration of carriage was affected by repeat hospitalization ($P = .001$) and clinical, as opposed to surveillance, culture ($P = .002$).
Conclusion: CRE carriers from a previous hospitalization have a lower probability of CRE carriage upon readmission if the index specimen was a surveillance culture and 1 year passed without further hospitalization. Multiple hospitalizations and CRE disease extend duration of carriage. This study better defines patients requiring cohorting and isolation, thus limiting spread of CRE and allowing for improved allocation of infection control measures.

Carbapenemases in gram-negative bacteria were initially described in Japan in the early 1990s.[1] The first clinically significant isolate in Europe was reported in Italy in 1999.[2,3] The European reports described resistance mechanisms involving metallo-β-lactamases of the VIM and IMP families.[4] In the United States, a carbapenemase-producing organism was first described in 2001. Unlike in Europe, the mechanism involved was a serine carbapenemase and was initially discovered in *Klebsiella pneumoniae*; hence, it was termed *Klebsiella pneumoniae* carbapenemase (KPC).[5] This resistance mechanism spread quickly, primarily via *Klebsiella pneumoniae* (especially sequence type 258) but also via other Enterobacteriaceae, and a number of other serine carbapenemases, including other KPC subtypes, were discovered.[6-8] In Israel, carbapenem-resistant Enterobacteriaceae (CRE) were first described in 2007, and their resistance was shown to be similar to that shown in the United States, primarily involving KPC and *Klebsiella pneumoniae*.[9] CRE resistance to carbapenems is in addition to resistance to penicillins and cephalosporins, thus leaving a very limited number of treatment options for patients infected with these strains.[10,11] CRE may cause serious infections, especially bacteremia and urosepsis, and carries a high associated mortality rate.[10,12-16]

Patients diagnosed as suffering from CRE infection or as CRE carriers are treated under conditions of cohorting and contact isolation.[17,18] Upon rehospitalization, repeat surveillance cultures are obtained; pending culture results, these patients are taken care off under identical isolation conditions.[12] At the current time, the duration of CRE carriage following hospital discharge is unknown, and the formerly CRE-positive patient population that requires isolation and cohorting upon rehospitalization is not well defined. As yet, only 1 small study has attempted to identify patients at risk for continued CRE carriage.[19] The current study was designed to determine the duration of CRE carriage following hospital

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discharge in patients with an in-hospital CRE-positive culture. We attempted to quantify the time period after which CRE carriage can be ruled out without necessitating isolation. As a secondary objective, we endeavored to identify risk factors for continuing carriage of CRE.

METHODS

The study was conducted in the Shaare Zedek Medical Center, a 700-bed university-affiliated general hospital in Jerusalem, Israel. The hospital includes all major departments and services, including 3 medical and 2 geriatric wards, hematology and oncology, pediatrics, a surgical department including a vascular surgery unit, gynecology and obstetrics, cardiothoracic surgery, urology, orthopedics, plastic surgery, ophthalmology, otorhinolaryngology, and several intensive care units.

Patients

We retrieved medical records of adult patients hospitalized from January 2009 through December 2010 who had at least 1 CRE-positive culture. We excluded patients with a CRE-positive culture prior to 2009 (n = 4), organisms with resistance mechanisms other than KPC (as determined by the modified Hodge test[20] and polymerase chain reaction [PCR],[13] n = 95), patients whose initial culture was taken as an outpatient (n = 21), and patients who died during the hospitalization in which CRE was initially isolated (n = 67). Thus, 137 patients were included in the study population (Fig 1).

Patients were followed up by several methods. Following the initial hospitalization, many patients were subsequently readmitted, and a surveillance culture was taken as per protocol, or CRE was isolated from a clinical culture. Such cultures were included in the present study as follow-up cultures. Other patients had surveillance or clinical cultures taken as part of follow-up in hospital outpatient clinics. Patients who did not have a follow-up culture as part of a readmission or in an outpatient clinic were contacted by the investigators. Many such patients had died subsequent to hospitalization. Follow-up was attempted among the patients who were alive at the time of the study, as follows: If a contacted patient had surveillance cultures taken as part of follow-up by his primary care physician, these cultures were included in the trial. Patients who were successfully contacted and did not have a follow-up culture subsequent to hospitalization were asked to give a rectal swab for purposes of the study. Cultures taken prior to initiation of data collection for the study (ie, cultures taken in 2009-2010) were considered to be retrospective; those taken during the data collection period (January 2011 through February 2012), whether taken for purposes of clinical follow-up, for purposes of the study, or both, were considered to be prospective. Culture negativity was assumed if a patient had at least 1 negative culture that was not followed by any positive cultures. Among patients with at least 1 negative culture, 56% (n = 32 out of 57) had multiple negative cultures.

Demographic data, comorbidities, and characteristics of the index culture were collected for all patients included in the study population, both for those whom follow-up was available and for those whom it was not. The study was approved by the Institutional Review Board of Shaare Zedek Medical Center.

Culture and susceptibility testing

Rectal swabs, whether obtained by the investigators or obtained as part of clinical follow-up, were plated directly onto CHROMagar (Paris, France) KPC screening plates for CRE.[21] In addition, each swab was placed into an enrichment tube containing Mueller Hinton broth with 2 μg/mL ertapenem and 6 μg/mL of vancomycin and incubated at 35°C for 24 hours (overnight). All tubes with apparent bacterial growth were plated onto CHROMagar KPC plates. From June 1 to December 31, 2008, 965 samples were tested for CRE, of which 870 (90.15%) were negative, and 95 (9.85%) were positive. Among these, 44 of 65 (68%) were positive before enrichment and 21 of 65 (32%) afterwards (the remaining 30 samples involved clinical samples). Because more than 95% of the enrichment tubes show turbidity, technicians have since then plated all the enrichment broths. Thus, for the entire period of the study, all enrichment tubes, with or without turbidity, were plated. All gram-negative isolates were identified by biochemical reactions (phenotypical method). All CRE strains were tested for the presence of KPC gene by PCR and by modified Hodge test.[13,20]

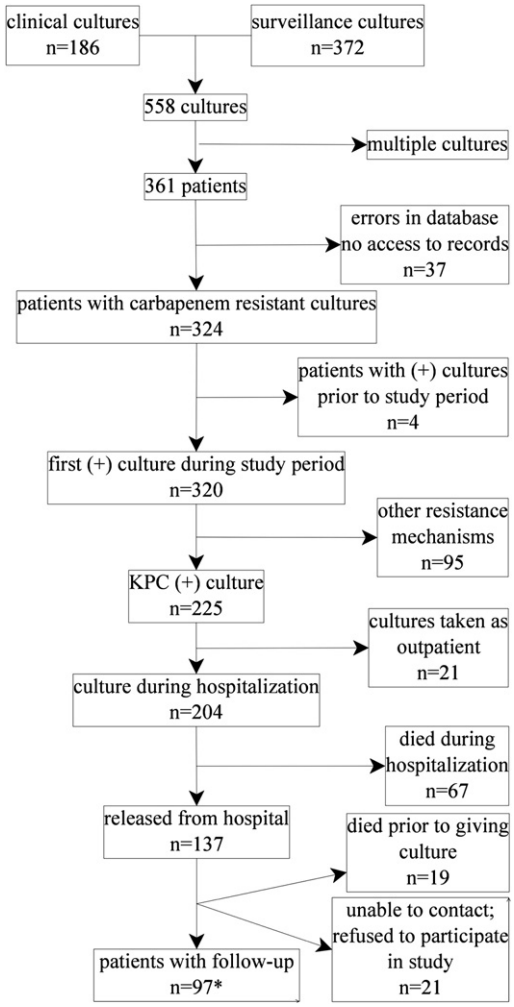

Fig 1. Study enrollment. *Of these, 18 (19%) had an index culture that was a clinical specimen, and 79 (81%) had an index culture that was a surveillance specimen.

Statistical analysis

To compare quantitative (continuous) variables between 2 independent groups, the 2-sample *t* test was applied as well as the non-parametric Mann-Whitney test. The association between 2 categorical variables was assessed using either χ^2 or Fisher exact test. Time to negative culture was analyzed using either Kaplan-Meier (KM) survival analysis with the log rank test for comparison of survival curves or the Cox regression model. All analysis was done using SPSS version 19 (IBM Corporation, Armonk, NY). All

Table 1
Characteristics of patients for whom follow-up was available versus patients for whom it was not

Variable	No follow-up culture available, n = 40 (%)	Follow-up culture available, n = 97 (%)	*P* value
Female	20 (50)	55 (57)	.474
Age at index culture; mean ± SD	75 ± 6 (range: 25-95)	78 ± 3 (range: 32-102)	.387
Alive at end of study/last follow-up	21 (53)	54 (56)	.735
Resident of a chronic care facility	21 (54)	59 (61)	.415
Hospitalized in medical wing			
At index culture	25 (63)	74 (76)	.269
At last follow-up	N/A	68 (70)	N/A
Foreign bodies			
Urinary catheter	15 (38)	39 (41)	.734
Gastrostomy	4 (10)	27 (28)	.023*
Nasogastric tube	11 (28)	10 (10)	.011*
Tracheostomy	3 (8)	7 (7)	.954
Comorbidities			
Diabetes mellitus	9 (23)	30 (31)	.320
Congestive heart failure	7 (18)	28 (29)	.165
Chronic lung disease	1 (3)	11 (11)	.096
Malignancy	11 (28)	13 (13)	.048*
Dementia	19 (48)	49 (51)	.748
eGFR (mL/min); mean ± SD	65 ± 8	71 ± 5	.218
Albumin (g/dL); mean ± SD	2.9 ± 0.2	3.1 ± 0.1	.054
Katz score; mean ± SD	2.2 ± 0.4	2.3 ± 0.3	.900
Karnovsky score; mean ± SD	50 ± 6	48 ± 3	.582
Index culture characteristics			
Days from admission to culture, mean ± SD	12.8 ± 2.5	10.9 ± 1.8	.240
Surveillance culture	28 (70)	79 (81)	.141
Clinical culture	12 (30)	18 (19)	.141
Urine	7 (18)	14 (14)	
Blood	0 (0)	2 (2)	
Other	5 (13)	2 (2)	
Klebsiella pneumoniae identified	33 (83)	84 (87)	.537
Multiple organisms identified	5 (13)	9 (9)	.571

eGFR, Estimated glomerular filtration rate; *N/A*, not applicable; *SD*, standard deviation.
NOTE. GFR estimated using Modification of Diet in Renal Disease Study formula.[22]
*Indicates statistical significance by univariate analysis.

statistical tests applied were 2-tailed, and a *P* value of 5% or less was considered statistically significant.

RESULTS

Of the 588 CRE-positive clinical or screening cultures in the 2 years from 2009 through 2010 in our database, representing 361 patients, 137 patients had carbapenemase-producing cultures that were taken during hospitalization, did not die during that hospitalization, and had no CRE-positive cultures prior to 2009. Thus, 137 patients met the eligibility criteria for inclusion in the study (Fig 1).

One or more follow-up cultures were successfully obtained from 97 of these patients, for a total of 242 follow-up cultures, with 41 patients with 1 follow-up culture, 19 patients with 2 follow-up cultures, and 37 with 3 or more follow-up cultures. Of these, 149 cultures were taken as clinical follow-up, whether at hospital readmission or in outpatient clinics, prior to the initiation of data collection for the present study. Thus, they were part of the initial database of cultures and were considered retrospectively. In addition, during the course of the study, 93 cultures were taken prospectively by investigators, by the patient's primary care physician, or as part of a hospital readmission. Demographic data of all patients meeting the eligibility criteria are shown in Table 1.

Patient and culture characteristics

Mean age of screened patients was 78 ± 3 years (range: 32-102 years). No significant difference in age was noted between those with follow-up and those for whom follow-up was not obtainable. In addition to their advanced age, patients in both groups were generally in poor health: 61% of those screened were residents of a chronic care facility, 51% were diagnosed with dementia, and only 56% were alive at the end of the study period. No significant difference was noted for the above variables between those with follow-up and those without. Among the patients with follow-up culture available, a higher percentage were discharged from the hospital with a feeding gastrostomy (28% vs 10%, $P = .023$), and a lower percentage were discharged with a nasogastric tube or were diagnosed with a malignancy ($P = .011$, $P = .048$, respectively).

In 87% of screened patients, *K pneumoniae* was isolated from the index culture, and, in 9%, multiple organisms were identified. This correlates with the endemic flora in Israel and is consistent with the increasing rate of carbapenemases in organisms other than *K pneumoniae*.[23] In all screened patients for whom multiple organisms were identified, *K pneumoniae* was one of the isolated organisms. No significant difference was noted between patients with and without follow-up cultures. In both groups, CRE was initially identified in a surveillance culture in 70% to 80% of patients.

Time to CRE negativity

Of the 97 patients with follow-up cultures, the mean time to culture negativity was 387 days (95% confidence interval (CI): 312-463 days; KM; range: 26-1,025 days,). The median time until culture became negative was 295 days (95% CI: 192-398 days; KM). At 3 months, 78% of patients remained culture positive by KM survival estimate; at 6 months, 65% remained positive; at 9 months, 51%; and, at 1 year, 39% of patients remained culture positive (number at risk: 82, 58, 42, and 30, respectively; Figure not shown).

The factors found to significantly affect the mean time to culture negativity were whether the patient was hospitalized between the index culture and the last follow-up culture, the number of hospitalizations, the number of hospitalization days, and whether the index culture was a clinical or surveillance culture (Table 2, Fig 2). In multivariate analysis, only the presence or lack of a hospitalization and clinical index culture were found to have an effect on the mean time to negativity ($P = .001$ and $P = .002$, respectively, by Cox regression).

DISCUSSION

CRE may cause serious invasive infections, especially bacteremia and urosepsis, and are associated with a high mortality rate,[10,14,15] including in our study (Fig 1), where 67 out of 204 patients (33%) died during the index culture hospitalization. This high mortality is not attributable solely to the CRE carrier status and probably reflects the multiple comorbidities and poor health of this population. As such, the Israeli Ministry of Health and subsequently the US Centers for Disease Control and Prevention issued recommendations and set up infrastructure to detect and control such infections.[12,17,18]

Patients diagnosed with CRE infection or carriage are treated under conditions of cohorting and contact isolation during the index hospitalization. Upon rehospitalization, surveillance cultures are obtained, and, pending results, these patients are placed under similar isolation conditions.[11,12,17,18,24] The period of time between admission and culture results is critical because these patients are cohorted with CRE-positive patients and cared for by separate staff protected by gowns and gloves, thus handicapping both patients

Table 2
Variables tested for their effect on mean time to first negative culture: n = 97

Variable	HR: 95% CI		*P* value	
			Univariate	Multivariate
Age at index culture	0.982-1.017		.953	
Days from admission to index culture	0.984-1.016		.994	
Hospitalizations after index culture	0.608-0.907		.004*	.209
Hospitalization days after index culture	0.965-0.998		.031*	.294
Katz score	0.892-1.102		.873	
Karnovsky score	0.985-1.017		.938	
Albumin (g/dL)	0.594-1.856		.867	
eGFR (mL/min)	0.997-1.023		.126	
Variable	No (95% CI)	Yes (95% CI)		
Female	393 (304-483)	404 (270-538)	.798	
Resident of a chronic care facility	395 (283-507)	380 (289-471)	.698	
Hospitalization between first and last culture	286 (215-357)	569 (403-735)	.001*	.001*
Hospitalized in medical wing				
At index culture	332 (259-405)	425 (287-562)	.493	
At last follow-up	328 (259-397)	453 (301-605)	.249	
Foreign bodies				
Urinary catheter	334 (254-414)	468 (325-610)	.164	
Gastrostomy	343 (259-428)	464 (334-594)	.148	
Nasogastric tube	386 (309-463)	217 (117-316)	.887	
Tracheostomy	370 (292-447)	508 (221-795)	.269	
Comorbidities				
Diabetes mellitus	396 (318-475)	360 (213-508)	.345	
Congestive heart failure	370 (282-459)	403 (288-518)	.317	
Chronic lung disease	402 (318-486)	286 (150-422)	.337	
Malignancy	394 (313-474)	301 (170-431)	.755	
Dementia	386 (278-494)	376 (281-472)	.761	
Index culture characteristics				
Clinical culture	337 (256-418)	641 (454-829)	.005*	.002*
Klebsiella pneumoniae identified	250 (173-328)	419 (332-506)	.081	.703
Multiple organisms identified	401 (321-481)	202 (137-267)	.218	

CI, Confidence interval; *eGFR*, estimated glomerular filtration rate; *HR*, hazard ratio.
NOTE. Continuous variables are expressed as hazard ratio, non-continuous variables are expressed in days. GFR estimated using Modification of Diet in Renal Disease Study formula.[22] Overall population mean: 387 days (95% CI: 312-463).
*Indicates statistical significance.

and staff, in addition to exposing patients to CRE reinfection. In this study, we found that the mean time until culture negativity was 387 days (95% CI: 312-436 days). As with a previous study,[19] the rate of carriage dissipated with time from index culture, with 78% positive at 3 months and only 39% positive at 1 year.

We also attempted to determine the risk factors for extended CRE carriage in the population studied. We found that the duration of carriage was affected by whether the index isolation was a clinical or a rectal surveillance culture, with a mean time to negativity of 641 versus 337 days, respectively ($P = .002$ by multivariate analysis). We also found that the duration of carriage was affected by whether the patient had been hospitalized between the first and last culture, with a mean time to negative of 569 days for those who had been hospitalized versus 286 days for those who had not ($P = .001$ by multivariate analysis). In contrast with the conclusions of a previous study and in contrast to known risk factors for initial CRE carriage, our study did not show a significant association between chronic care facility residence and continued CRE carriage. Other risk factors that have been shown in previous studies to be associated with initial CRE carriage and infection, including functional status and an indwelling urinary catheter,[11] were not found, in our study, to affect continued carriage in patients with a previous CRE-positive culture.

One possibility to explain our findings is that repeat hospitalizations reflect reinfection. Another explanation could be that repeat hospitalizations flag those patients who are more severely ill; as such, they may need more time to clear CRE. Furthermore, patients with clinical CRE infection may have a larger inoculum relative to those who are CRE positive by surveillance culture, thus

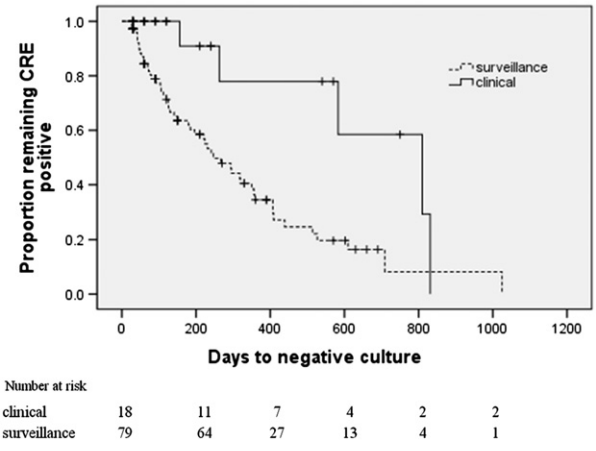

Fig 2. Time to negative culture: clinical index culture versus surveillance index culture.

contributing to longer colonization times. More study is needed to define further the factors leading to continued CRE carriage.

The results of this study suggest that, upon readmission, previously CRE-positive patients can be cared for in a general ward if more than 1 year has passed since the positive index culture, there were no interim hospitalizations, and the original CRE was isolated from a surveillance specimen rather than a clinical culture. Patients with multiple hospitalizations or those who were diagnosed with clinical CRE disease should be assumed to have a more

extended duration of CRE coverage and should therefore be admitted under conditions of isolation and cohorting until proven to be CRE negative. These measures will reduce the hospitalization of CRE-positive patients among the general population, potentially preventing the spread of CRE. Using these data can, furthermore, reduce the unnecessary cohorting of formerly CRE-positive patients who are most likely to be CRE negative.

This study has several limitations. First, although our study population was much larger than that of the previous study, it still included only 97 patients and, naturally, became smaller with longer follow-up, including 44% (43/97 patients) who had died by the end of the study. Nevertheless, we did not detect significant differences between those with and without follow-up cultures. Thus, it would appear that our results can be generalized to a larger population. A second limitation is that follow-up cultures were evaluated both prospectively and retrospectively, and, as such, cultures were taken at differing lengths of time relative to the index culture. Third, although multiple hospitalizations in our institution were included in our analysis, we were unable to evaluate whether the patients studied were hospitalized in other acute care institutions between the index culture and the last follow-up. Fourth, we evaluated comorbidities and foreign bodies at initial hospital discharge but not at subsequent follow-up and did not evaluate antimicrobial use; both of these are possible predictors of continuing CRE carriage. Fifth, although 56% of patients who had negative cultures (32/57) had multiple negative cultures, we defined a patient as CRE negative if they had at least 1 CRE-negative culture with no further positive cultures. This may be an overly lenient definition of CRE negativity. Finally, we used a positive culture as marker for CRE fecal carriage. The Israeli Ministry of Health has recommended that a culture-negative status should be confirmed by a direct PCR from a rectal swab. This recommendation was based on interim data and has not been adopted by all clinical microbiology laboratories. The European regulation recommendations (EUCAST guidelines and ECDC technical report) are to screen for CRE carriage by stool culture or rectal swab and not to use PCR for this purpose, although Nordmann et al cites PCR for KPC as an alternative possibility.[25] The optimal method for CRE detection remains an evolving issue.

In conclusion, this study found that patients with an initially positive CRE culture had a mean time from index culture to CRE culture negativity of 387 days (95% CI: 312-463). Upon readmission, previously CRE-positive patients can probably be cared for in a general ward if more than 1 year has passed since the positive index culture, there were no interim hospitalizations, and the original CRE was isolated from a surveillance specimen rather than a clinical culture. Patients with multiple hospitalizations or those who were diagnosed with clinical CRE disease should be assumed to have a more extended duration of CRE coverage and should therefore be admitted under conditions of isolation and cohorting until proven to be CRE negative.

References

1. Ito H, Arakawa Y, Ohsuka S, Wacharotayankun R, Kato N, Ohta M. Plasmid-mediated dissemination of the metallo-β-lactamase gene blaIMP among clinically isolated strains of *Serratia marcescens*. Antimicrob Agents Chemother 1995;39:824-9.
2. Cornaglia G, Riccio ML, Mazzariol A, Lauretti L, Fontana R, Rossolini GM. Appearance of IMP-1 metallo-β-lactamase in Europe. Lancet 1999;353:899-900.
3. Kurokawa H, Yagi T, Shibata N, Shibayama K, Arakawa Y. Worldwide proliferation of carbapenem-resistant gram-negative bacteria. Lancet 1999;354:955.
4. Walsh TR, Bolmström A, Qwärnström A, Gales A. Evaluation of a new Etest for detecting metallo-β-lactamases in routine clinical testing. J Clin Microbiol 2002;40:2755-9.
5. Yigit H, Queenan AM, Anderson GJ, Domenech-Sanchez A, Biddle JW, Steward CD, et al. Novel carbapenem-hydrolyzing β-lactamase, KPC-1, from a carbapenem-resistant strain of *Klebsiella pneumoniae*. Antimicrob Agents Chemother 2001;45:1151-61.
6. Deshpande L, Rhomberg P, Sader H, Jones R. Emergence of serine carbapenemases (KPC and SME) among clinical strains of Enterobacteriaceae isolated in the United States Medical Centers: report from the MYSTIC Program (1999-2005). Diagn Microbiol Infect Dis 2006;56:367-72.
7. Bratu S, Landman D, Haag R, Recco R, Eramo A, Alam M, et al. Rapid spread of carbapenem-resistant *Klebsiella pneumoniae* in New York City: a new threat to our antibiotic armamentarium. Arch Intern Med 2005;165:1430-5.
8. Kitchel B, Rasheed JK, Patel JB, Srinivasan A, Navon-Venezia S, Carmeli Y, et al. Molecular epidemiology of KPC-producing *Klebsiella pneumoniae* isolates in the United States: clonal expansion of multilocus sequence type 258. Antimicrob Agents Chemother 2009;53:3365-70.
9. Leavitt A, Navon-Venezia S, Chmelnitsky I, Schwaber MJ, Carmeli Y. Emergence of KPC-2 and KPC-3 in carbapenem-resistant Klebsiella pneumoniae strains in an Israeli hospital. Antimicrob Agents Chemother 2007;51:3026-9.
10. Schwaber MJ, Carmeli Y. Carbapenem-resistant Enterobacteriaceae: a potential threat. JAMA 2008;300:2911-3.
11. Wiener-Well Y, Rudensky B, Yinnon AM, Kopuit P, Schlesinger Y, Broide E, et al. Carriage rate of carbapenem-resistant *Klebsiella pneumoniae* in hospitalised patients during a national outbreak. J Hosp Infect 2010;74:344-9.
12. Ben-David D, Maor Y, Keller N, Regev-Yochay G, Tal I, Shachar D, et al. Potential role of active surveillance in the control of a hospital-wide outbreak of carbapenem-resistant *Klebsiella pneumoniae* infection. Infect Control Hosp Epidemiol 2010;31:620-6.
13. Schechner V, Straus-Robinson K, Schwartz D, Pfeffer I, Tarabeia J, Moskovich R, et al. Evaluation of PCR-based testing for surveillance of KPC-producing carbapenem-resistant members of the Enterobacteriaceae family. J Clin Microbiol 2009;47:3261-5.
14. Patel G, Huprikar S, Factor SH, Jenkins SG, Calfee DP. Outcomes of carbapenem-resistant *Klebsiella pneumoniae*: infection and the impact of antimicrobial and adjunctive therapies. Infect Control Hosp Epidemiol 2008;29:1099-106.
15. Schwaber MJ, Klarfeld-Lidji S, Navon-Venezia S, Schwartz D, Leavitt A, Carmeli Y. Predictors of Carbapenem-resistant *Klebsiella pneumoniae* acquisition among hospitalized adults and effect of acquisition on mortality. Antimicrob Agents Chemother 2007;52:1028-33.
16. Borer A, Saidel-Odes L, Eskira S, Nativ R, Riesenberg K, Livshiz-Riven I, et al. Risk factors for developing clinical infection with carbapenem-resistant *Klebsiella pneumoniae* in hospital patients initially only colonized with carbapenem-resistant *K pneumoniae*. Am J Infect Control 2012;40:421-5.
17. Seigal JD, Rhinehart M, Jackson M, Chiarello L, Healthcare Infection Control Practices Advisory Committee. 2007 Guideline for isolation precautions: preventing transmission of infectious agents in healthcare settings. Available from: http://www.cdc.gov/hicpac/pdf/isolation/isolation2007.pdf. Accessed December 10, 2012.
18. CDC. Guidance for control of infections with carbapenem-resistant or carbapenemase-producing Enterobacteriaceae in acute care facilities. MMWR Morb. Mortal Wkly Rep 2009;58:256-60.
19. Schechner V, Kotlovsky T, Tarabeia J, Kazma M, Schwartz D, Navon-Venezia S, et al. Predictors of rectal carriage of carbapenem-resistant Enterobacteriaceae (CRE) among patients with known CRE carriage at their next hospital encounter. Infect Control Hosp Epidemiol 2011;32:497-503.
20. Lee K, Chong Y, Shin HB, Kim YA, Yong D, Yum JH. Modified Hodge and EDTA-disk synergy tests to screen metallo-β-lactamase-producing strains of *Pseudomonas* and *Acinetobacter* species. Clin Microbiol Infect 2001;7:88-91.
21. Samra Z, Bahar J, Madar-Shapiro L, Aziz N, Israel S, Bishara J. Evaluation of CHROMagar KPC for rapid detection of carbapenem-resistant Enterobacteriaceae. J Clin Microbiol 2008;46:3110-1.
22. Levey AS, Bosch JP, Lewis JB, Greene T, Rogers N, Roth D. A more accurate method to estimate glomerular filtration rate from serum creatinine: a new prediction equation. Modification of Diet in Renal Disease Study Group. Ann Intern Med 1999;130:461-70.
23. Geffen Y, Finkelstein R, Oren I, Shalaginov R, Tavleva I, Sprecher H. Changing epidemiology of carbapenem-resistant Enterobacteriaceae carriage during an outbreak of carbapenem-resistant *Klebsiella pneumoniae*. J Hosp Infect 2010;76:355-6.
24. Friedmann R, Raveh D, Zartzer E, Rudensky B, Broide E, Attias D, et al. Prospective evaluation of colonization with extended-spectrum β-lactamase (ESBL)-producing Enterobacteriaceae among patients at hospital admission and of subsequent colonization with ESBL-producing Enterobacteriaceae among patients during hospitalization. Infect Control Hosp Epidemiol 2009;30:534-42.
25. Nordmann P, Gniadkowski M, Giske CG, Poirel L, Woodford N, Miriagou V, European Network on Carbapenemases. Identification and screening of carbapenemase-producing Enterobacteriaceae. Clin Microbiol Infect 2012;18:432-8.