

Nosocomial Infections and Agents Determined by Consultations in Intensive Care Unit

Yoğun Bakım Ünitesinde Konsültasyonlarla Belirlenen Hastane İnfeksiyonları ve Etkenleri

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Objectives: We investigated nosocomial infections diagnosed via consultations with the Department of Infectious Diseases and Clinical Microbiology at Reanimation I-II intensive care units.

Patients and Methods: Of 3750 patients hospitalized at Reanimation I-II intensive care units, 1221 patients were followed up via consultations with the Department of Infectious Diseases and Clinical Microbiology. Additionally, main diseases that require intensive care, other concomitant diseases, demographical data, hospital stays and isolated microorganisms were evaluated.

Results: Seven hundred and fifty-six patients (61.9%) were diagnosed with nosocomial infections according to the criteria of Centers for Disease Control and Prevention. Among these infections, nosocomial pneumonia took the first place. As infectious agent, *Pseudomonas spp.* (19.7%) took the first place, followed by *Acinetobacter spp.* (17.3%) and *Staphylococcus spp.* (16.7%).

Conclusion: Nosocomial infections are common at intensive care units. Besides infection control precautions, consultations with Infectious Diseases are also important in quick identification and treatment of these infections.

Key words: Intensive care units; infectious diseases; consultation.

Amaç: Reanimasyon I-II Yoğun Bakım Ünitelerinde, İnfeksiyon Hastalıkları ve Klinik Mikrobiyoloji Anabilim Dalı konsültasyonlarıyla tanı konulan nozokomiyal infeksiyonlar incelendi.

Hastalar ve Yöntemler: Yoğun bakım ünitelerinde yatan 3750 hastanın 1221'i İnfeksiyon Hastalıkları ve Klinik Mikrobiyoloji Anabilim Dalı konsültasyonlarıyla izlendi. Ayrıca yoğun bakıma yatış gerektiren primer ve diğer eşlik eden hastalıklar, demografik veriler, hastanede kalış ve izole edilen mikroorganizmalar da bu çalışmada değerlendirildi.

Bulgular: Centers for Disease Control and Prevention kriterlerine göre 756 hasta (%61.9) nozokomiyal infeksiyon tanısı aldı. Bu infeksiyonlar arasında nozokomiyal pnömoni ilk sırada yer aldı. İnfeksiyon etkenleri olarak ilk sırada yer alan *Pseudomonas spp.*'i (%19.7), *Acinetobacter spp.* (%17.3) ve *Staphylococcus spp.* (%16.7) takip etti.

Sonuç: Nozokomiyal infeksiyonlarla yoğun bakımlarda sık karşılaşılmaktadır. Bu infeksiyonlarda İnfeksiyon Hastalıkları konsültasyonları infeksiyon kontrolün yanısıra doğru ve hızlı tanı ve tedavide önem arz etmektedir.

Anahtar sözcükler: Yoğun bakım ünitesi; infeksiyon hastalıkları; konsültasyon.

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Patients at intensive care units (ICU) make up only 5-10% of all inpatients. They are important units for nosocomial infections. About 25% of all nosocomial infections and 45-50% of all nosocomial pneumonia and bacteremia take place at these units. Agents of nosocomial infections at ICUs may differ among hospitals, even among different ICUs of the same hospital. The most well-known characteristics of these infections are resistant pathogens often to play role at the infection and the difficulty to treat the infections. The facts that underlying diseases of the patients at these units are serious and higher probability for patients to encounter resistant microorganisms cause the infections to result in serious mortality and morbidity. Hospital stay gets longer due to these infections and important financial detriments develop. For the optimization of antibiotic treatment at ICU infections, it is important to profile the agent according to body parts and to follow the antibiotic resistance patterns of these agents.^[1-3]

Need to control resistance at these microorganisms and to use antibiotics rationally has seriously increased the share of consultations among duties performed by Infectious Diseases and Clinical Microbiology (IDCM) specialists.^[4]

In this study, we aimed to investigate nosocomial infections diagnosed with IDCM Department's consultations, at Reanimation I-II ICUs.

PATIENTS AND METHODS

Of 3750 patients hospitalized at Reanimation I-II ICUs between April 1, 2003 and December 31, 2006, 1221 patients were followed up via consultations with the Department of Infectious Diseases and Clinical Microbiology. Seven hundred and fifty-six patients (61.9%) who were diagnosed with nosocomial infections according to the criteria of Centers for Disease Control and Prevention (www.cdc.gov/ncidod/dhqp) were investigated retrospectively.

Our university hospital is a regional reference hospital made up of three blocks and it has a capacity of 700 hospital beds. There are two reanimation units with a total of 23 beds. Except newborns and postoperative cardiac surgery patients, patients at all age groups from surgical and internal departments are followed

up here and all modern intensive care applications are performed. The Department of Infectious Diseases and Clinical Microbiology serves since 1982.

Infectious Diseases consultations requested from the reanimation unit were followed regularly by IDCM residents accompanied by IDCM teaching staff since April 2003. The follow-up card has been arranged for every patient evaluated. After information about the patient is recorded on the card, microbiological follow-up of samples derived from the patients are noted down. Antibiotic choice is determined daily at teaching staff-accompanied visits, according to antibiotic sensitivity of producing microorganisms.

In this study, main diseases of patients at admission to ICU, other concomitant diseases, demographical data, hospital stays, isolated microorganisms and nosocomial infections were recorded daily to follow-up cards and data were transferred to SPSS 10.0 software and evaluated.

RESULTS

Of 756 patients included in the study, 508 (67.2%) were male and 248 (32.8%) were female. Mean age of the patients were 48.4 ± 21.4 years and mean stay at ICU was 26.5 ± 23.3 days. Total inpatients at ICUs and patients who acquired infections according to years were summarized at Table 1, primary diseases causing the need for administration to ICUs were summarized at Table 2.

It was detected that, of 1221 patients who were consulted, 756 patients developed 1855 nosocomial infections. Among these infections, nosocomial pneumonia took the first place (Table 3). As infection agent, *Pseudomonas spp.* took the first place, followed by *Acinetobacter spp.* and *Staphylococcus spp.* (Table 4).

The first five primary reasons of administration to ICUs for patients who have been consulted with Infectious Diseases were trauma (32.8%), cerebrovascular event (20.7%), malignancy (11.3%), postoperative follow-up (4.7%), and intra-abdominal abscess (3.8%). During the long ICU stay of these patients, various invasive methods and wide-spectrum antibiotics have been used.

Table 1. Total number of inpatients at ICUs and patients who acquired infections, according to years

Year	Number of inpatients	Number of follow-up patients	Number of patients who acquired infections	Total number of infections
2003 (April-December)	688	151	144	428
2004	1004	409	207	436
2005	1076	387	216	531
2006	982	274	189	460
<i>Total</i>	3750	1221	756	1855

Table 2. Primary diseases of the patients causing the need for administration to ICUs

Reason of administration	n	%	Reason of administration	n	%
Trauma	248	32.8	Injury with knife	4	0.52
Cerebrovascular event	157	20.76	HELLP (Hemolysis, elevated liver enzyme concentrations, low platelet counts)	4	0.52
Malignancy	86	11.37	Encephalitis	4	0.52
Postoperative	36	4.76	Tetanus	3	0.39
Intra-abdominal abscess	29	3.83	Fournier's gangrene	3	0.39
Chronic obstructive pulmonary disease	27	3.57	Gastrointestinal system bleeding	3	0.39
Burns	23	3.04	Idiopathic pulmonary fibrosis	2	0.26
Sepsis	22	2.91	Diabetic ketoacidosis	2	0.26
Respiratory failure	20	2.64	Amyotrophic lateral sclerosis	2	0.26
Intoxication	13	1.71	Rheumatoid arthritis	1	0.13
Congestive heart failure	12	1.58	Chronic renal failure	1	0.13
Pneumonia	10	1.32	Cholangitis	1	0.13
Meningitis	7	0.92	Tubo-ovarian abscess	1	0.13
Gunshot injury	7	0.92	Interstitial pulmonary disease	1	0.13
Suffocation with water	6	0.79	Peritonitis	1	0.13
Electricity shock	6	0.79	Cirrhosis of liver	1	0.13
Cardiac arrest	5	0.66	Anorexia nervosa	1	0.13
Pancreatitis	4	0.52	Pulmonary thromboembolism	1	0.13

DISCUSSION

Patients at ICUs make up a patient group who need invasive life support, in frequent contact with the healthcare staff, with a high probability of infection with antibiotic-resistant bacteria.^[5] The knowledge of local antibiotic resistance patterns of infectious diseases which cause important morbidity and mortality at ICU is as important as to diagnose, in point of determining treatment options. Recently, with new and wide-spectrum antibiotics entering the market, inappropriate antibiotics use has increased. As a result, an increase in the frequency of microorganisms causing resistant infections has been observed. In order to control the use of antimicrobial agents and resistance development, most hospital managements need IDCM specialists.^[2,4,6-8] Less usage of wide-spectrum antibiotics, fast switch to oral treatment and multidisciplinary approach by Infectious Diseases specialists cause a decline at antibiotic-resistant infections. Akalin et al.^[9] have observed that after continuous

and systematic consultations with Infectious Diseases and rational antibiotics applications, sensitivity patterns of pathogens causing ICU infections were revealed.

Previous studies point out that Infectious Diseases consultations have been demanded for 40% of ICU patients. In our study, the rate of consultation demand for Reanimation I and II ICU patients was 32.6%. By the help of Infectious Diseases consultations, antibiotics expenses and resistance development rates decrease, and morbidity and mortality rates stay lower.^[4]

The most frequent infections acquired at the ICUs are pneumonia, urinary tract infections (UTI), bloodstream infections (BSI) and surgical site infections (SSI). According to the results of the European Prevalence of Infection in Intensive Care (EPIC); pneumonia takes the first rank with 46.9%, UTI have the rate of 17.6% and BSI have the rate of 12%.^[5,10] In a study performed by Erbay et al.^[11] in 2003 at Pamukkale University Medicine

Table 3. Distribution of infections according to years and infection areas

Year	Urinary tract infections		Bloodstream infections		Pneumonia		Surgical site infections	
	n	%	n	%	n	%	n	%
2003 (April-December)	91	21.3	101	23.6	173	40.4	63	14.7
2004	108	24.7	96	22	176	40.4	56	12.9
2005	109	20.5	136	25.6	202	38	84	15.8
2006	93	20.2	132	28.6	159	34.6	76	16.5
Total	401	21.6	465	25	710	38.3	279	15

Table 4. Distribution of microorganisms according to years

Agent	2003 (April-December)		2004		2005		2006	
	n	%	n	%	n	%	n	%
<i>Pseudomonas spp.</i>	106	20.8	97	20.6	119	19	101	18.6
<i>Acinetobacter spp.</i>	96	19.4	84	17.8	114	18.2	75	13.8
<i>Candida spp.</i>	48	9.4	70	14.8	62	9.9	48	8.8
<i>E. coli</i>	17	3.3	27	5.7	41	6.5	38	7
<i>Enterococcus spp.</i>	30	5.9	37	7.8	51	8.1	55	10.2
<i>Klebsiella spp.</i>	45	8.8	43	9.1	54	8.6	57	10.5
MSSA	37	7.3	27	5.7	34	5.4	33	6
MRSA	37	7.3	18	3.8	36	5.7	16	2.9
MRCNS	30	5.9	18	3.8	40	6.4	36	6.6
<i>Enterobacter spp.</i>	24	4.7	17	3.6	25	3.9	31	5.7
Other	36	7	34	7.2	50	7.9	51	9.4
Total	509		472		626		541	

Faculty, the rate of pneumonia was found as 40.9%, BSI 30.2%, UTI 23.6% and SSI 15.3%.

When the results of the consultations were evaluated, it was observed that, taking the occurrence areas of all the nosocomial infections at ICU patients into account, nosocomial pneumonias took the first place with a rate of 38.6%. Pneumonias were followed by BSI with a rate of 25%, UTI with a rate of 21.6% and SSI with a rate of 15%. When frequency rates of nosocomial infections in our references were evaluated, it was observed that at different centers, bloodstream infections or urinary tract infections differed for the second place after pneumonias.

Microorganisms causing the infections at ICUs and resistance patterns may differ among hospitals and among ICUs at the same hospital with different purposes. In the past years, Gram negative bacteria were more

frequent as infection agents but recently an increase in the frequency of Gram positive bacteria has been reported.^[12] Namiduru et al.^[13] reported that Gram positive bacteria were isolated with a rate of 31.5% and Gram negative bacteria with a rate of 68.4%. Palabıykoğlu et al.^[14] reported that, for nosocomial infections developing at ICUs, microorganisms isolated were Gram negative with a rate of 63.9%, Gram positive with 28.5% and *Candida spp.* with 7.6%. Considering the frequency of bacteria isolated at ICUs, *P. aeruginosa* takes the first place among Gram negative bacteriae, where *S. aureus* and Coagulase Negative Staphylococci (CNS) are frequent among Gram positive bacteria.^[14,15] In a study by Orrett,^[16] the frequency of isolated Gram negative bacteria was reported as *P. aeruginosa* (36.6%), *K. pneumoniae* (20.6%), *Enterobacter spp.* (16.8%). The frequency of isolated Grampositive bacteria was determined as *S. aureus* (41.8%), CNS (30.9%), *Enterococcus spp.* (20%).

Table 5. Distribution of microorganisms according to infection areas

Agent	Urinary tract infections		Bloodstream infections		Surgical site infections		Pneumonia	
	n	%	n	%	n	%	n	%
<i>Pseudomonas spp.</i>	106	20.8	97	20.6	119	19	101	18.6
<i>Acinetobacter spp.</i>	96	19.4	84	17.8	114	18.2	75	13.8
<i>Candida spp.</i>	48	9.4	70	14.8	62	9.9	48	8.8
<i>E. coli</i>	17	3.3	27	5.7	41	6.5	38	7
<i>Enterococcus spp.</i>	30	5.9	37	7.8	51	8.1	55	10.2
<i>Klebsiella spp.</i>	45	8.8	43	9.1	54	8.6	57	10.5
MSSA	37	7.3	27	5.7	34	5.4	33	6
MRSA	37	7.3	18	3.8	36	5.7	16	2.9
MRCNS	30	5.9	18	3.8	40	6.4	36	6.6
<i>Enterobacter spp.</i>	24	4.7	17	3.6	25	3.9	31	5.7
Other	36	7	34	7.2	50	7.9	51	9.4
Total	509		472		626		541	

According to our consultation evaluations, Gram negative bacteria were isolated with a rate of 64.5%, Gram positive with 24.7% and *Candida spp.* with 10.7%. Among the most isolated agents *Pseudomonas spp.* took the first place with a rate of 19.7%, followed by *Acinetobacter spp.* with 17.3%, *Staphylococcus spp.* with 16.7%, *Candida spp.* with 10.7%, *Klebsiella spp.* with 9.2%. The results were consistent with the literature. Distribution of infection agents according to infection type may differ among hospitals or countries. Pneumonias take the first place among ICU infections. The most frequent agents causing pneumonia at ICUs are *P. aeruginosa*, *S. aureus*, *Enterobacteriaceae* and *Acinetobacter spp.*^[12] In the study about adult medical ICUs carried out by National Nosocomial Infections Surveillance, pneumonia agent frequency rates were 21% for *P. aeruginosa*, 20% for *S. aureus*, 9% for *Enterobacter spp.*, 8% for *Klebsiella pneumoniae*.^[17] In a study performed by Nag et al.,^[18] among 39 pneumonia patients with microbiological analysis, 25.6% had *P. aeruginosa* and 17.9% had *K. pneumoniae*. Recently, it has been reported that there is an increase in the frequency of Gram positive bacteria, especially *S. aureus*, as pneumonia agent. In a study carried out by Gastmeier et al.,^[19] when distribution of pathogens as pneumonia agent was evaluated, the most frequent ones were determined as *S. aureus* (24.1%), *P. aeruginosa* (16.8%), *Klebsiella spp.* (12.1%). In our consultation evaluations, the most frequent agent at pneumonias was determined as *Pseudomonas spp.* (29.4%). It was followed by *Acinetobacter spp.* (22.7%), *Staphylococcus spp.* (16.2%), *Klebsiella spp.* (11%).

Clinical view of urinary tract infection are not generally serious, but mortality is high when secondary bacteremia develops. Urinary catheter has an important role in its pathogenesis.^[20] The most frequent agents are *E. coli*, *Enterococci*, fungi like *Candida spp.* and *P. aeruginosa*.^[12,20] In a study carried out by Richards et al.,^[21] the agents with their frequencies were *Candida spp.* with 24.8%, *E. coli* with 18.5%, *Enterococcus spp.* with 14.3%. In another study carried out by Parlak et al.,^[22] the most frequent urinary tract infection agents were *Candida spp.* (27.2%), *E. coli* (27.2%) and *Staphylococcus spp.* (12.9%). When our results were evaluated, *Candida spp.* took the first place with 35.8%, followed by *E. coli* with 13.6% and *Pseudomonas spp.* with 11.9%. All these results were consistent with the literature.

Blood stream infections are 2-7 times more frequent at ICUs than in the other hospital units. Its contribution to mortality changes between 27-35%. The most common agent among BSIs is CNS group with a rate of 30%. The other agents are *S. aureus*, *Enterococcus spp.*, fungi such as *Candida spp.* and Gram negative enteric bacteria.^[23] In the study about adult medical ICUs carried out by National Nosocomial Infections Surveillance, BSI agent frequency rates were reported as 36% for CNS, 16% for *Enterococcus spp.* and 13% for *S. aureus*.^[21] In our consultation evalu-

ations, *Staphylococcus spp.* (30.3%) group was the most frequent among BSIs, followed by *Enterococcus spp.* (16.8%) and *Acinetobacter spp.* (12.2%). Frequency rates among *Staphylococcus spp.* were evaluated as 18.9% for methicillin-resistant coagulase-negative *Staphylococcus*, and 11.4% for *S. aureus* (Table 5).

In a study carried out by Erbay et al.,^[11] among patients who were diagnosed with SSI, the most frequent infection agents were reported as MRSA, *Acinetobacter spp.* and CNS. In our study, the most frequent agents were *Acinetobacter spp.* (23.7%), *Pseudomonas spp.* (16.3%), *Staphylococcus spp.* (13.4%) (Table 5). These results were similar to the previous results.

Nearly one-half of hospitalized patients receive antimicrobial agents, and antimicrobial usage varies widely across hospitals. Infection control committee should monitor the antimicrobial susceptibility profiles produced by the microbiology laboratory on a regular basis to observe for trends in the development of antimicrobial resistance. The primary administrative function of the infection control program is to develop, implement, and continually evaluate policies and procedures designed to minimize the risk of nosocomial infection.^[1]

As a result, health-care related infections develop often at intensive care units. When the data of our country and of foreign countries are evaluated, it was revealed that the most common infection among ICU infections is pneumonia, and Gram negative bacteria is the first among the agents. By virtue of its control over hospital formularies and of the distribution of medications within the hospital, the hospital pharmacy is often in a position to contribute significantly to defining and directing the appropriate use of antibiotics.^[24] We believe that early determination of these infections and treatment with proper antibiotics according to the agent and resistance data with the help of Infectious Diseases consultations, will help decrease the frequency of infections caused especially by resistant microorganisms, with effective infection control precautions.

REFERENCES

1. Edmond MB, Wenzel RP. Organization for infection control. In: Mandell GL, Bennett JE, Dolin R, editors. Principles and practice of infectious diseases. 6th ed. New York: Elsevier Churchill Livingstone; 2005. p. 3323-6.
2. Esposito S, Leone S. Antimicrobial treatment for Intensive Care Unit (ICU) infections including the role of the infectious disease specialist. *Int J Antimicrob Agents* 2007;29:494-500.
3. Çetin ÇB, Turgut H, Kaleli İ, Yalçın AN, Orhan N. Pamukkale Üniversitesi Tıp Fakültesi Hastanesi yoğun bakım ünitesinde nozokomiyal infeksiyonlar. *Hastane İnfeksiyonları Dergisi* 2002;6:98-101.
4. Beşirbellioğlu BA. Dünyada ve Türkiye'de infeksiyon hastalıkları konsültasyonları. *Klimik Dergisi* 2005;18:91-3.
5. Eggimann P, Pittet D. Infection control in the ICU. *Chest* 2001;120:2059-93.
6. Schlesinger Y, Paltiel O, Yinnon AM. Analysis and impact

- of infectious disease consultations in a general hospital. *J Hosp Infect* 1998;40:39-46.
7. Petrak RM, Sexton DJ, Butera ML, Tenenbaum MJ, MacGregor MC, Schmidt ME, et al. The value of an infectious diseases specialist. *Clin Infect Dis* 2003;36:1013-7.
 8. Yapar N, Erdenizmenli M, Oğuz VA, Kuruüzüm Z, Senger SS, Cakir N, et al. Infectious disease consultations and antibiotic usage in a Turkish university hospital. *Int J Infect Dis* 2006;10:61-5.
 9. Akalin H, Kahveci F, Ozakin C, Helvacı S, Gedikoğlu S, Kutlay O, et al. Influences of alternate therapy protocol and continuous infectious disease consultation on antibiotic susceptibility in ICU. *Intensive Care Med* 1999;25:1010-2.
 10. Vincent JL, Bihari DJ, Suter PM, Bruining HA, White J, Nicolas-Chanoin MH, et al. The prevalence of nosocomial infection in intensive care units in Europe. Results of the European Prevalence of Infection in Intensive Care (EPIC) Study. EPIC International Advisory Committee. *JAMA* 1995;274:639-44.
 11. Erbay H, Yalcin AN, Serin S, Turgut H, Tomatir E, Cetin B, et al. Nosocomial infections in intensive care unit in a Turkish university hospital: a 2-year survey. *Intensive Care Med* 2003;29:1482-8.
 12. Strausbaugh LJ. Nosocomial respiratory infections. In: Mandell GE, Bennett JE, Dolin R, editors. *Mandell, Douglas, and Bennett's principles and practice of infectious diseases*. 6th ed. New York: Elsevier Churchill Livingstone; 2005. p. 3362-70.
 13. Namıduru M, Karaoğlan İ, Göksu S, Dikensoy Ö, Karaoğlan M. Cerrahi yoğun bakım ünitesinde hastane infeksiyonu etkeni olan bakteriler ve antibiyotiklere direnç durumları. *İnfeksiyon Dergisi* 2003;17:39-44.
 14. Palabıyıkoğlu İ, Tekeli E, Çokça F, Arıkan Akan Ö, Ünal N, Aysev D, et al. Ankara Üniversitesi Tıp Fakültesi hastaneleri yoğun bakım ünitelerinde hastane infeksiyonları surveyansı: alet kullanım ve alet ilişkili infeksiyon oranları. *Flora Dergisi* 2006;11:89-95.
 15. Eltahawy AT. Gram-negative bacilli isolated from patients in intensive care unit: prevalence and antibiotic susceptibility. *J Chemother* 1997;9:403-10.
 16. Orrett FA. Nosocomial infections in an intensive care unit in a private hospital. *West Indian Med J* 2002;51:21-4.
 17. Richards MJ, Edwards JR, Culver DH, Gaynes RP. Nosocomial infections in medical intensive care units in the United States. National Nosocomial Infections Surveillance System. *Crit Care Med* 1999;27:887-92.
 18. Nag VL, Ayyagari A, Venkatesh V, Dash NR, Ghar M, Prasad KN. Bacterial isolates from mechanically ventilated patients with nosocomial pneumonia within intensive care unit of a tertiary care center. *J Commun Dis* 2005;37:281-7.
 19. Gastmeier P, Geffers C, Sohr D, Schwab F, Behnke M, Rüdten H. Surveillance of nosocomial infections in intensive care units. Current data and interpretations. [Article in German] *Wien Klin Wochenschr* 2003;115:99-103.
 20. Warren JW. Nosocomial urinary tract infections. In: Mandell GL, Bennett JE, Dolin R, editors. *Mandell, Douglas, and Bennett's principles and practice of infectious diseases*. 6th ed. New York: Elsevier Churchill Livingstone; 2005. p. 3370-81.
 21. Richards MJ, Edwards JR, Culver DH, Gaynes RP. Nosocomial infections in combined medical-surgical intensive care units in the United States. *Infect Control Hosp Epidemiol* 2000;21:510-5.
 22. Parlak E, Erol S, Kizilkaya M, Altoparlak U, Parlak M. Nosocomial urinary tract infections in the intensive care unit patients. [Article in Turkish] *Mikrobiyol Bul* 2007;41:39-49.
 23. Suljagić V, Cobeljić M, Janković S, Mirović V, Marković-Denić L, Romić P, et al. Nosocomial bloodstream infections in ICU and non-ICU patients. *Am J Infect Control* 2005;33:333-40.
 24. Hopkins CC. Pharmacy service. In: Mayhall CG, editor. *Hospital epidemiology and infection control*. 3rd ed. Philadelphia: Lippincott Williams and Wilkins; 2004. p. 1315-22.