

ORIGINAL ARTICLE

Outpatient Parenteral Antimicrobial Therapy Practices among Adult Infectious Disease Physicians

Michael A. Lane, MD;¹ Jonas Marschall, MD;¹ Susan E. Beekmann, MPH;² Philip M. Polgreen, MD;² Ritu Banerjee, MD;³ Adam L. Hersh, MD;⁴ Hilary M. Babcock, MD¹

OBJECTIVE. To identify current outpatient parenteral antibiotic therapy practice patterns and complications.

METHODS. We administered an 11-question survey to adult infectious disease physicians participating in the Emerging Infections Network (EIN), a Centers for Disease Control and Prevention–sponsored sentinel event surveillance network in North America. The survey was distributed electronically or via facsimile in November and December 2012. Respondent demographic characteristics were obtained from EIN enrollment data.

RESULTS. Overall, 555 (44.6%) of EIN members responded to the survey, with 450 (81%) indicating that they treated 1 or more patients with outpatient parenteral antimicrobial therapy (OPAT) during an average month. Infectious diseases consultation was reported to be required for a patient to be discharged with OPAT by 99 respondents (22%). Inpatient (282 [63%] of 449) and outpatient (232 [52%] of 449) infectious diseases physicians were frequently identified as being responsible for monitoring laboratory results. Only 26% (118 of 448) had dedicated OPAT teams at their clinical site. Few infectious diseases physicians have systems to track errors, adverse events, or “near misses” associated with OPAT (97 [22%] of 449). OPAT-associated complications were perceived to be rare. Among respondents, 80% reported line occlusion or clotting as the most common complication (occurring in 6% of patients or more), followed by nephrotoxicity and rash (each reported by 61%). Weekly laboratory monitoring of patients who received vancomycin was reported by 77% of respondents (343 of 445), whereas 19% of respondents (84 of 445) reported twice weekly laboratory monitoring for these patients.

CONCLUSIONS. Although use of OPAT is common, there is significant variation in practice patterns. More uniform OPAT practices may enhance patient safety.

Infect Control Hosp Epidemiol 2014;35(7):839-844

Over the past 30 years, outpatient parenteral antimicrobial therapy (OPAT) has gained in popularity as a cost-effective strategy for treating a variety of infectious diseases, including skin and soft-tissue infections,^{1,2} osteomyelitis,^{3,4} prosthetic joint infections,^{5,6} and endocarditis.⁷ In a 2006 survey of infectious disease (ID) physicians, 94% indicated that patients are commonly set up for OPAT at hospital discharge.⁸ In addition to patients' preference for being treated outside the hospital setting,⁹ there are clear cost savings associated with OPAT. Use of OPAT is significantly less expensive than continued inpatient care.¹⁰⁻¹²

In 2004, the Infectious Disease Society of America (IDSA) published practice guidelines suggesting standards for OPAT practices. These guidelines provide recommendations on patient evaluation and selection for OPAT services, antibiotic selection and administration, OPAT team structure, and laboratory monitoring.¹³ A survey of ID physicians, conducted before the publication of these guidelines, revealed diverse

OPAT practices.⁸ Little is known about OPAT practice patterns, complication rates, and safety systems since the publication of these guidelines. The aim of this study was to survey adult ID physicians on their current OPAT practices.

METHODS

The Emerging Infections Network (EIN) is a network of ID physicians in North America who provide care to adult and pediatric patients. The network was established in 1995 by the Centers for Disease Control and Prevention (CDC) to establish a provider-based emerging infections sentinel network.¹⁴ The network is also used for surveys of current knowledge and practices of providers. This survey was sent electronically or via facsimile to the 1,244 EIN members who provide care to adult patients. The survey was conducted from November to December 2012. After the survey distribution, email reminders were sent to nonrespondents 2 and 4 weeks

Affiliations: 1. Department of Internal Medicine, Washington University in St. Louis School of Medicine, St. Louis, Missouri; 2. Department of Internal Medicine, Carver College of Medicine, University of Iowa, Iowa City, Iowa; 3. Department of Pediatric and Adolescent Medicine, Mayo Clinic, Rochester, Minnesota; 4. Pediatric Infectious Diseases, University of Utah, Salt Lake City, Utah.

Received November 17, 2013; accepted February 9, 2014; electronically published May 9, 2014.

© 2014 by The Society for Healthcare Epidemiology of America. All rights reserved. 0899-823X/2014/3507-0009\$15.00. DOI: 10.1086/676859

after the initial invitation. The survey consisted of brief introductory text and 11 questions. Survey questions addressed OPAT practice patterns and safety issues. Participants were asked about their participation in OPAT services and the role of ID consultation before patient discharge or placement of a vascular catheter for designated OPAT recipients. Participants were also asked about who was responsible for monitoring and acting upon laboratory results from patients receiving OPAT. Respondents were queried on their perceptions of the frequency and consequences of OPAT-related complications, including laboratory abnormalities, catheter-associated complications, and the development of *Clostridium difficile* or bloodstream infections. One question focused on barriers to providing safe OPAT services to patients. Finally, participants were asked to indicate the frequency of laboratory monitoring during OPAT for several frequently used antibiotics. The survey may be found at <http://ein.idsociety.org/surveys/survey/62/>. Differences in frequencies were analyzed for statistical significance using χ^2 tests, Student *t* test, and Mann-Whitney *U* test as appropriate. A *P* value of less than .05 was considered to be statistically significant.

RESULTS

Overall, 555 (44.6%) of 1,244 physicians participating in the EIN responded to the survey. Respondents came from all US census regions.¹⁵ Response rates were similar across all census regions. Respondents were significantly more likely than non-respondents to have 15 years or more of ID experience ($P < .0001$). EIN members with 25 years or more of experience were the largest group of respondents (150 [55%] of 274), followed by those with 15–24 years of experience (147 [50%] of 292).

Among respondents, 105 (19%) did not provide care to any patients discharged with OPAT in an average month. Among those who did manage patients who were receiving OPAT, monthly patient volume varied widely; 114 respondents (20%) managed 1–5 patients/month, 214 respondents (39%) managed 6–15 patients/month, 80 respondents (14%) managed 16–25 patients/month, and 42 respondents (8%) managed more than 25 patients/month. Respondents ranked the patient's home as the most common location for receiving OPAT, followed by infusion centers, dialysis centers, and emergency rooms.

Twenty-two percent of respondents reported that ID consultation is required to discharge any patient who is receiving intravenous antibiotics. Of those requiring ID consultation to discharge a patient with OPAT, only 28 (28%) required ID consultation to approve vascular access placement for OPAT. The inpatient (63%) and outpatient (52%) ID physicians were the most commonly identified as being responsible for monitoring and acting upon laboratory results. Ninety-four respondents (21%) indicated that the patient's primary care physician was responsible for monitoring laboratory results. Dedicated OPAT teams whose primary job is to monitor pa-

tients receiving OPAT were uncommon, with 118 (26%) reporting this service at their primary hospital or clinic. Respondents providing OPAT services to 16 or more patients per month were more likely to have a dedicated OPAT team, compared with lower-volume providers (40% vs 21%; $P < .001$). Lack of a dedicated OPAT team was the single most common barrier reported to providing safe OPAT services (median rank, 2), followed by the large number of locations at which patients receive OPAT, communication issues, and volume of laboratory results (median rank, 3).

Only 97 (22%) of the respondents have a system to track the frequency of errors, adverse events, or "near misses" associated with OPAT. Those providing OPAT services to more than 16 patients per month were more likely to have error-reporting systems than were lower-volume providers (32% vs 18%; $P = .023$). Line occlusion or clotting, rash, and nephrotoxicity were the most commonly reported complications associated with OPAT (Figure 1). Respondents indicated that patients commonly required line exchange or removal or change in antibiotic therapy because of complications from OPAT; hospitalization for OPAT complications was less common (Figure 2). Over the past 5 years, 98 (22%) and 214 (48%) of the respondents reported OPAT-related complications to be less frequent or unchanged, respectively. A minority (67 [15%]) reported OPAT-related complications to be more frequent than 5 years ago. Although there is some variation, weekly laboratory monitoring was reported to be the most common practice for several common antibiotics (Table 1).

DISCUSSION

We report the results of a survey of a large network of adult ID physicians regarding their experiences providing OPAT. We found that the use of OPAT is common among ID physicians, with over 80% of respondents discharging 1 or more patients with OPAT during an average month. We found significant variability in the involvement of ID physicians in selecting patients for OPAT, practice infrastructure, and laboratory monitoring practices.

Selecting patients who would benefit from OPAT is critical to treatment success. International OPAT guidelines recommend careful review of patients who might be appropriate for OPAT.^{13,16} Patients discharged with OPAT must be medically stable to receive continued treatment outside the inpatient hospital setting. In addition, IDSA guidelines recommend an assessment of the patient and caregivers who will be responsible for administering the medications and caring for vascular access devices.¹³ In addition to assessing the patient and caregiver's ability to provide daily OPAT care at home, formal ID consultation facilitates the appropriate selection of antibiotic therapy. Sharma et al¹⁷ found that requiring ID consultation before discharge with OPAT frequently altered the patient's care and resulted in a significant cost savings. At the Cleveland Clinic, ID consultation is re-

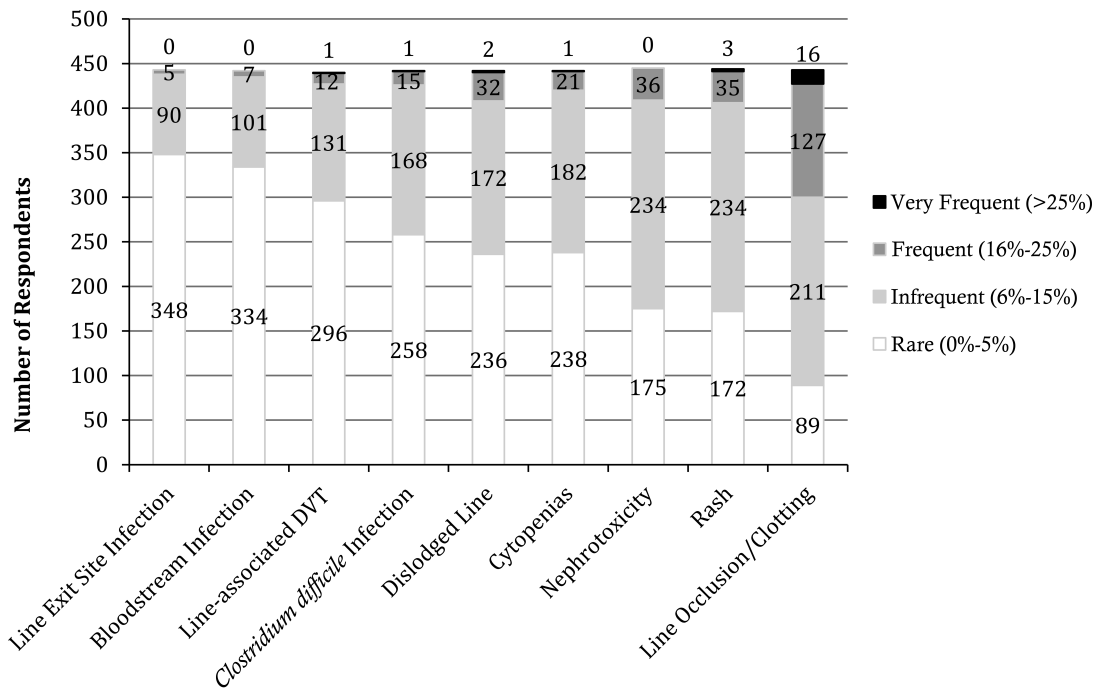


FIGURE 1. Number of respondents reporting perceived frequency of specified outpatient parenteral antimicrobial therapy complications. DVT, deep vein thrombosis.

quired before patient discharge with OPAT. In a study of 263 candidates for OPAT, ID consultation resulted in optimization of the antibiotic treatment regimen or significant alterations in the patient's assessment in 84% and 52%, respectively, of patients evaluated by OPAT physicians. Additionally, OPAT was determined to be unnecessary in 27% of patients evaluated, almost half of whom were deemed not to need any antibiotic therapy at all following discharge.¹⁸ Although these studies demonstrate significant benefit to patients, few hospitals require ID consultation before discharge. In our study, only 22% of respondents indicated that ID consultation was required to initiate OPAT. Our results suggest that there are significant opportunities for improvement in antibiotic stewardship through the use of routine ID consultation before OPAT initiation.

Additionally, our survey found that a wide variety of providers are responsible for monitoring and acting upon laboratory results for patients treated with OPAT, including inpatient ID physicians (reported by 63% of respondents), outpatient ID physicians (52% of respondents), patient primary care physicians (21% of respondents), and pharmacists (9% of respondents). Although it is possible that some variation may be attributable to different models of OPAT delivery,¹⁹ our findings suggest a lack of consensus regarding standard processes to ensure that patients receive appropriate monitoring after hospital discharge. Only 26% of respondents indicated that their primary hospital or clinic had a specified provider or team whose primary purpose was to monitor

patients receiving OPAT; it is possible that some clinical practices use various personnel to perform these duties even though it is not their primary role. Respondents reported many barriers to providing safe OPAT services. The lack of dedicated personnel was the single most common barrier reported by respondents. Although IDSA guidelines recommend a multidisciplinary team to coordinate care and monitor laboratory results, our study suggest that these recommendations may be poorly implemented in current practice.

Although earlier surveys of ID physicians suggest OPAT complications are common, there are limited data on the frequency of OPAT-related adverse events or hospital readmission.⁸ In a retrospective study of 302 courses of OPAT, significant adverse events were noted in 25%. Renal failure was the most common adverse event, occurring in 7% of OPAT courses.²⁰ Among patients with osteomyelitis treated with OPAT, 5% experienced some adverse event.²¹ This OPAT registry also demonstrated that 25.2% of patients treated with vancomycin experienced a vancomycin or intravenous line-related adverse event.²² Other reports have shown significant rates of decreased renal function, as high as 3.08 patients per 1,000 therapy-days among patients treated with select antibiotics.²³ Hospital readmission because of complications associated with OPAT therapy occurs in 12%–16% of patients.^{6,24} In our study, respondents reported line occlusion or clotting, rash, and nephrotoxicity occur commonly, although most believe there has been no change in the frequency of OPAT-related complications over the past 5 years.

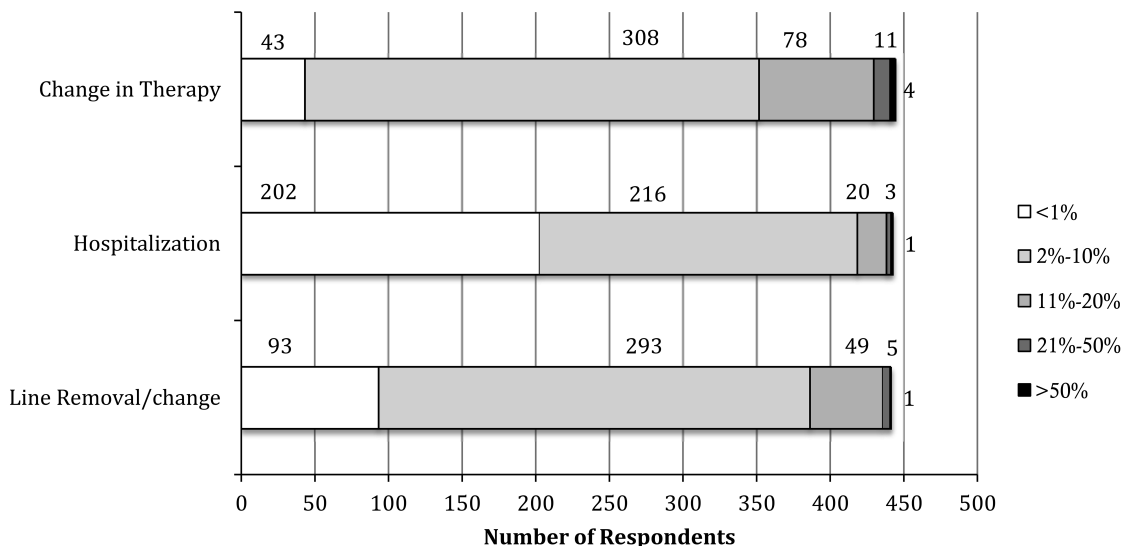


FIGURE 2. Number of respondents reporting perceived frequency of specified consequences of outpatient parenteral antimicrobial therapy complications.

However, despite the frequency of these complications, fewer than one-quarter have systems to track the frequency of errors, adverse events, or “near-misses” associated with OPAT. Given the widespread lack of reporting systems or registries, it is possible that error rates reported by respondents underestimate the true number of patients who experience harm while treated with OPAT.

Although weekly laboratory monitoring was most common for many antibiotics, our results demonstrated some variability in practice. Vancomycin use has become more common as rates of methicillin-resistant *Staphylococcus aureus* infection have increased among hospitalized patients. Vancomycin-associated nephrotoxicity rates have been reported to vary widely from 5%–35%.²⁵ Clinical guidelines on vancomycin use suggest once weekly monitoring for hemodynamically stable patients;²⁶ however, these guidelines do not address the safety of high vancomycin dose strategies that target a trough concentration of 15–20 mg/L. A subsequent

meta-analysis demonstrated an increased risk of nephrotoxicity among patients with vancomycin trough greater than or equal to 15 mg/L compared with those with a trough less than 15 mg/L (odds ratio, 2.67 [95% confidence interval, 1.95–3.65]).²⁷ Most respondents in our study report monitoring laboratories on a weekly basis for patients treated with vancomycin. However, more frequent laboratory monitoring, favored by 86 (19%) of 445 respondents, may allow for early identification and intervention for patients who develop nephrotoxicity.

This study has several limitations that may limit the generalizability of the results. Although we had more than 550 respondents, these respondents may not be representative of the entire ID community. Additionally, a significant number of respondents indicated they were not required to be involved in the management of patients discharged with OPAT. Because our survey targeted only EIN members, it is possible that OPAT practices and complication rates identified in our

TABLE 1. Laboratory Antibiotic Monitoring Frequency

Antibiotic	No. (%) of respondents, by no. of times per week that antibiotic is monitored					Total respondents
	<1	1	2	3	>3	
Daptomycin	33 (8)	385 (88)	20 (5)	1 (0)	0 (0)	439
Vancomycin	16 (4)	343 (77)	84 (19)	2 (0)	0 (0)	445
Oxacillin-nafcillin	38 (9)	385 (87)	17 (4)	2 (0)	0 (0)	442
Cephalosporins	44 (10)	384 (87)	11 (2)	1 (0)	1 (0)	441
Carbapenems	44 (10)	388 (87)	12 (3)	0 (0)	0 (0)	444
Amphotericin	22 (5)	98 (24)	194 (47)	91 (22)	10 (2)	415
Aminoglycosides	23 (5)	130 (30)	247 (57)	31 (7)	4 (1)	435

survey are not representative of patients discharged with OPAT by other medical providers. Additionally, recall bias is an inherent limitation of surveys.

Although OPAT has been used for decades to successfully treat a wide array of infectious diseases, our study demonstrates there is tremendous variability in practice patterns among physicians who provide OPAT services. With increasing focus on improving the quality of medical care and reducing hospital readmissions, standardization of OPAT practices has the potential to provide significant benefit to patients. To improve clinical outcomes, robust tracking systems or OPAT registries will need to be developed to support evidence-based practices and monitor individual patient outcomes.

ACKNOWLEDGMENTS

Financial support. M.A.L. reports having received career development support from the Goldfarb Patient Safety and Quality Fellowship program and the Barnes-Jewish Hospital Foundation. M.A.L. also reports being supported by Washington University Institute of Clinical and Translational Sciences (ICTS) grants (UL1 TR000448 and KL2 TR000450) from the National Center for Advancing Translational Sciences and a KM1 Scholars Program grant (KM1CA156708) through the National Cancer Institute (NCI) at the National Institutes of Health (NIH). M.A.L. has also received loan repayment support from L30 AR063363. J.M. reports being supported by the NIH Clinical and Translational Sciences award (UL1RR024992) and being the recipient of a KL2 career development grant (KL2RR024994); he is currently supported by a Building Interdisciplinary Careers in Women's Health KL2 career development award (5K12HD001459-13). J.M. also reports being the section leader for a subproject of the Centers for Disease Control and Prevention Epicenters Program grant (CU54 CK 000162). In addition, J.M. reports being funded by the Barnes-Jewish Hospital Patient Safety and Quality Fellowship Program and a research grant by the Barnes-Jewish Hospital Foundation and Washington University's ICTS. This publication was supported by cooperative agreement 1U50CK000187 from the Centers for Disease Control and Prevention. Its contents are solely the responsibility of the authors and do not necessarily represent the official views of the Centers for Disease Control and Prevention.

Potential conflicts of interest. All authors report no conflicts of interest relevant to this article. All authors submitted the ICMJE Form for Disclosure of Potential Conflicts of Interest, and the conflicts that the editors consider relevant to this article are disclosed here.

Address correspondence to Michael Lane, MD, Washington University School of Medicine, Campus Box 8051, 660 South Euclid Avenue, St. Louis, MO 63110 (mlane@dom.wustl.edu).

REFERENCES

- Leder K, Turnidge JD, Grayson ML. Home-based treatment of cellulitis with twice-daily cefazolin. *Med J Aust* 1998;169(10):519–522.
- Nathwani D. The management of skin and soft tissue infections: outpatient parenteral antibiotic therapy in the United Kingdom. *Chemotherapy* 2001;47(suppl 1):17–23.
- Eron LJ, Goldenberg RI, Poretz DM. Combined ceftriaxone and surgical therapy for osteomyelitis in hospital and outpatient settings. *Am J Surg* 1984;148(4A):1–4.
- Tice AD. Outpatient parenteral antimicrobial therapy for osteomyelitis. *Infect Dis Clin North Am* 1998;12(4):903–919.
- Esposito S, Noviello S, Leone S, et al. Outpatient parenteral antibiotic therapy (OPAT) in different countries: a comparison. *Int J Antimicrob Agents* 2004;24(5):473–478.
- Duggal A, Barsoum W, Schmitt SK. Patients with prosthetic joint infection on IV antibiotics are at high risk for readmission. *Clin Orthop Relat Res* 2009;467(7):1727–1731.
- Rehm SJ. Outpatient intravenous antibiotic therapy for endocarditis. *Infect Dis Clin North Am* 1998;12(4):879–901, vi.
- Chary A, Tice AD, Martinelli LP, Liedtke LA, Plantenga MS, Strausbaugh LJ. Experience of infectious diseases consultants with outpatient parenteral antimicrobial therapy: results of an emerging infections network survey. *Clin Infect Dis* 2006;43(10):1290–1295.
- Montalto M. Patients' and carers' satisfaction with hospital-in-the-home care. *Int J Qual Health Care* 1996;8(3):243–251.
- Hindes R, Winkler C, Kane P, Kunkel M. Outpatient intravenous antibiotic therapy in medicare patients: cost-savings analysis. *Infect Dis Clin Pract* 1995;4(3):211–217.
- Poretz DM, Woolard D, Eron LJ, Goldenberg RI, Rising J, Sparks S. Outpatient use of ceftriaxone: a cost-benefit analysis. *Am J Med* 1984;77(4C):77–83.
- Williams DN, Bosch D, Boots J, Schneider J. Safety, efficacy, and cost savings in an outpatient intravenous antibiotic program. *Clin Ther* 1993;15(1):169–179; discussion 168.
- Tice AD, Rehm SJ, Dalovisio JR, et al. Practice guidelines for outpatient parenteral antimicrobial therapy. IDSA guidelines. *Clin Infect Dis* 2004;38(12):1651–1672.
- Executive Committee of the Infectious Diseases Society of America Emerging Infections Network. The emerging infections network: a new venture for the Infectious Diseases Society of America. *Clin Infect Dis* 1997;25(1):34–36.
- US Department of Commerce. Census regions and divisions of the United States. http://www.census.gov/geo/maps-data/maps/pdfs/reference/us_regdiv.pdf. Accessed May 1, 2014.
- Chapman AL, Seaton RA, Cooper MA, et al. Good practice recommendations for outpatient parenteral antimicrobial therapy (OPAT) in adults in the UK: a consensus statement. *J Antimicrob Chemother* 2012;67(5):1053–1062.
- Sharma R, Loomis W, Brown RB. Impact of mandatory inpatient infectious disease consultation on outpatient parenteral antibiotic therapy. *Am J Med Sci* 2005;330(2):60–64.
- Shrestha NK, Bhaskaran A, Scalera NM, Schmitt SK, Rehm SJ, Gordon SM. Contribution of infectious disease consultation toward the care of inpatients being considered for community-based parenteral anti-infective therapy. *J Hosp Med* 2012;7(5):365–369.
- Tice AD. Outpatient parenteral antibiotic therapy (OPAT) in the United States: delivery models and indications for use. *Can J Infect Dis* 2000;11(suppl A):17A–21A.
- Berman SJ, Johnson EW. Out-patient parenteral antibiotic therapy (OPAT): clinical outcomes and adverse events. *Hawaii Med J* 2001;60(2):31–33.
- Tice A. The use of outpatient parenteral antimicrobial therapy in the management of osteomyelitis: data from the Outpatient Parenteral Antimicrobial Therapy Outcomes Registries. *Chemotherapy* 2001;47(suppl 1):5–16.
- Tice AD, Hoaglund PA, Nolet B, McKinnon PS, Mozaffari E.

- Cost perspectives for outpatient intravenous antimicrobial therapy. *Pharmacotherapy* 2002;22(2 pt 2):63S–70S.
23. Rehm SJ, Longworth DL. Rates of adverse events associated with community-based parenteral anti-infective therapy. *J Clin Outcomes Manage* 2000;7(10):23–28.
 24. Cervera C, del Rio A, Garcia L, et al. Efficacy and safety of outpatient parenteral antibiotic therapy for infective endocarditis: a ten-year prospective study. *Enferm Infecc Microbiol Clin* 2011;29(8):587–592.
 25. Elyasi S, Khalili H, Dashti-Khavidaki S, Mohammadpour A. Vancomycin-induced nephrotoxicity: mechanism, incidence, risk factors and special populations: a literature review. *Eur J Clin Pharmacol* 2012;68(9):2143–2155.
 26. Rybak M, Lomaestro B, Rotschafer JC, et al. Therapeutic monitoring of vancomycin in adult patients: a consensus review of the American Society of Health-System Pharmacists, the Infectious Diseases Society of America, and the Society of Infectious Diseases Pharmacists. *Am J Health Syst Pharm* 2009;66(1):82–98.
 27. van Hal SJ, Paterson DL, Lodise TP. Systematic review and meta-analysis of vancomycin-induced nephrotoxicity associated with dosing schedules that maintain troughs between 15 and 20 milligrams per liter. *Antimicrob Agent Chemother* 2013;57(2):734–744.