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Practice Guidelines for Outpatient Parenteral Antimicrobial Therapy

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EXECUTIVE SUMMARY

These guidelines were formulated to assist physicians and other health care professionals with various aspects of the administration of outpatient parenteral antimicrobial therapy (OPAT). Although there are many reassuring retrospective studies on the efficacy and safety of OPAT, few prospective studies have been conducted to compare the risks and outcomes for patients who receive treatment as outpatients rather than as inpatients. Because truly evidence-based studies are lacking, the present guidelines are formulated from the collective experience of the committee members and advisors from related organizations.

Important aspects of OPAT are described in the text and tables and include the following:

1. The literature supports the effectiveness of OPAT for a wide variety of infections (table 1 and the Appendix).
2. A thorough assessment of the patient's general medical condition, the infectious process, and the home situation is necessary before starting therapy (table 2)
3. Prescribing physicians should be aware of a number of aspects of OPAT which distinguish it from

other forms of therapy. These include the required teamwork, communication, monitoring, and outcome measurements (tables 3 and 4).

4. The physician has a unique role on the OPAT team, which may also include nursing, pharmacy, and social services. These responsibilities include establishing a diagnosis, prescribing treatment, determining the appropriate site of care, monitoring during therapy, and assuring the overall quality of care.

5. Antimicrobial selection for OPAT is different from that for therapy in the hospital. Once-daily drug administration has many advantages. Potential for adverse effects and the stability of an antimicrobial once it is mixed must be considered (tables 5–7).

6. The importance of administering the first dose of an antibiotic in a supervised setting is emphasized.

7. Regular clinical and laboratory monitoring of patients receiving OPAT is essential and varies with the antimicrobial chosen (table 8).

8. Outcomes measures should be an integral part of any OPAT program, to assure the effectiveness and quality of care (table 9).

9. Children receiving OPAT must be considered differently because of their special needs.

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INTRODUCTION

The practice of administering intravenous antimicrobial therapy in the home and in alternate care settings has grown rapidly since it was first described in 1974 by Rucker and Harrison [1–9]. The most common infections treated and antimicrobials used by a variety of programs are shown in table 1. In the United States,

Table 1. Infections treated with outpatient parenteral antimicrobial therapy (OPAT) and the antibiotics used in 4 studies or sites.

OPAT Network (1996–2002) ^a	Cleveland Clinic (1986–2000) ^b	Minneapolis area (1978–1990) ^c	Children's Hospital San Diego (2000) ^d
Type of infection, ranked by frequency (% of OPAT courses)			
Skin and soft tissue (23)	Musculoskeletal	Cellulitis (15)	Bacteremia (16)
Osteomyelitis (15)	Infected devices	Osteomyelitis (13)	Pyelonephritis (13)
Septic arthritis/bursitis (5)	Bacteremia	Late-stage Lyme disease (10)	Meningitis (13)
Bacteremia (5)	Intra-abdominal	Pyelonephritis and UTI (9)	Intra-abdominal (8)
Wound (4)	Skin and soft tissue	Septic arthritis (7)	Cellulitis (7)
Pneumonia (4)	...	Other (46)	Osteomyelitis (7)
Pyelonephritis (3)	Wound (7)
Antimicrobial, ranked by frequency of use (% of OPAT courses)			
Ceftriaxone (33)	Vancomycin (31)	...	Ceftriaxone (42)
Vancomycin (20)	Penicillins (20)	...	Meropenem (11)
Cefazolin (6)	Antivirals (12)	...	Cefazolin (11)
Oxacillin/nafcillin (5)	Cephalosporins (9)	...	Cefepime (6)
Aminoglycosides (5)	Aminoglycosides (5)	...	Ceftazidime (6)
Clindamycin (3)	Other β -lactams (4)	...	Vancomycin (6)
Ceftazidime (3)

NOTE. UTI, urinary tract infection.

^a Data from OPAT Outcomes Registry (available at <http://www.opat.com>).

^b Data from Susan Rehm, personal communication. Percentage of infections not recorded.

^c Data from [138].

^d Data from John Bradley, personal communication.

OPAT is estimated to be a multibillion-dollar-a-year industry and is provided to 1 in 1000 Americans each year [10]. The growth of OPAT has been fueled by a variety of factors including the push for cost containment, the development of antimicrobial agents that can be administered once daily, technological advances in vascular access and infusion devices, increased acceptance of such therapy by both patients and health care personnel, and the availability of reliable and skilled services for OPAT in the community. Although OPAT has become widely accepted as a form of medical therapy (see Appendix), more information is needed regarding its benefits, safety, and limitations. This is especially true with the economic incentives for early discharge that exist for payors.

These guidelines update those written in 1997 [11] and are intended to ensure successful implementation of parenteral antimicrobial services for patients in varied community settings, including the home and outpatient facilities, such as physicians' offices, hospital clinics, ambulatory-care centers, day hospitals, and skilled nursing facilities. They have been formulated to incorporate the perspectives of the team of physicians, nurses, pharmacists and other health care professionals necessary for an effective and safe program [6, 8, 12]. Advice and participation were requested of the leading infusion-nurse, pharmacy, infection control, internal medicine, pediatric medicine, and

home-care societies to gain a broad perspective on the multidisciplinary approach needed.

The recommendations were formulated from the collective clinical experience of the Infectious Diseases Society of America Guidelines Committee and representatives from the invited organizations. In the majority of cases, the strength and quality of evidence in support of OPAT is limited by a lack of prospective studies and a large number of confounding variables, therefore no ratings are given here. The information herein, however, can provide a guide for programs to develop the best practices possible in their environment.

These guidelines are general and need to be adapted to many variables in each treatment setting. Because of the focus on OPAT, the related topics of duration of therapy, when to switch to oral anti-infective therapy, and infusion therapies other than antimicrobials are not addressed.

BASIC DEFINITIONS

In these guidelines, the acronym "OPAT" is used in place of "CoPAT" (community-based parenteral anti-infective therapy), because "OPAT" is the more commonly used term. "OPAT" is generally used to refer to the provision of parenteral antimicrobial therapy in at least 2 doses on different days without

intervening hospitalization. The term “outpatient” is used to refer to the varied settings in which intravenous antimicrobial therapy can be provided without an overnight stay in a hospital. These include the home, physician’s offices, hospital-based ambulatory-care clinics, emergency departments, hemodialysis units, freestanding infusion centers, skilled nursing or long-term care facilities, and rehabilitation centers. The term “parenteral” encompasses intravenous, subcutaneous, and intramuscular routes of administration. “Antimicrobial” refers to antiviral, antifungal, and antibacterial medications. “Caregiver” refers to any family member, friend, or paid nonprofessional individual with the ability and willingness to administer treatment and to observe and report significant events.

PATIENT EVALUATION AND SELECTION

Initiation of OPAT requires that a physician determine that such therapy is needed to treat a defined infection, that hospitalization is not needed to control the infection, and that alternate routes of drug delivery are not feasible or appropriate. Factors to consider in patient evaluation and selection are outlined in table 2.

The primary goals of outpatient therapy programs are to allow patients to complete treatment safely and effectively in the comfort of their home or another outpatient site and to avoid the inconveniences, complications, and expense of hospitalization. However, OPAT is not appropriate if the patient’s medical care needs would be better met in the hospital. Financial concerns in selection of patients for OPAT should not take precedence over the patient’s welfare.

There is potential for both overuse and underuse of OPAT. A careful analysis of patients referred for home therapy will demonstrate that a subset of referrals may be inappropriate [6]. Some patients require hospitalization for ongoing care; for others, oral therapy is appropriate, and, for some, antimicrobial therapy may not be needed. Because of the risks of progressive infections and for adverse events, physicians with training in the specialty of infectious diseases or with experience and

knowledge of OPAT should be involved in the evaluation of candidates for therapy.

Medical assessment. Determination of the status of the patient’s infection and any underlying medical condition is a critical component of the assessment process. The increasing use of OPAT without initial hospitalization makes the challenge of medical assessment even more important. The patient’s risk of sudden or life-threatening changes in health should be low. OPAT may be appropriate for patients with terminal conditions, if the therapy contributes to their quality of life and comfort. Often the patient’s participation is more dependent on medical and psychosocial factors other than the type of infection present. Table 1 lists the more common infections and antimicrobials used at several different OPAT centers. For most programs, soft-tissue and bone infections are the most common diagnoses.

Patients with a sepsis syndrome or infections such as meningitis, endocarditis, septic arthritis, or severe pneumonia should usually be hospitalized for initiation of parenteral antimicrobial therapy because of the risk that the patient’s medical condition may suddenly worsen or that hospital-based procedures may be needed. Once their condition has stabilized, however, many of these patients may be appropriately discharged to receive OPAT.

Recent guidelines for community-acquired pneumonia indicate that OPAT may be useful for selected patients [13–16]. Studies by Fine and coworkers [17, 18] suggest OPAT can be much more widely used for pneumonia, if community resources are available and physicians are aware of them. Selected patients with endocarditis are also candidates for OPAT [19]. There is a significant experience in treating nonenterococcal endocarditis on an outpatient basis, usually with once-daily ceftriaxone and sometimes without hospitalization [20–22]. However, patients with endocarditis who have prosthetic valves, persistently positive blood culture results, poorly controlled congestive heart failure, large vegetations (>10 mm in length), recurrent embolic events, *Staphylococcus aureus* etiology, or conduction abnormalities are at increased risk for complications that may be more quickly recognized and

Table 2. Specific considerations in evaluating patients for outpatient parenteral antimicrobial therapy (OPAT).

1. Is parenteral antimicrobial therapy needed?
2. Do the patient’s medical care needs exceed resources available at the proposed site of care?
3. Is the home or outpatient environment safe and adequate to support care?
4. Are the patient and/or caregiver willing to participate and able to safely, effectively, and reliably deliver parenteral antimicrobial therapy?
5. Are mechanisms for rapid and reliable communications about problems and for monitoring of therapy in place between members of the OPAT team?
6. Do the patient and caregiver understand the benefits, risks, and economic considerations involved in OPAT?
7. Does informed consent need to be documented?

treated in the hospital. A conservative approach suggests inpatient care or daily outpatient follow-up during the first 2 weeks of therapy because of the increased risk of life-threatening events, such as acute congestive heart failure, embolus, or myocardial abscess [19]. Andrews and von Reyn [23] suggest that patients with uncomplicated endocarditis due to viridans group streptococci could be discharged to receive OPAT after 1 week of hospitalization.

Injection drug use or alcohol abuse problems should be specifically evaluated before therapy is initiated. Patients who are likely to abuse a vascular access system are poor candidates for OPAT [24]. A skilled nursing facility may be the most appropriate model for care. Intramuscular injections or daily infusions with removal of the catheter may be appropriate for some patients [25]. Some computerized infusion pumps can monitor therapy and may reduce the likelihood of tampering. The patient's ability to adhere to the prescribed regimen and the threat of unauthorized vascular access will determine whether therapy outside of the hospital setting is advisable and whether a long-lasting venous line is appropriate.

Patient and caregiver ability assessment. The capabilities of patients who will receive OPAT and of their caregivers must be carefully evaluated before they are accepted into the program. Patients or their caregivers must be able to assume responsibility for the infusion, the care of the vascular access device (VAD), and the care of the catheter infusion site, and be able to recognize and report new problems, such as rash, diarrhea, or fever. Home care of children requires the involvement of parents or guardians and requires standards the same as, if not higher than, those for adults. Daily treatment in a physician's office or infusion center is an option for selected patients with unstable diseases or inadequate housing or because of personal preference or insurance restrictions. Patients receiving OPAT should have their VAD and health status assessed by a licensed health-care practitioner. Participation in OPAT by selected patients with physical limitations may be facilitated through the use of electronic and mechanical infusion devices [26].

Patients should be informed of the economic and the medical aspects of OPAT before the initiation of therapy. Patients should be counseled regarding insurance coverage and anticipated out-of-pocket costs to allow an informed decision before OPAT begins. Documentation of informed consent with written information may be appropriate.

Ongoing communication among patient, caregiver, nurse, pharmacist, and physician is critical to the success of OPAT. Patients must have means of immediate communication (telephone or cellular telephone) and transportation for physician appointments and emergency services. Communications should be undertaken in such a way that patient confidentiality is preserved. Telemedicine with home monitors or in-

teractive audio/video devices for home assessment and compliance may be helpful [27, 28].

Home assessment. The health care team must also have knowledge of the patient's home environment prior to initiation of OPAT. This information is ideally obtained by a visit to the home before or at the time of initiation of therapy, but verbal assessment may suffice [29]. Potential problems, such as the functioning of utilities, safety issues, cleanliness, substance abuse, access to transportation, and social strife need to be assessed. Home visits may also pose a risk to health-care practitioners, which should be considered.

KEY ELEMENTS OF AN OPAT PROGRAM

Physician-directed OPAT program. The key elements of physician-directed OPAT programs are outlined in table 3. Although any physician can legally order OPAT, not all physicians are expert in doing so. The responsible physician should be knowledgeable about infectious diseases and OPAT so that poor clinical responses or problems such as therapeutic failure, adverse events, drug toxicity, and infusion device and vascular access issues are avoided or appropriately and promptly addressed. In some clinical settings, an infectious diseases consultation is required before a patient can be sent home to receive OPAT [6, 30]. Some organizations have focused on accreditation requirements to establish minimum standards for physician supervision and management of home care agencies [31]. Although there has been enormous growth in home care services nationwide, direct physician involvement has not kept pace, largely because of low levels of reimbursement for management or direct patient care in the home setting [32, 33].

Infusion nurse specialists and pharmacists should also be knowledgeable and experienced with OPAT, as should other members of the health care team, which may include social workers, physical therapists, dietitians, and occupational therapists. The American Society of Health System Pharmacists has developed specific guidelines on the pharmacist's role in home care [34, 35].

OPAT programs must have systems for rapid communication between nurses, pharmacists, physicians, and patients. Such systems are required both for initial treatment planning and for monitoring of ongoing care. Communication via pagers, cellular telephones, facsimile machines, and electronic mail has become increasingly important, although it must comply with the Health Insurance Portability and Accountability Act (HIPAA). Programs should have written policies and procedures that outline the responsibilities of the team members and address issues such as patient selection criteria, drug preparation, vascular access, laboratory monitoring, and disposal of waste and needles. Patient and caregiver education materials should provide specific information about the program, a list of emer-

Table 3. Key elements required for an outpatient parenteral antimicrobial therapy (OPAT) program.

-
1. Health care team
 - A. An infectious diseases specialist or physician knowledgeable about infectious diseases and the use of antimicrobials in OPAT
 - B. Primary care or referring physicians available to participate in care
 - C. Nurse expert in intravenous therapy, access devices, and OPAT
 - D. Pharmacist knowledgeable about OPAT
 - E. Case manager and billing staff knowledgeable about therapeutic issues and third party reimbursements
 - F. Access to other health care professionals, including a physical therapist, a dietitian, an occupational therapist, and a social worker
 2. Communications
 - A. Physician, nurse, and pharmacist available 24 h per day
 - B. System in place for rapid communication between patient and team members
 - C. Patient education information for common problems, side effects, precautions, and contact lists
 3. Outline of guidelines for follow-up of patients with laboratory testing and intervention as needed
 4. Written policies and procedures
 - A. Outline of responsibilities of team members
 - B. Patient intake information
 - C. Patient selection criteria
 - D. Patient education materials
 5. Outcomes monitoring
 - A. Patient response
 - B. Complications of disease, treatment, or program
 - C. Patient satisfaction
-

gency-access telephone numbers, a statement regarding precautions and risks of OPAT, and when possible, specific information about the disease process and the antimicrobials used. Plans for quality assurance and outcomes monitoring should also be incorporated into OPAT programs. Policies and procedures may be developed for an individual program or developed with one of several commercial sources.

Referral to OPAT programs. The key elements for OPAT programs to which a patient is referred are listed in table 4. These relate to criteria for programs that the prescribing physician does not control even though the physician is ultimately responsible for the patient's care and outcome. Specific administrative elements, in addition to those listed in table 3, should be in place. Because prescribing physicians remain responsible for clinical care decisions, it is important for them to assess the quality of care provided by the OPAT delivery organization and to document deficiencies. Physicians are considered legally responsible for deciding whether a patient should be treated as an outpatient and to assure the quality of care during OPAT [36]. In addition, consultants should clarify their postdischarge role with other doctors involved in the patient's care [37].

An experienced physician director or advisor for an OPAT delivery organization is important for the success of the program. This position is analogous to that of the medical director

for hospice programs. Such persons provide clinical input into policies and procedures and oversee quality-of-care activities.

A home-infusion company should have written policies available regarding the qualifications of their staff, the procedures used, and the quality assurance systems in place. The company should be willing to share this information as well as the charge estimates for the proposed course of therapy. Patient education materials are an important resource, which can be helpful for conveying information about safety, responsibilities, and compliance and general advice.

The choice of a model for administering OPAT varies with individual patient needs, the program resources available, and the payor. It is possible to change the type of delivery model depending on the anti-infective agent used, the patient's capability for self-care, and the need for other medical services. The delivery models can be roughly classified according to whether the antimicrobial is administered in an infusion center, at a skilled nursing facility, or at home by a nurse or is self-administered [11, 38].

In the self-administration model, antimicrobials are infused by the patient, a family member, or another responsible person. Infusions may occur in the home, at work, or any other site. Methods by which therapy can be self-administered include gravity infusion systems and a variety of administration systems that can be adapted to the needs of the patient, the VAD, and

Table 4. Key elements required for evaluating an outpatient parenteral antimicrobial therapy (OPAT) program when the patient is to be referred.

-
1. Medical director or physician adviser knowledgeable about infectious diseases and OPAT
 2. An outline of roles for the prescribing physician in relation to the case manager, the medical director, the nurse, and the pharmacist
 3. Written standards that outline the required training, experience, and licensure for nurses, pharmacists, physicians, and other patient care personnel
 4. Information on whether the program is accredited or certified by the Joint Commission for the Accreditation of Health Care Organizations, the state health department, or other responsible agency
 5. Information on the experience the organization has in providing OPAT
 6. Established policies regarding the following issues:
 - A. Frequency of physician's and nurse's clinical assessment of the patient
 - B. Staffing and on-call policies
 - C. Frequency of clinical status reports to physicians
 - D. Reporting laboratory results to assure delivery to physicians within 24 h
 - E. Prompt reporting of patient problems and critical laboratory values
 7. Willingness to share program quality and outcomes information
 8. Willingness to share information regarding individual patient charges
 9. Policies available regarding the following issues:
 - A. Antimicrobial preparation, storage, and dispensing
 - B. Vascular access systems used and site care
 - C. Monitoring guidelines for physician visits, nurse evaluations, and laboratory studies
 - D. Disposal of waste and needles
 - E. Health care worker safety
 10. Provision of patient education and resource materials, including the following:
 - A. Instructions for emergencies
 - B. Information about antimicrobial use and possible adverse effects
 - C. Information about the potential risks, problems, and patient responsibilities regarding OPAT
 11. A developed, ongoing system to monitor quality indicators, including outcomes and complications of therapy
-

the drug used. This model has the advantages that it provides autonomy for the patient and reduces expense.

If a visiting nurse–service provider has staff that is experienced in home infusion, medications may be infused in the home under the direct supervision of a nurse. Antimicrobials may be administered by gravity infusion, by pump, or by intravenous pressure infusion (“IV push”) [39]. The number of nursing visits authorized by third-party payors, the availability of infusion nurses, and other considerations may limit the applicability of this model.

The infusion-center model has been established in many locations, including physician offices, outpatient centers, hospital outpatient clinics, and, less frequently, an emergency department or extended care facility. These centers offer the advantage of ready access to medical equipment and personnel but require the patient to travel to the facility for treatment.

Skilled nursing facilities may provide parenteral antimicrobial therapy and have replaced prolonged hospitalization in situations where patients are not capable of self-care, do not have satisfactory caregivers, have multiple medical problems,

are undergoing rehabilitation, do not have insurance coverage for home therapy, or are not likely to be compliant. Subacute care facilities and rehabilitation centers offer additional options for patients who require skilled therapy beyond infusion of antimicrobial agents.

ROLES OF THE TEAM MEMBERS IN OPAT

An effective OPAT program requires an interdisciplinary team of professionals committed to high-quality patient care [6, 11, 12, 40–43]. The typical OPAT team consists of the patient, a physician, an infusion nurse, and, often, a pharmacist. In many situations, a case manager for the hospital or third-party payor will play a vital role. Social workers are often involved in the selection of patients and coordination of therapy. Family members or other caregivers should participate in the planning and delivery of therapies outside of the hospital. There are inevitably areas of overlapping responsibilities, such as selection of intravenous access devices, determination of the most appropriate site of care, and monitoring of laboratory results. Several phy-

sicians (the primary physician, an infectious disease consultant, and other specialists) may be involved in follow-up, which adds to the challenges in coordinating care. For OPAT to be effective, not only optimal patient selection and education but also communication and coordination of care are essential. Reports of laboratory values, discussions of patient assessments, troubleshooting, and changes in orders are often handled by telephone, electronic mail, or facsimile. Continual availability of most members of the care team is critical to the success and safety of OPAT.

Expertise and experience in the management of antimicrobial therapy and VADs are required to optimize outcomes and minimize risk in OPAT programs. Because no specific OPAT certification is currently available for physicians, nurses, or pharmacists, OPAT expertise may be assessed by a combination of elements.

The physician. The role of the physician in OPAT has several unique aspects, and includes establishment of a diagnosis, determination of whether OPAT is appropriate, selection of antimicrobials, ordering of monitoring tests, and assessment at follow-up visits [6, 1112, 42, 43]. The physician, the infusion nurse specialist, and the patient should determine the appropriate type of vascular access. In consultation with other members of the team, the physician selects the site of care. The physician is responsible for the ongoing assessment of the patient's clinical response to therapy, monitoring for drug toxicity, management of vascular access problems, care of concurrent medical problems, and coordination of the efforts of other members of the team. The OPAT physician should approve any changes in treatment orders, including changes in doses or intervals for administration of antimicrobial agents. Collaboration between the primary physician and physician managing OPAT is imperative to avoid the possibility that potential problems will be overlooked or that efforts will be duplicated.

The issue of physician certification or credentialing to provide OPAT is evolving. The American Academy of Home Care Physicians offers a certifying examination in home care; however, measurements of competence specific to the provision of OPAT are only a small portion of the examination. The Residency Review Committee of the American Board of Internal Medicine, in its standards for training programs in infectious diseases, lists "appropriate use and management of antimicrobial agents in a variety of clinical settings, including the hospital, ambulatory practice and the home" as a curriculum component [44].

The infusion nurse. The role of the infusion nurse varies with the OPAT model and the site of care [26, 45, 46]. At the time of initial patient assessment, nurses provide valuable input as to the patient's suitability for parenteral therapy outside of the hospital. They usually assume the lead role in recommendations for the type of VAD to be selected and in the care of

the infusion device. Patient education, training, and monitoring fall within the realm of responsibility of the infusion nurse as well. When patients receive OPAT at home, nurses can provide a valuable home assessment. They may infuse the antimicrobial agent or provide oversight to others providing care. They may also serve bridging functions for the team and play a pivotal role in coordination of care. Nurses may achieve specialty certification in infusion therapy through the Infusion Nurses Certification Corporation (INCC), the sister organization of the Infusion Nurses Society, which has established standards for nurses in all care settings [26].

The pharmacist. The pharmacist on the team is usually responsible for the acquisition, storage, compounding, dispensing, and delivery of the antimicrobials, as well as for monitoring for adverse events and potential drug interactions [34, 43, 47]. The American Society of Health-System Pharmacists (ASHP) suggests that pharmacists conduct a preadmission assessment and that they educate patients about the antimicrobial agent and possible side effects [34]. The ASHP Section of Home, Ambulatory and Chronic care has published guidelines for pharmacists practicing in this setting [35].

The patient and the caregiver. The roles of the patient and caregiver in OPAT must not be underestimated; they both should play a part in planning the OPAT program and follow-up [29, 42]. Education about the infection, complications, treatment plans, potential problems, communication, and expected outcome is necessary. Their responsibilities of the patient and the caregiver are far greater than for hospitalized patients, and their adherence to therapy is essential. Patients and caregivers are often pleased to be involved in their own care and often come away with a sense of pride and satisfaction in their role.

The safety of the medical staff should also be considered, especially with home visits after dark and in high-crime neighborhoods. Concerns bearing on US Occupational Safety and Health Administration regulations with regard to worker safety and needlesticks should be as great, if not greater, with outpatient care than with inpatient care [48]. Bloodborne pathogens remain a problem and exposure remains a risk, although the risks are less than in a hospital [49]. Use of needleless administration systems is recommended.

ANTIMICROBIAL SELECTION AND ADMINISTRATION

When selecting an antimicrobial for OPAT, multiple factors must be taken into account, including the probable infecting organism, the pharmacodynamic and pharmacokinetic properties of candidate drugs, and drug stability. The antimicrobials frequently used for OPAT are listed in table 1. Although almost any antimicrobial can be used, drugs with long half-lives continue to be extensively prescribed, although specific choices will

Table 5. Properties of commonly prescribed antimicrobials at various temperatures.

Drug	Half-life in h	Phlebitis risk rating ^b	Optimal dilution, mg/mL ^c	Duration of stability, by storage temperature ^a		
				−20°C	5°C	25°C
Acyclovir ^d	2–3.5	1	5	ND	37 d	>37 d
Amphotericin B	24–360	3	0.1	ND	35 d	5 d
Liposomal amphotericin B	24–360	2	4	ND	24 h	5 d
Amphotericin B lipid complex	24–360	2	1	ND	48 h	6 h
Ampicillin	1	2	30	ND	48 h	8 h
Ampicillin-sulbactam	1	2	20	ND	48 h	8 h
Caspofungin	>48	1	0.2–03	ND	24 h	1 d
Cefazolin	1–2	1	10–20	30 d	10 d	1 d
Cefoperazone	1.5–25	1	40	96 d	80 d	80 d
Ceftazidime	1.4–2	1	1–40	90 d	21 d	2 d
Ceftriaxone	5.4–10.9	1	10–40	180 d	10 d	3 d
Cefuroxime	1–2	1	5–10	30 d	180 d	1 d
Chloramphenicol	1.5–4	1	10–20	180 d	30 d	30 d
Clindamycin	2–3	1	6–12	56 d	32 d	16 d
Doxycycline ^e	22–24	2	0.1–1	56 d	48 h	3 d
Erythromycin lactobionate	1.5–2	3	0.1–0.2	30 d	14 d	1 d
Ertapenem	4	2	20	ND	24 h	6 h
Ganciclovir	2.5–3.6	1	5	364 d	35 d	5 d
Gentamicin	2–3	1	0.6–1	30 d	30 d	30 d
Imipenem-cilastatin	0.8–1.3	2	2.5–5	ND	2 d	10 h
Linezolid	4.5	1	2	ND	ND	ND
Meropenem	1.5	1	5–20	ND	24 h	4 h
Nafcillin	0.5–1.5	3	2–40	90 d	3 d	1 d
Oxacillin	0.3–0.8	2	10–100	30 d	7 d	1 d
Penicillin G ^f	0.4–0.9	2	0.2	84 d	14 d	2 d
Quinupristin-dalfopristin	3/1	3	2	ND	54 h	5 h
TMP-SMZ ^d	8–11/10–13	2	8	ND	ND	6 h
Tobramycin	2–3	1	0.2–3.2	30 d	4 d	2 d
Vancomycin	4–6	2	5	63 d	63 d	7 d

NOTE. D, day(s); ND, no data; TMP-SMZ, trimethoprim-sulfamethoxazole.

^a Data from [47].

^b Degree of tendency to cause phlebitis: 1, mild; 2, moderate; 3, high.

^c Optimal solutions may vary from saline to 5% dextrose, depending on the antibiotic.

^d Should not be refrigerated.

^e Protect from sunlight.

^f Degradation products can form after a few hours.

vary with the patient population, the likely diagnosis, the anticipated duration of therapy, and physician preference. Use of agents that can be administered once daily reduces disruption of daily activities and limits the potential for complications. The choice of antimicrobials for OPAT needs to be continually evaluated as new oral agents may replace some parenterally administered choices, and antimicrobial resistance is an ongoing issue.

The initial dose of an intravenous agent should be administered in a supervised setting, such as a physician's office, ambulatory care department, or the hospital, before a patient's discharge to home care. Personnel trained in resuscitation and appropriate equipment should be readily available.

For patients with pneumonia, there is evidence that prompt administration of an intravenous antimicrobial may improve outcomes with respect to 30-day mortality [50] and lessen the length of hospital stay [51]. Administration of a parenteral antibiotic in the physician's office before hospitalization may also improve outcomes [52].

Table 5 displays the parameters of antimicrobials that are used for OPAT. The half-life of a drug determines the frequency with which it can be administered. The likelihood that phlebitis will develop influences the decision about the type of VAD needed. Drug-stability information is important for determining how often a drug must be mixed and how long it can be stored. The rate of administration must also be

monitored closely, especially with vancomycin, amphotericin B, acyclovir, ganciclovir, and foscarnet. Although IV push administration has been advocated for some of the β -lactam antibiotics, it has not been well studied and may cause minor symptoms [53–56]. The pH, osmolality, and irritative qualities of a drug need to be considered with this type of rapid intravenous administration.

Research regarding pharmacokinetics and pharmacodynamic factors has influenced the dosing of antimicrobial agents [11]. Aminoglycosides, which show concentration-dependent killing and a prolonged postantibiotic effect (i.e., a prolonged effect on bacterial growth after antibiotic therapy ceases), may be given in a once-daily dose. Such a regimen may offer therapeutic advantages and may also reduce the incidence of nephrotoxicity and ototoxicity [57–59]. However, the use of once-daily aminoglycoside therapy by pregnant women, children, elderly persons, and critically ill patients has not been fully evaluated. Once-daily dosing recommendations for patients with renal dysfunction, neutropenia, burns, liver disease, or endocarditis should be used with caution [57].

The β -lactam antimicrobials, because of their short half-lives and time-dependent killing with only a brief postantibiotic effect, might best be given by continuous infusion [60, 61]. However, β -lactams, such as ampicillin, that have short half-lives and that are unstable at body temperature may need to be mixed daily and administered as frequently as every 4 h, depending on renal function.

Ceftriaxone and ertapenem have sufficiently long half-lives to provide serum concentrations above the MICs for most susceptible organisms for 12–24 h and thus can be given once daily. Vancomycin has been used extensively in outpatient settings because of its attractive dosing characteristics and the increasing prevalence of infections due to oxacillin-resistant *S. aureus*. It is usually given every 12 h, but less frequent administration is indicated for patients with renal dysfunction and for elderly patients [62]. The increasing concern regarding vancomycin-resistant enterococci and the emergence of vancomycin-resistant *S. aureus* has necessitated limiting the use of vancomycin to clear indications [63, 64].

Although many drugs are stable both at room temperature and when refrigerated, the stabilities of ampicillin, quinupristin-dalfopristin, lipid formulations of amphotericin B, imipenem-cilastatin, and trimethoprim-sulfamethoxazole in solution are of concern. These drugs are stable in solution at room temperature for <8 h, so they should not be administered by continuous infusion therapy. Body temperatures likely result in even more rapid drug deterioration. An alternative to premixed antibiotics is to mix them with a prepackaged system just before use. A number of drugs are not approved for pediatric use—for example, fluoroquinolone and quinupristin-dalfopristin.

Multiple factors need to be weighed when considering use of a VAD, and the type of infusion system chosen must be individualized [26, 65]. Issues to be considered include the patient's overall clinical status, age, and vein condition; the diagnosis; current vascular access; antimicrobials prescribed and their frequency of administration; need for a programmable infusion pump; and the anticipated duration of therapy [66].

Peripheral short catheters are appropriate for patients with good vein status who will receive a short course of therapy (generally <2 weeks for adults and <1 week for children) with an agent that has low potential for causing phlebitis or soft-tissue damage if infiltrated. Midline catheters (7.5–20 cm in length) are also available for patients with moderately difficult venous access or whose treatment is anticipated to last >1 week. A wide range of central VADs are available for longer durations of therapy and are usually placed when the use of a programmable ambulatory infusion pump is planned. Implantable ports are not commonly used for OPAT unless already in place.

The use of peripherally inserted central catheters (PICCs) has increased since the previous OPAT guidelines were published [67, 68]. These catheters are appropriate in many circumstances in which the need for prolonged (more than 1–2 weeks) vascular access is present and the risks of complications or expense of other types of central lines is not warranted. PICCs are also appropriate for use with programmable pumps. When a PICC is placed, the catheter length should be recorded and checked again when it is removed. A chest radiograph should be performed after PICC placement to confirm the position of the catheter tip, especially if irritative or vesicant agents are to be used [69–72].

Tunneled and nontunneled central catheters are also widely used for longer-term access and for the infusion of irritative agents. They may be preferred over PICCs in patients who are active or in infants and children from whom it is necessary to obtain blood samples frequently. For patients who require multilumen catheters, a tunneled catheter may be more appropriate, although double-lumen PICCs are available.

MONITORING CLINICAL AND LABORATORY ASPECTS

The clinical aspects of OPAT encompass a broad range of patient care issues. These include monitoring the patient for response to treatment and potential adverse events, in addition to care of the VAD. Obtaining blood samples at regular intervals (as appropriate for the drug administered) is required to monitor laboratory values during most courses of therapy. Table 6 displays the frequency of adverse effects serious enough to stop antimicrobial therapy, which differ according to the drug being administered [73].

Table 6. Frequency of adverse effects due to intravenously administered antimicrobials used for outpatient parenteral antimicrobial therapy (OPAT).

Variable	Antimicrobial								Total
	Cfz	Ctz	Ctrx	Cm	Gm	Oxa	Naf	Van	
Courses administered	781	456	4670	442	327	479	266	2881	10,302
Courses stopped early ^a									
<i>n</i>	32	16	136	34	26	40	26	144	454
%	4.1	3.5	2.9	7.7	8.0	8.4	9.8	5.0	4.4
Adverse effect, % of courses									
Rash	1.92	2.19	1.39	5.43	0.61	3.55	4.51	2.29	2.05
Diarrhea	0.38	0.00	0.45	0.90	0.00	0.63	0.38	0.07	0.33
Nausea	0.77	0.22	0.36	0.90	0.92	1.88	1.50	0.24	0.50
Renal	0.13	0.22	0.00	0.00	2.75	0.21	0.75	0.42	0.25
Leukopenia	0.26	0.22	0.09	0.23	0.00	0.42	2.26	0.21	0.21
Urticaria	0.51	0.00	0.19	0.45	0.00	0.21	0.00	0.49	0.29
Fever	0.00	0.44	0.41	0.45	0.00	0.42	0.75	1.18	0.59
Vestibular	0.00	0.00	0.00	0.00	3.06	0.00	0.00	0.10	0.13
Hepatic	0.13	0.00	0.04	0.00	0.00	1.04	0.38	0.00	0.09
Anaphylaxis	0.26	0.00	0.04	0.00	0.31	0.21	0.00	0.14	0.10
Anaphylactoid	0.26	0.00	0.02	0.00	0.00	0.00	0.00	0.07	0.05
Anemia	0.00	0.22	0.00	0.00	0.00	0.21	0.75	0.00	0.04

NOTE. Information gathered from the OPAT Outcomes Registry as of October 2002 [73]. Cm, clindamycin; Ctrx, ceftriaxone; Ctz, ceftazidime; Cfz, cefazolin; Gm, gentamicin; Naf, nafcillin; Oxa, oxacillin; Van, vancomycin.

^a Reactions recorded were only those serious enough to stop therapy with that antimicrobial. More than 1 reason for stopping therapy was noted in 20.1% of cases.

Clinical monitoring. The frequency of patient follow-up visits with the supervising physician needs to be determined when a patient begins a course of OPAT. In most circumstances, patients see the managing physician once or twice each week. Some patients need to be seen daily by a physician, especially at the beginning of OPAT. Patients with endocarditis, meningitis, or other life-threatening infections may also require more frequent visits [23]. Less frequent visits may be appropriate for patients with stable chronic infections, few comorbid conditions, and appropriate caregiver support. Nurse and pharmacist assessments and monitoring should not substitute for face-to-face physician evaluations of patients. Visits to the referring or primary care doctor may also be helpful. If there are transportation difficulties, care may be coordinated with a local physician. Patients should also be seen after completion of OPAT to be sure they have responded to therapy are doing well and have had no adverse events.

The frequency of nursing visits will vary with the patient's condition, needs, and diagnosis. More frequent nursing visits may be needed at the outset of therapy for clinical monitoring and teaching purposes. A growing number of patients and their caregivers are being taught self-administration of antimicrobials, with a resulting decrease in the number of nursing visits.

Laboratory monitoring. The guidelines displayed in table 7 address the minimum frequency of monitoring for adverse

reactions and toxicity. Additional studies may be needed for determination of the response to therapy.

Adverse effects in patients receiving antimicrobial therapy are not unusual [11, 73–76]. Table 6 displays information from the OPAT Outcomes Registry, which indicates that 3%–10% of antimicrobial courses are stopped prematurely because of an adverse reaction. If laboratory parameters show an adverse trend, the frequency of laboratory monitoring should be increased; in some cases, the medication may need to be changed or its use discontinued. Data suggest that some adverse reactions, such as renal or vestibular toxicity and leukopenia, become more frequent as the length of therapy increases [73]. Even though an infection is responding, the need for regular laboratory monitoring remains [77].

Patients receiving aminoglycoside therapy should have serum creatinine determinations twice weekly [11]. Weekly monitoring may be considered for infants and children if they are clinically stable. Patients receiving prolonged courses of aminoglycoside therapy should have an initial determination of the trough and peak serum concentration around the third or fourth dose and after any dosage change. Determination of trough or midpoint serum concentrations should be considered for those patients receiving aminoglycoside therapy as a single daily dose, to document serum concentrations [78, 79]. When aminoglycoside trough serum concentrations in-

Table 7. Suggestions for laboratory parameters that should be monitored weekly during outpatient parenteral antimicrobial therapy (OPAT).

Antimicrobial agent(s), by class	Frequency of testing, no. of times per week				Other
	Complete blood count ^a	Renal function tests ^b	Potassium level	Liver enzyme levels	
Aminoglycosides (gentamicin, tobramycin, amikacin)	Once	Twice	Clinical monitoring for vestibular and hearing dysfunction at each visit; serum concentrations as clinically indicated (see text)
β -Lactams (penicillins, cephalosporins, aztreonam, carbapenems)	Once	Once ^c	
Antipseudomonal penicillins	Once	Once	Once	...	
Fluoroquinolones	Once	
Miscellaneous					
Clindamycin	Once	Once	...	Once	
Daptomycin	Once	Once	...	Once	CPK at least weekly
Linezolid	Once	
Pentamidine	Twice	Twice	Twice	...	Blood glucose level daily; chemistry profile ^d twice per week
Quinupristin-dalfopristin	Once	Monitor for arthralgias
Trimethoprim-sulfamethoxazole	Once	Once	Once	...	
Vancomycin	Once	Once	Serum levels as clinically indicated
Antifungals					
Amphotericin B, including lipid formulations	Once	Twice	Twice	Once	Magnesium level once per week
Azole antifungal agents	Once	Once	...	Once	
Caspofungin	Once	
Antivirals					
Ganciclovir	Twice	Once	
Acyclovir	Once	Once	Magnesium level once per week
Foscarnet	Once	Twice	Twice	Once	Chemistry profile ^d with calcium and magnesium level once per week
Cidofovir	Once	Once	Once	...	Urinalysis and chemistry profile ^d once per week

NOTE. Frequencies are minimal criteria for patients with normal or stable renal function. Different criteria may apply for children.

^a Should include a differential count of leukocytes and platelet count.

^b Renal function tests may include serum creatinine and blood urea nitrogen levels and urinalysis. Trough levels appear to be the earliest indication of aminoglycoside toxicity.

^c Weekly liver enzyme tests with oxacillin, nafcillin, and carbapenems.

^d A chemistry profile should include liver enzyme levels as well as electrolyte levels.

crease, more frequent determination of serum creatinine levels may be necessary [80]. Nomograms may be helpful [78, 79]. Serum drug and serum creatinine levels should be used to adjust aminoglycoside dosing, although aminoglycoside concentrations do not always correlate with the renal or vestibular toxicity [80–83].

When an aminoglycoside is used, patients and caregivers should be instructed to monitor otologic symptoms by clinical means, such as the volume of conversation, the development of tinnitus, vertigo, or a feeling of fullness in the ears [84]. Any changes noted should prompt consideration of an audiometric evaluation and/or discontinuation of aminoglycoside therapy. The patient's understanding of these instructions should be

clearly documented in the medical record and consideration should be given to including the possibility of an adverse drug reaction in the written consent to receive OPAT that is obtained at the start of therapy. For infants and young children, audiometric screening should be considered for those scheduled to receive prolonged therapy (4–6 weeks). Symptoms of vestibular dysfunction should be reviewed during each visit with the physician and nurse. Physical examination may also be helpful. Formal vestibular testing is not practical in most settings. The “dynamic illegible E test” is an inexpensive method of screening for vestibular dysfunction that can be performed in the physician's office [85, 86].

Audiometry is no longer routinely recommended when ami-

noglycosides are administered to adults, as it has not been documented to be of value for either healthy individuals or hospitalized patients [87]. Infectious diseases practitioners do not routinely obtain audiograms during aminoglycoside therapy [88, 89].

The value of vancomycin serum concentration data is controversial in the published literature [90–92]. Toxicity does not appear to be related to serum levels of vancomycin [93–95], although it does increase when vancomycin is given with other ototoxic or nephrotoxic agents [96, 97]. A correlation between serum vancomycin levels and clinical outcomes has not been convincingly demonstrated in humans [92, 98, 99]. but there is some evidence of a relationship in an animal model [100]. There have been a number of attempts to develop formulae and nomograms for vancomycin dosing, with variable success [101–103]. Specific patient populations have been shown to have poorly predictable serum concentrations when dosages are based on standard parameters [104–115]. In addition, vancomycin clearance decreases and serum concentrations increase during the course of prolonged treatment [116].

Given the high incidence of adverse drug reactions and to assure effective levels, it is recommended that both trough and peak serum levels be determined, until further studies of these relationships are undertaken [96, 97]. There are also concerns that inadequate dosing of antimicrobials, including vancomycin, may promote the development of bacterial resistance [117].

Of particular note is the need to monitor for hepatic toxicity in patients receiving oxacillin, caspofungin, or quinupristin-dalfopristin therapy [118]. Leukopenia is a common adverse effect with penicillin or vancomycin therapy [119, 120].

VAD care. The care of the VAD will vary with the type of device. Dressing changes, frequency of flushes, and site maintenance are based upon specific protocols for the individual VAD. In 2002, the Centers for Disease Control and Prevention (CDC) published guidelines for the prevention of catheter-related infection [121–123]. The Infusion Nurses Society has also published practice standards for insertion, care, and maintenance [26]. Catheters need to be secured well, especially for infants and children, to avoid accidental or purposeful manipulation of the device.

Patients and caregivers should be instructed in the monitoring and care of the VAD and should inspect the device daily. A health care practitioner should examine short and midline catheters at least twice per week and central catheters at least weekly. The entrance site should be examined for evidence of local phlebitis, induration, erythema, tenderness, and leakage [122]. The development of ipsilateral edema of the neck or arm in association with a PICC or other central catheter should prompt evaluation for a deep venous thrombosis [53], which usually requires removal of the device [121, 124]. Peripheral catheters should be assessed for replacement every 72 h when

used in adults, although, with close monitoring, a longer duration may be considered for patients receiving OPAT [122, 125].

OPAT OUTCOMES AND PATIENT SAFETY

The measurement of outcomes by an OPAT program is a part of the continuous performance improvement process through which health-care providers attempt to improve and assure the quality of their care and service. Parameters are chosen to assess the safety, efficacy, and cost of the OPAT program [1–9, 19–22, 74–78]. The best-studied OPAT outcomes indicators have been those related to cost savings and financial analyses [126]. Results of outcomes analyses may also be useful for marketing and contracting with payors. Accrediting bodies such as the Joint Commission for the Accreditation of Health Care Organizations (JCAHO) and the National Committee for Quality Assurance require outcomes measurements as a part of their certification process but do not specify the parameters or indicators to use. The JCAHO requires reporting and root cause analysis of “sentinel events” resulting in unexpected death or permanent injury arising from therapy [127, 128]. As the financial pressures mount for earlier hospital discharge of sicker patients, the importance of monitoring outcomes to assure patient safety increases.

Since the 1997 OPAT guidelines were published, some progress has been made in defining the appropriate outcomes to monitor and the techniques for their measurement; however, available data are sparse and rarely prospective [74, 75, 77, 129–138]. The articles referenced in the Appendix support the effectiveness of OPAT for many indications [11]. Recent studies have been published that demonstrate the effectiveness of OPAT for patients with osteomyelitis [131, 137, 139, 140] and children with complicated appendicitis [130]. Studies of pneumonia in patients with cystic fibrosis indicate at least comparable outcomes and higher patient satisfaction with OPAT than hospital care [7, 17, 18, 141–145]. Some studies show earlier return to normal function if hospital admission can be avoided [15, 146].

Adverse-event rates among patients receiving OPAT vary with the antimicrobial administered and the type and duration of placement of (“dwell time”) the VAD [66]. For OPAT, as for hospital-administered antimicrobial therapy, adverse drug reactions occur with sufficient frequency to require continuous monitoring of data specific to the antimicrobial used [74, 75, 77].

OPAT centers should have an active performance improvement program that can track clinical and program outcomes. Limited data are available to allow for comparison of a program’s performance with a national database for benchmarking purposes. The OPAT Outcomes Registry is a national database [135, 136, 147] that is accumulating data that can help compare

a program's performance with that of an aggregate of >30 centers with over 14,000 cases [147–149]. An OPAT center collects data on outcomes for the patients and can monitor its own clinical performance over time. This is particularly useful in the absence of published outcomes standards for infections treated with OPAT. Parameters which are monitored in the OPAT Outcomes Registry are listed in table 8 [136, 147].

Patient safety and health care–related infections are of particular concern with OPAT. The home environment is rarely constructed for safety; hence, application of hospital infection control polices may not be appropriate. Fortunately, the risk of infection related to home care appears to be much less than the risk of hospital-acquired infection and the chances of acquiring an antimicrobial-resistant organism from the home environment appear to be lower [33, 66]. Long-term care facilities are challenged with a concentrated population of debilitated but mobile patients, many of whom are recovering from hospital-acquired infections [150].

Patient safety issues with OPAT are similar to the hospital with potential medication errors, adverse drug effects, and complications from infusion devices. Patients and staff should be educated with regard to these risks and be immediately available if they occur. OSHA standards for health care worker safety and needlestick prevention are to be incorporated into the patient's plan of care in the outpatient setting [151].

CONSIDERATIONS FOR PEDIATRIC PATIENTS

Although many of these guidelines apply to both adults and children, particular aspects of OPAT require some degree of specialization in the care of neonates, infants, and children. For this vulnerable population, safety should be the most important consideration. Although OPAT offers many advantages, it should not be undertaken in neonates, infants, or children unless care can be delivered to the child with the same or a greater degree of safety as provided by inpatient therapy. Certain competencies in physical examination are unique to pediatrics (e.g., assessment of seizures in a newborn infant with meningitis), certain infections are more common in children (including omphalitis, mastoiditis, and meningitis), and certain antimicrobial toxicities may be specific to children (e.g., fluoroquinolones and cartilage toxicity). Moreover, a family member other than the infected child must be capable of providing the necessary care. Some problems are unique to children, such as Munchausen syndrome by proxy. Literature on OPAT specific to children is not as extensive as literature on the outpatient treatment of adults, but a number of articles on pediatric therapy and complications have been written for community-acquired infections, meningitis, fever and neutropenia, and cystic fibrosis [130, 141, 145, 152–168].

An important difference of OPAT in pediatrics pertains to

Table 8. Outcome measures for outpatient parenteral antimicrobial therapy (OPAT).

1. Clinical status (as reported by the responsible physician)
A. Improved
B. Clinical failure
C. No change
2. Bacterial infection status (if a pathogen was identified and repeat culture was done)
A. Culture negative for pathogen
B. Persistent pathogen
C. New pathogen
3. Program outcome (i.e., end of therapy)
A. Therapy completed as planned
B. Therapy not completed because of patient's death, noncompliance with therapy, complication, patient's preference, hospitalization (give reason), or other
4. Antibiotic use (i.e., end of treatment course)
A. Course completed as planned
B. Course not completed because of adverse drug reaction (note type), resistant organism, persistent organism, patient's preference, clinical failure
5. Vascular access complications, such as phlebitis, infection, thrombosis, infiltration, or becoming dislodged
6. Additional outcome measurements
A. Patient returned to work or school during OPAT (if applicable)
B. Did outcome meet physician expectations?
C. Survival status (patient alive, died of infection, died of other causes, lost to follow-up, or status unknown)

the nursing component of the team. In particular, the skills of physical assessment to evaluate the response to the infection and complications of the infection or medications clearly require experience and competence in the care of newborns, infants and children [166]. For the safety of the child, it is essential that the nursing provider be capable of a skilled assessment of the medical condition and response to treatment. In most situations, a registered nurse should provide nursing care, rather than a nurse's aide or a nursing assistant. The determination of competencies for the various levels of nursing, and the licensing procedures for nursing personnel are specific to each state. Physicians should be aware of the qualifications of the nursing personnel given responsibility for assessment of infants in their particular state. A nationally recognized pediatric infusion nurse society does not exist but the INCC certification examination does provide a component related to pediatrics [169]. Physicians, nurses, and pharmacy staff should all have proficiency and validated competency with the unique antimicrobials and dosing used for newborns, infants, and children to prevent errors in dosing or adverse drug events [170].

The need for home nursing visits in the majority of children follows the same guidelines as summarized for adults. However, in certain situations in which the clinical findings may be dif-

difficult to assess and the potential complications of the infection are great, daily visits by home care nurses may be required. Examples include infections during the neonatal period and CNS infections for children of any age. Both the qualifications of the visiting nurse for medical assessment of the child and authorization for the medically required number of nursing visits should be confirmed prior to discharge into an OPAT program. On occasion, direct communication with the medical director of a third party payor may be required to authorize the visits required for the safety of the infant or child. Similar to situations involving adults in which a caregiver is expected to administer antimicrobials, the competence of the parent or caregiver to administer medication and care for VADs should be demonstrated prior to beginning OPAT. Such preparation may avoid complications that result from parents or caregivers who are not capable of either a medical assessment, care of the child's catheter, or infusion of medication. The physician who discharges and treats the child as an outpatient has the ultimate responsibility for the intended outcome.

Selection of antimicrobials for children generally follows the same guidelines as those for inpatient parenteral therapy. However, the number of US Food and Drug Administration–approved antibacterials, antivirals, and antifungals for children is substantially fewer than those for adults, usually because of lack of data on efficacy and safety in children. As with inpatient management of pediatric infections, the physician must select the safest and most effective antimicrobials for the child. Selection of drugs with the least frequent dosing is an important consideration, as is the ability to administer the medication intramuscularly. Secure vascular access is essential before discharge as vascular access for an infant in the home with limited equipment resources and no support from other medical personnel may be difficult. Data on treatment of neonatal infections with newer agents is particularly limited. In general, sulfa-containing antibiotics are to be avoided during the neonatal period of physiologic jaundice. Fluoroquinolones are currently not used routinely in children because of concerns about cartilage toxicity.

The spectrum of equipment used for antimicrobial infusion in children is similar to adults, although some products are available specifically for children. The availability of vascular access by peripheral catheters, PICCs [68], and subcutaneously tunneled central catheters is virtually universal. A variety of infusion techniques are used in children, from direct injection of drugs via syringe (i.e., IV push administration) to infusion devices that vary from small kinetic “balloon” or elastomeric pumps to sophisticated electronic programmable infusion pumps.

Most of the outcome parameters for pediatric patients are similar to those for adults, even though the catheters and equipment used to administer medication, the antibiotics used, and

the infections and pathogens treated may be unique to the pediatric age group. The complications and outcomes in one pediatric program should be compared with those of similar pediatric programs, rather than with adult programs. Improved standardization of definitions used for outcomes and reporting in pediatrics will make comparisons between institutions increasingly relevant and important.

FUTURE STRATEGY

OPAT is now a standard part of medical practice in North America. Although it is commonplace, it is not without risk and responsibilities, especially for the physician, who must provide a quality of care with OPAT as good as that that would be provided if the patient remained hospitalized. It is also a method of delivery of medication that requires the expertise of and close coordination of services from physicians, nurses, pharmacists, and others.

The opportunities for further developing OPAT need to be explored with caution and ongoing assessments of effectiveness and patient safety. There are a number of ways by which information can be gathered concerning patient outcomes and the evolving trends in different health care organizations shared.

Additional studies of OPAT are needed in multiple areas. Randomized trials to answer important questions are rare. Vascular access is of continued concern, both with regard to device selection and ongoing care. The safety of midline catheters and PICCs in relation to peripheral short catheters for use with OPAT has not been studied fully. Policies for changing of catheters and dressings vary among providers, although guidelines and standards have been developed by the Infusion Nurses Society and the CDC that limit short peripheral catheter dwell time to 72 h [26, 37]. These recommendations were largely derived from hospital studies and may not always be appropriate for OPAT. Administration of antibiotics by IV push may save time but, in OPAT, its safety has not been documented. The complications associated with use of PICCs and the ability to recognize them early in the outpatient setting are of concern and require close monitoring. Concerns remain about infusing the first dose of an intravenous antibiotic in the home, especially because of the potential for anaphylaxis.

The answers to these questions can only be found through concentrated, cooperative efforts to gather and analyze data with the same rigor that applies in studies of therapy in hospitals. Clinical research on outcomes and patient safety issues can be accomplished through networks of providers and registries with outcomes information. These data can also be used to learn more about the optimal therapy for infectious diseases and about the agents used to treat them [147].

Table 9. Internet resources with information on outpatient parenteral antimicrobial therapy (OPAT).

Organization	URL	Notes
American Academy of Home Care Physicians	http://www.aahcp.org	Information on home care, house calls, and membership
American College of Physicians/American Society of Internal Medicine	http://www.acponline.org	References, teaching tools, patient handouts, and information for personal digital assistants
American Society of Health-System Pharmacists	http://www.ashp.org	Recent drug information
Association for Professionals in Infection Control and Epidemiology	http://www.apic.org	Guidelines for hand hygiene and prevention of infections, as well as educational materials
Association for Vascular Access	http://www.avainfo.org	Newsletter and information on networks, meetings, and membership
US Food and Drug Administration	http://www.fda.gov/cder/drug	Consumer and physician information on shortages and recall
Infectious Diseases Society of America	http://www.idsociety.org	Guidelines
Infusion Nurses Society and Infusion Nurses Certification Corporation	http://www.ins1.org	Newsletter and information on publications, credentialing, membership, meetings, nurse competence program, patient education, and teaching resources
OPAT Outcomes Registry	http://www.opat.com	Information about OPAT, data from the OPAT Outcomes Registry, network for patient referrals, references, posters, newsletter, slide sets, and information on membership
OPIT (Outpatient Intravenous Therapy) Source Book	http://www.opitsourcebook.com	Sourcebook catalog and display of different vascular access devices

FINAL COMMENTS

The contributors to these guidelines considered what could be done to optimize their understanding and use. Timely publication of the guidelines or their abstracts in the various society journals is possible. In addition, the Internet offers the ability to disseminate information and support it through links to documents from other societies and to patient education materials. The potential exists for continual updating and close cooperative activities among the societies represented in these guidelines. Many of these resources are available through the Web page of the Infectious Diseases Society of America (<http://www.idsociety.org>). Additional information about OPAT can be found at the OPAT Outcomes Registry Web site (<http://www.opat.com>) and at the Web pages of the contributing societies listed in table 9.

The future role of physicians in outpatient and home care is uncertain. Although their role in the hospital and office as specialists continues to be rewarded, their management of ancillary services and home care has significant disincentives [171]. Reimbursement mechanisms should be adjusted to rec-

ognize the added time and skill needed to manage these complex infections outside the hospital.

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APPENDIX

Table A1. Summary of reports that support the effectiveness outpatient parenteral antimicrobial therapy for various infectious conditions.

Type of infection or condition	References
Soft-tissue infection, including cellulitis and wound infection	[2, 5, 6, 8, 53, 60, 66, 74, 75, 77, 134, 138, 153, 155–157, 166, 172–196]
Osteomyelitis	[1–6, 8, 32, 53, 60, 66, 74, 75, 77, 131, 134, 137–140, 155, 157, 166, 172, 174–176, 178–183, 185, 187, 189, 191–196, 197–204]
Septic arthritis or bursitis	[3–5, 8, 66, 75, 77, 134, 138, 153, 155–157, 166, 179–182, 185, 187, 191, 192, 194, 196, 199, 203, 205]
Prosthetic joint infection	[3, 77, 175, 181, 196, 200]
Pneumonia and/or severe lower respiratory infection	[5, 8, 13–16, 66, 74, 75, 77, 134, 138, 155–157, 166, 172, 174, 176, 177, 179, 180, 182, 184, 189, 192–196, 206–208]
Cystic fibrosis (infectious exacerbation)	[7, 9, 138, 141–145, 166, 180, 189, 192, 209–215]
Sinusitis (complicated)	[5, 8, 66, 74, 75, 138, 156, 166, 179, 181, 184, 189, 193, 216]
Chronic otitis and/or mastoiditis	[5, 75, 134, 138, 155–157, 166, 189, 192, 217, 218]
Endocarditis	[1–6, 8, 19–22, 53, 60, 66, 74, 75, 77, 138, 174, 176, 178–182, 185, 187, 192–196, 200, 204, 205, 219–225]
Bacteremia	[1, 66, 74, 75, 77, 134, 138, 153, 157, 166, 167, 174, 176, 179, 182, 184, 189, 191–194, 196, 200]
IV catheter-associated infection	[5, 53, 74, 77, 138, 172, 189, 192, 195]
Vascular graft infection	[2, 3, 195]
Hepatic or splenic abscess	[60, 138, 196]
Intra-abdominal infection or peritonitis	[53, 60, 66, 75, 130, 138, 156, 157, 172, 179, 182, 189, 191, 192]
Complicated urinary tract infection	[5, 8, 66, 74, 75, 77, 138, 153, 155, 156, 166, 172, 174, 176, 177, 179, 180, 182, 189, 192–194, 226]
Pelvic inflammatory disease and/or tubo- ovarian abscess	[5, 8, 134, 138, 172, 176, 180, 189]
Meningitis or encephalitis	[66, 74, 75, 138, 152, 153, 155, 172, 174, 180–182, 189, 195, 196, 225, 227, 228]
Brain or epidural abscess	[6, 60, 66, 74, 75, 77, 179–182, 189, 196, 229]
Neutropenic fever	[74, 159, 161–164, 168, 172, 181, 230–235]
Lyme disease	[8, 60, 66, 74, 138, 179, 195]
Fungemia and/or systemic mycosis	[3, 60, 66, 174, 179, 180, 192]
Cytomegalovirus infection	[3, 8, 53, 60, 66, 75, 77, 138, 174, 189, 193, 195, 236, 237]

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