INFECTIOUS DISEASES II

PSAP

INFECTIONS IN THE LONG-TERM CARE SETTING

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Learning Objectives

1. Implement facility policies and procedures for assessment of residents with suspected infection to identify appropriate candidates for antibiotic drug therapy.
2. Evaluate the appropriateness of antibiotic drug therapy on the basis of clinical presentation and accompanying diagnostic data.
3. Develop clinical pathways for appropriate antibiotic drug selection, dosage, administration, and monitoring on the basis of principles of age-related changes in pharmacokinetics and pharmacodynamics.
4. Develop drug use evaluation criteria for evaluating the appropriateness of antibiotic drug use within a long-term care population.
5. Interpret infection control information to prevent or track the spread of infection in a long-term care facility.

Introduction

Prevalence of Infections in the Long-term Care Setting

Residents of long-term care facilities (LTCFs) are among the frailest patients in our health system. The rapid growth of the population segment older than 65 years is widely publicized, but what is less often discussed is the growing proportion of this group requiring long-term care. According to 2004 census data, 1.6 million Americans reside in LTCFs, and more than 45% are older than 85 and have dementia. It has been estimated that 40% of individuals who reach the age of 65 may require some kind of services from an LTCF during their lives. Therefore, the number of individuals cared for in this environment is expected to double or even triple within the next 10–20 years.

The meaning of the term *long-term care facility* will vary depending on the type of facility discussed and the type of care it is licensed to provide. Facility types can range from communal dwelling residential homes to skilled nursing facilities that provide Medicare Part A services. Skilled nursing facilities can either be hospital or community based, and a skilled license can apply to an entire facility or to a single unit within a community facility or a hospital. Therefore, environmental exposures, infection control processes, intensity of care, characteristics and training of staff, and access to diagnostic testing will differ from facility to facility.

Older residents of LTCFs are particularly vulnerable to infections. In this population, multiple factors contribute to increased incidence of infection and mortality associated with infection. These factors include age-related changes in physiology that alter immune response or drug sensitivity. An estimated 4.1 infections (range, 0.8–9.5) per 1000 patient care-days occur in this setting. However, the determination of accurate prevalence rates for each type of infection is challenging because patients who are elderly are at risk of both underdiagnosis and overdiagnosis of infection.

Potential for Underdiagnosis or Overdiagnosis of Infection

Underdiagnosis increases the risk of inappropriate prescribing when drug therapy is directed at symptoms and not the underlying cause. Overdiagnosis often leads to unnecessary exposure to antibiotic drugs, exacerbating the growing problem of antibiotic resistance of pathogens. Misdiagnosis can occur when atypical illness presentation leads to misinterpretation of signs and symptoms or when characteristics of the long-term care environment affect access to physician assessment and diagnostic testing. This chapter discusses the characteristics of infection presentation in patients who are elderly. The most reliable findings that support a diagnosis of infection are identified, and geriatric syndromes commonly confused with infection are described.

The potential for inaccurate diagnosis of infection has direct implications for the appropriateness of drug therapy. Even when infection is appropriately diagnosed, age-related changes in pharmacokinetics and pharmacodynamics can influence the magnitude or quality of drug response. Common areas of drug therapy intervention by the pharmacist to

Abbreviations in This Chapter

APIC	Association for Professionals in Infection Control and Epidemiology
CBC	Complete blood cell count
IDSA	Infectious Diseases Society of America
LTCF	Long-term care facility
MRSA	Methicillin-resistant *Staphylococcus aureus*
UTI	Urinary tract infection
VRE	Vancomycin-resistant enterococci

optimize drug selection, dosage, administration, and duration are discussed.

Pathophysiology

Age-Related Immunosenescence

Aging is associated with many changes in the immune system, the most significant and well documented of which appear to be changes in T-cell and B-cell function. The precise relationship between immunosenescence and infection in the long-term care population is not known. It can be stated that, in general, the immune response is diminished among elderly individuals; however, the degree of variability within this population is large. The quality of a patient's immune response appears to correlate with overall health status. In addition, genetics, environmental exposures, nutrition, comorbid condiions, drugs, and institutional infection control processes may all confound this relationship. Therefore, individual risk factors must be considered for each of the most common types of infection in this setting, which include, in order of prevalence, infections of the urinary tract (UTIs), respiratory tract, skin and soft tissues, gastrointestinal tract, and bloodstream (Table 1-1).

The risk of poor outcomes associated with infections is compounded by rising antibiotic resistance rates. High rates of use perpetuate a cycle of resistance, virulent infection, and resultant increased morbidity and mortality. This cycle can potentially be disrupted, because there is a significant degree of inappropriate antibiotic drug exposure in LTCFs. One of the best defenses against inappropriate antibiotic drug use is accurate diagnosis of infection, which admittedly is easier to describe than to achieve. The following sections describe various challenges to accurate identification of infection.

Atypical Disease Presentation

Atypical disease presentation is an important concept in geriatric medicine. Patients who are elderly may not manifest the classic signs and symptoms associated with a given medical condition in younger patients. Instead, illness presentation can include new or worsening delirium and other changes in baseline function, such as new or worsening confusion, agitated behavior, incontinence, falls, or other functional decline. This atypical presentation is particularly likely in frail, elderly LTCF residents, and diagnosis is especially difficult when dementia prevents an individual from articulating what he or she is experiencing. Although any medical condition can present atypically, infection has been identified as the root cause in as many as 77% of the illnesses presenting with atypical characteristics.

Atypical disease presentation can be associated with both underdiagnosis and overdiagnosis of infection. Underdiagnosis can occur when atypical symptoms either go unrecognized or are attributed to another medical condition. It can also occur when a symptom is treated as a condition instead of a sign of an underlying problem. For instance, an LTCF resident might be prescribed anxiolytic or antipsychotic drugs to treat agitated behavior associated with acute mental status change without caregivers performing an evaluation to determine the precipitating cause. Inappropriate intervention can leave the resident vulnerable to a spiral of poor outcomes such as a prescribing cascade. This occurs because exposure to unnecessary drugs can cause adverse effects (possibly resulting in the prescribing of additional drugs), and the unaddressed precipitating condition can lead to patient deterioration.

In many respects, awareness of the potential for underdiagnoses of infection can also cause the pendulum to swing too far in the opposite direction. The fear of failing to identify an underlying medical condition can result in a lowered threshold to consider infection. This lowered threshold is not bad if the clinical assessment and diagnostic work-up are adequate to exclude all the possible causes of the resident's presentation. However, assumptions about the likelihood of infection can lead to inaccurate diagnosis.

Challenges to Accurate Infection Diagnosis

Resident Access to Assessment by Health Professionals

The frailest of the patients who are elderly, such as those residing in LTCFs, may not have frequent access to a physician. Every LTCF has a physician medical director, but this person is usually not the attending physician of record for most residents. Medical services are most often provided by physicians outside the LTCF environment. Depending on the licensure status of the facility, physician visits may be required as frequently as monthly or as infrequently as yearly. Physicians may also delegate visits to a physician's assistant or advance practice nurse. Intervention for acute problems arising between visits is prompted at the discretion of facility staff. The Infectious Diseases Society of America (IDSA) advocates that the results of on-site evaluation be reported to the physician or mid-level practitioner for decisions about further evaluation. However, these recommendations fall short of making a statement about whether the LTCF resident should be evaluated in person by a physician or mid-level practitioner. In many cases, such face-to-face evaluations do not occur. Hands-on assessment will be performed by the facility nursing staff, and clinical and laboratory data will be shared via telephone or facsimile with the individual making diagnostic and prescribing decisions.

Most hands-on care in LTCFs is provided by certified nurse assistants. These individuals will have the greatest familiarity with an LTCF resident's day-to-day baseline status and are in a better position to recognize signs and symptoms of illness. These staff members are supervised by charge nurses who are, in most facilities, licensed vocational

Table 1-1. Common Infections in Long-term Care Residents

Infection Type	Prevalence and Risk Factors	Common Causative Organisms	Antibiotic Drug Options
Urinary tract infection	1–2.4 per 1000 resident-days; most common reason for antibiotic drug exposure Genitourinary abnormalities; prior antibiotic drug use; previous stroke; diabetes mellitus; decreased cognitive or physical function; incontinence; neurogenic bladder; urinary catheters; cystoceles (women); decreased estrogen (women); benign prostatic hyperplasia (men); urethral strictures (men)	*E. coli* (women) *P. mirabilis* (men) *K. pneumoniae* *Citrobacter* spp. *Enterobacter* spp. *Providencia* spp. *M. morganii* *P. aeruginosa* *S. aureus* *Enterococcus* spp. Coagulase-negative staphylococci Group B streptococci	Oral Trimethoprim/sulfamethoxazole; trimethoprim; cephalexin; amoxicillin/clavulanate; cefadroxil; cefixime; cefuroxime; cefpodoxime; ciprofloxacin; norfloxacin Intravenous Ampicillin; cefazolin; gentamicin; tobramycin
Pyelonephritis			Third-generation cephalosporin; fluoroquinolone
Prostatitis			Trimethoprim/sulfamethoxazole; fluoroquinolone
Pneumonia	1.2 per 1000 resident-days Most common reason for hospital transfer Advanced age; male; swallowing difficulty; feeding tube; bedridden state; chronic lung disease; congestive heart failure; cardiovascular disease; dementia; incontinence; low serum albumin	Non-intubated *S. pneumoniae* *H. influenza* *M. catarrhalis* *C. pneumoniae* *K. pneumoniae* *M. pneumoniae* *S. aureus* Gram-negative bacilli Viruses Intubated *S. aureus* Gram-negative bacilli *S. pneumoniae* *P. aeruginosa* Anaerobes	Levofloxacin or moxifloxacin; amoxicillin/clavulanate plus macrolide; ceftriaxone or cefotaxime plus macrolide; ampicillin/sulbactam plus macrolide Cefepime or ceftazidime; piperacillin/tazobactam plus ciprofloxacin plus vancomycin; imipenem or meropenem
Pneumonitis	Prior stroke; swallowing difficulty; dementia; poor dentition	Anaerobes ± bacteria listed above	Piperacillin/tazobactam plus ciprofloxacin plus vancomycin; clindamycin or metronidazole plus cefepime or ceftazidime or imipenem or meropenem
Bacterial diarrhea	0–2.6 cases per 1000 resident-days, 25% of hospitalizations and 85% of mortality related to diarrhea are among individuals older than 60 years Poor hygiene and food-handling procedures; recent hospitalization; prior antibiotic drug use	Prior antibiotic drugs *C. difficile* Other *V. cholerae* Enterotoxigenic *E. coli* *Shigella* *Salmonella* *Campylobacter*	Metronidazole; oral vancomycin Doxycycline; tetracycline; trimethoprim/sulfamethoxazole; ciprofloxacin; norfloxacin; erythromycin; clarithromycin

C. difficile = Clostridium difficile; C. pneumoniae = Chlamydia pneumoniae; E. coli = Escherichia coli; H. influenzae = Haemophilus influenzae; K. pneumoniae = Klebsiella pneumoniae; M. catarrhalis = Moraxella catarrhalis; M. morganii = Morganella morganii; P. aeruginosa = Pseudomonas aeruginosa; P. mirabilis = Proteus mirabilis; S. pneumoniae = Streptococcus pneumoniae; V. cholerae = Vibrio cholerae.

nurses. The ratio of licensed nurses to residents will vary by facility but may be as low as 1:20. Although most state regulations will require LTCFs to retain the services of at least one full-time registered nurse, these requirements can be waived. This waiver is often necessary when workforce shortages impede the hiring of such personnel.

There are no published studies that differentiate resident outcomes on the basis of illness evaluation by certified nurse assistants, licensed vocational nurses, registered nurses, physician's assistants, nurse practitioners, general physicians, or geriatricians. In general, abnormalities in vital signs or changes in baseline functional status are reported by nurse assistants to the charge nurse. The initial assessment is performed by the charge nurse, who relays information, usually over the telephone, to the physician, physician's assistant, or nurse practitioner. Orders for further diagnostic testing and treatment are then given. Each individual must be optimally trained to perform the assessments appropriate to his or her scope of practice, not only to recognize infection but also to exclude other possible causes of the resident's illness presentation. Breakdowns or shortcuts in this chain of reporting are often responsible for inappropriate diagnosis or treatment.

Minimal criteria for the assessment of residents with suspected infection include an evaluation of temperature; a microbiologic culture; an evaluation by a physician; and, for residents with suspected pneumonia, a chest radiograph. A significant proportion of LTCF residents will not receive this complete assessment. Because in-person visits by the physician may be relatively infrequent, it might be expected that the criteria for evaluation by a physician could not feasibly be met for a high number of residents. The current system is not optimal for our frailest patients, because up to one-third of residents may not have any of these criteria fulfilled. Reporting the initial assessment via telephone to a prescriber who is remote to the site of care provides few safeguards against incorrect diagnosis caused by incomplete data.

Access to Diagnostic Testing

An LTCF resident's access to diagnostic testing will also vary with the type of facility in which they reside. Hospital-based facilities provide the fastest and most convenient access to testing, because the necessary laboratory equipment and personnel are on-site. Community-based facilities must contract with external vendors for phlebotomy, clinical laboratory, and mobile radiology services if residents are to receive diagnostic tests on-site. Otherwise, medical transportation must be arranged to the hospital or to a diagnostic evaluation clinic. Sometimes, the pursuit of such testing is precluded by a resident's advance directives or by the wishes of their responsible party. However, such directives cannot necessarily be interpreted to imply that antibiotic drug therapy is to be withheld in instances of suspected infection. Therefore, it is not uncommon that the decision to initiate an antibiotic drug must be made in the absence of optimal diagnostic confirmation.

Findings That Support Infection Diagnosis

Fever

In an adult, fever is often defined as an elevation in body temperature of at least 1°F (0.5°C) above 98.6°F (37°C). However, this definition of fever is not always appropriate when interpreting body temperature in a patient who is elderly. These patients may have lower baseline body temperatures and, in up to 50% of cases, may not exhibit a significant febrile response during illness. When present, a temperature of greater than 100°F (37.8°C) has a 70% sensitivity and 90% specificity for infection; additionally, repeated temperatures greater than 99°F (37.2°C) or an increase of more than 2°F (1.1°C) from baseline are predictive of infection. Any of these temperature changes should prompt further evaluation.

Body temperature is a parameter that can be easily measured by facility staff, although there has been some debate over which method of temperature assessment is optimal. Some data suggest that rectal measurement is more accurate than oral, but considerations of resident cooperation and preference preclude any general recommendations for a "gold standard" method. If rectal measurement is used, repeated temperatures of 99.5°F (37.5°C) or higher are highly suggestive of infection; however, the absence of fever does not exclude infection. Drugs and other noninfectious causes also can be associated with elevated temperature, so fever by itself is not diagnostic for infection. However, when present, fever is an important clinical sign that should prompt further evaluation.

Complete Blood Cell Count

A complete blood cell count (CBC) should be obtained in all patients with suspected infection. An elevated white blood cell count is one of the best predictors of infection, regardless of whether fever is present. A leukocyte count of 14,000 cells/mm^3 or greater, a band count greater than 1500/mm^3, a neutrophil count of 90% or higher, or a left shift is indicative of infection. The IDSA recommends no further diagnostic testing in the absence of fever, leukocytocis, and left shift, especially if there is no specific sign of focal infection, because the likelihood of true infection is low. These recommendations as they pertain to long-term care are endorsed by the American Geriatrics Society. This recommendation should not be interpreted to mean that work-ups for other medical conditions are unnecessary if a nonspecific change in baseline status is a concern. The IDSA guidelines do recommend additional diagnostic tests if infection is considered likely based on the caregiver's initial assessment.

Urinary Tract Infections

Asymptomatic Bacteriuria

Asymptomatic bacteriuria is one of the most common reasons an LTCF resident will be inappropriately diagnosed with infection. Definitions of asymptomatic bacteriuria vary. One of the earliest accepted definitions of asymptomatic bacteriuria is the presence of positive cultures (10^5 colony-forming units [CFU] per milliliter or greater) of the same microorganism in two consecutive urine samples; and, by definition, the presence of microorganisms cannot be associated with urinary symptoms. More recently, this definition has been amended to include the absence of fever (temperature less than 100.4°F [38°C]) and a lower threshold (102 CFU/mL or greater) for defining asymptomatic bacteriuria in the presence of an indwelling catheter.

The prevalence of asymptomatic bacteriuria increases with age. Up to 25% of women older than 65 have asymptomatic bacteriuria, and this estimate increases to more than 50% in women older than 80. In men, the prevalence also increases with age, from 10% in men older than 65% to 35% in men older than 80. The prevalence is particularly high in residents of LTCFs. It has been estimated that 30% to 50% of residents in LTCFs and 100% of those residents with indwelling catheters will have a positive urine culture at any given time.

It would seem straightforward that urinalysis, and subsequent antibiotic drug therapy, should not be pursued in patients without symptoms. The challenge, however, is defining which residents of LTCFs are truly without symptoms. The atypical characteristics of illness presentation among people who are frail and elderly can make the assessment of LTCF residents confusing. A sudden onset of cognitive or behavioral changes, nonspecific functional decline, falls, incontinence, lethargy, or any other phenomenon that represents a change in the resident's baseline level of function can certainly herald some kind of illness. The trap into which caregivers fall, however, is to assume a UTI as the easy explanation for the illness presentation. Understanding both the prevalence of UTIs in long-term care and the principles of atypical disease presentation, there is a low threshold for ordering a urinalysis when change of status is reported for a facility resident; however, this practice can lead to an inappropriate diagnosis. Given the high prevalence of bacteriuria in LTCF residents, it is possible for a resident to have both a positive urine culture and a change in baseline status, even if the presence of bacteria in the urine is coincidental to the presenting symptoms and not the cause of the illness.

Another factor that will confound accurate UTI diagnosis is dark, foul-smelling urine. This clinical sign often prompts urinalysis when reported by facility staff, and in some caregivers' opinions, this negates the definition of "asymptomatic," because dark, foul-smelling urine is often interpreted as a urinary symptom. However, noninfectious causes such as foods and drugs can result in dark, foul-smelling urine, and increased concentration secondary to dehydration is the most common cause. In the absence of other symptoms, diagnosis of UTI on the basis of urine appearance or smell, even with a positive urine culture, is likely to be inaccurate, and a more appropriate intervention would be to assess hydration status. Dehydration often accompanies fever in LTCF residents. Although most guidelines do not include evaluation of hydration status as part of the work-up for infection, both physical and laboratory evaluation for dehydration is reasonable in a patient presenting with dark, foul-smelling urine accompanied by fever.

Symptomatic Infection

According to the Association for Practitioners in Infection Control and Epidemiology (APIC) criteria for diagnosing a UTI, at least three of the following signs and symptoms must be present: fever or chills; worsening of mental or functional status, which may include new or increased incontinence; new flank or suprapubic pain or tenderness; change in the character of the urine (e.g., blood, foul smell); or new or increased burning or pain on urination, frequency, or urgency. Of note is that various aspects of worsened mental or functional status satisfy only one of the five criteria. Strict application of the APIC criteria should preclude symptoms such as new-onset confusion, agitated behavior, falls, and other forms of decline from being enumerated individually when building the case for UTI diagnosis. When multiple symptoms of this nature are present, but at least two of the other diagnostic criteria are not satisfied, the clinician should consider other medical problems.

Application of these criteria is less straightforward in a catheterized individual; in this instance, only two of the first four criteria are required (urinary symptoms such as frequency or urgency are not applicable). In catheterized LTCF residents, there is a greater possibility that even strict adherence to APIC criteria could result in misdiagnosis, because there are many reasons why a catheterized resident might satisfy two criteria. Mental or functional status changes due to a noninfectious cause could be misinterpreted in the presence of a change in urine character. For instance, hematuria or foul smell could be caused by blood associated with catheter insertion or by dehydration. Mental status or functional changes in the presence of fever could satisfy criteria for infection but would not necessarily be specific for infections originating from the urinary tract. The likelihood of positive urine cultures increases the potential for misdiagnosis; therefore, APIC criteria alone cannot reliably confirm UTI diagnosis.

If a UTI is suspected on the basis of the above criteria, the APIC recommends a urinalysis. This recommendation deviates from the IDSA recommendation to obtain a CBC as the initial test, and there are potential drawbacks to obtaining a urinalysis without first obtaining a CBC. Historically, bacterial counts of 10^4 CFU/mL or greater in the urine have been considered diagnostic for UTI, because counts less than 10^4 CFU/mL are less likely to be reproducible when cultures are repeated, suggesting contamination or colonization rather than infection. However, up to one-third of women with lower UTIs may have bacterial counts that are below the 10^4-CFU/mL cutoff. Some literature suggests that colony counts as low as 100 CFU/mL in a properly obtained sample are clinically significant for infection. However, understanding the dilemma associated with the presence of bacteriuria in asymptomatic patients, it is difficult to advocate any threshold for bacterial counts. If clinically relevant infections can be associated with such low colony counts, yet colony counts greater than 10^4 CFU/mL can be associated with asymptomatic bacteriuria, then UTI diagnosis cannot be determined on the basis of this parameter alone.

Pyuria is an important sign, but it can be inappropriately interpreted when considered alone. Neither a positive dipstick test for leukocyte esterase nor the presence of white blood cells identified through microscopic analysis of the urine is a good predictor of UTI. In contrast, the absence of pyuria assessed by either of these methods has a negative predictive value close to 100%. Therefore, although the presence of pyuria cannot reliably confirm a diagnosis of UTI, the absence of pyuria makes a UTI unlikely.

Testing for urinary nitrite can increase the sensitivity and specificity of the leukocyte esterase test. Evaluation of urinary nitrite alone is not recommended because not all bacteria produce nitrite; therefore, the test has very low sensitivity. A positive result on both tests has good predictive

value for infection; however, the sensitivity is still less than 80%.

Logistically, it is unlikely that the ordering practitioner will wait for the results of a CBC before deciding what other diagnostic tests to order. Such an approach might be feasible in a hospital-based LTCF with access to an on-site laboratory. However, in a community facility that must contract with an outside vendor for phlebotomy and clinical laboratory services, it is more realistic that most of the required tests would be ordered at one time so as not to delay diagnosis and treatment. Therefore, for a suspected UTI, the urinalysis and culture with sensitivity would be ordered together with the CBC. Although there is the potential that this approach will result in unnecessary tests, it is an acceptable concession to make. Too often, the urinalysis is ordered first and interpreted without a CBC. Interpreting the urinalysis within the context of the CBC results may help avoid the alternative scenario in which an unnecessary antibiotic drug is prescribed for an inappropriate UTI diagnosis. For this reason, it is important to remember that the CBC is the test advocated by the IDSA guidelines as the initial test to obtain for infection evaluation.

The IDSA guidelines do not formally state that serum chemistries must be obtained with the CBC and urinalysis, but these tests could be advocated as appropriate. Serum chemistries might be especially important when there is a history of poor oral intake, weight loss, or clinical signs consistent with dehydration. In addition, if the presenting signs of illness are atypical and nonspecific, an evaluation of electrolytes, glucose, blood urea nitrogen, serum creatinine, and, possibly, liver enzymes can provide clues to an alternative explanation for the resident's change of status. When the clinical signs do not present a clear picture, the triad of CBC, serum chemistries, and urinalysis may provide clues to a variety of possible disease states and syndromes, whereas the urinalysis alone may simply identify bacteriuria.

Respiratory Tract Infection

Differentiating Pneumonia from Noninfectious Respiratory Conditions

Appropriate antibiotic drug treatment depends on an accurate diagnosis of pneumonia, because there are a number of respiratory symptoms that can be associated with noninfectious causes. Cough, shortness of breath, wheezing, nasal drainage, sneezing, and increased respiratory rate can be associated with exacerbations of chronic obstructive lung disease, heart failure, asthma, or allergies; aspiration; and other diseases. The need to differentiate pneumonia from influenza often presents a dilemma. An LTCF resident's limited access to the diagnostic testing needed to accurately confirm the presence of pneumonia often forces treatment decisions based on clinical symptoms only. The desire to avoid antibiotic drugs in a patient with a viral illness is offset by the concern that pneumonia is associated with a high 30-day mortality rate among the frail elderly, even with appropriate treatment.

A resident presenting with nonspecific respiratory symptoms should receive not only a physical assessment but also a medical record assessment, including a drug regimen review. As stated previously, the initial report of the resident's change of status is often communicated via telephone to a practitioner who is not at the site of care. Without direct access to the medical record, it is easy to rush to a conclusion regarding infection while forgetting that there may be comorbid medical conditions that could offer an alternative explanation for the presenting symptoms. Although such data may not be immediately accessible by the practitioner over the telephone, the nursing staff reporting the change of status should provide this information. A "refresher" report of the resident's active medical conditions should be considered part of the pertinent data to be provided during the telephone report of any suspected illness.

Undiagnosed medical conditions can also result in symptoms that are misattributed to infection. A drug regimen review can provide clues to such situations. For instance, use of inhaled ß-agonists, ipratroprium, or even oxygen in the absence of a documented respiratory diagnosis or the use of furosemide in the absence of a documented cardiovascular diagnosis are circumstances that can alert the clinician that a drug was prescribed at some point to treat a symptom, such as respiratory distress or edema, but that an adequate evaluation was not performed to identify the cause of symptoms. The potential that a chronic respiratory condition such as emphysema or asthma, or a cardiovascular condition such as heart failure, has not been optimally identified and treated might result in occasional exacerbations of the symptoms that could be misinterpreted as infection.

Although a pharmacist is not the health professional who will diagnosis such conditions, the drug regimen review can identify drugs without appropriate indications. The presence of drugs without indications is a potential problem for any LTCF resident but is a particular red flag when the drug circumstances described occur for a resident with a history of recurrent antibiotic drug orders. Such residents are good candidates for retrospective review. The clinical parameters documented in the history at the time of each antibiotic drug order can be evaluated to determine whether the diagnostic criteria for infection were met or whether an alternative medical condition should be considered the true cause of the respiratory symptoms.

Clinical Signs Supporting Pneumonia Diagnosis

For residents with suspected respiratory infection, one of the most important clinical parameters is respiratory rate. An elevated respiratory rate has the best predictive value for infection compared with other vital signs. Tachypnea, as defined by a respiratory rate greater than 25 breaths/minute, has 90% sensitivity and 95% specificity for pneumonia and a positive and negative predictive value of 95%. For residents with a respiratory rate greater than 25 breaths/minute, pulse oximetry should be performed. Pulse oximetry is another assessment that can be performed on-site in most LTCFs, and hypoxemia is an important parameter that predicts respiratory failure and 30-day mortality. If oxygen saturation less than 90% is identified, a decision to transfer the resident to an acute care facility or to pursue evaluation and treatment in-house must be made. Other nonrespiratory symptoms that may be observed in LTCF residents with pneumonia include fever, confusion, fatigue, chills, sweats, nausea, diarrhea, loss of appetite, and headache.

After evaluation of these clinical parameters, the IDSA guidelines state that a chest radiograph must be obtained

to identify signs of pneumonia and to exclude other causes. However, this test is not routinely performed in all LTCFs. Rates of obtaining a chest radiograph for residents with suspected pneumonia range from 20% to 85%, with lower rates being reported in community-based facilities and higher rates reported in hospital-based facilities.

When a chest radiograph is not available or not desired, a scoring system has been proposed to determine the probability of pneumonia based on other clinical signs (Table 1-2, Predictive scale). With this scoring system, a score of 4 or more is associated with a 69.4% probability of pneumonia on a chest radiograph. A score of 0 or -1, however, is associated with a 24.5% probability of a positive radiographic result; thus, a low score cannot be used to exclude pneumonia. However, the predictive value of a high score provides a reasonable basis on which to assume a diagnosis and initiate treatment when a chest radiograph is not an option. A second scoring system has been developed to determine the severity of suspected pneumonia and the need for a chest radiograph (Table 1-2, Severity scale). Access to appropriate diagnostic testing becomes more critical as risk factors accumulate, because mortality approaches 80% when all five of the possible points are scored. If a nursing facility cannot provide such access, or cannot provide the level of care necessary to adequately treat a severe infection, patients with higher scores are good candidates for hospital transfer, if patient or family wishes allow. A set of criteria, based on this severity scale score, have also been developed to provide guidance regarding which residents might be successfully treated without transfer to a hospital (Table 1-2, In-house treatment criteria).

Table 1-2. Scoring Systems for Predicting Pneumonia, Staging Pneumonia Severity, and Identifying Candidates for In-house Treatment

Predictive scale[a]		
White blood cell count (cells/mm^3)	< 10,000	0
	10,000–14,999	1
	≥ 15,000	2
Respiratory rate (breaths/minute)	< 30	0
	≥ 30	1
Somnolence or decreased alertness	Absent	0
	Present	1
Wheezes	Absent	0
	Present	−1
Acute confusion	Absent	0
	Present	1
Temperature	< 38°C	0
	≥ 38°C	1
Crackles	Absent	0
	Present	1
Pulse (beats/minute)	< 110	0
	110–129	1
	≥ 130	2
Severity scale[b]		
Respiratory rate > 30 breaths/minute		2
Pulse > 125 beats/minute		1
Altered mental status		1
Dementia		1
In-house treatment criteria		
Severity scale score of ≤ 2		
Respiratory rate < 30 breaths/minute		
Oxygen saturation > 92% on room air		
Pulse < 90 beats/minute		
Blood pressure within 10 mm Hg of baseline		
Temperature between 97.7°F (36.5°C) and 100.6°F (38.1°C)		
Resident is conscious		
Resident does not have a feeding tube		
Facility can provide adequate care		
Resident or family does not want transfer		

[a]Mehr DR, Binder EF, Kruse RL, Zweig SC, Madsen RW, D'Agostino RB. Clinical findings associated with radiographic pneumonia in nursing home residents. J Fam Pract 2001;50:931–7.

[b]van der Steen JT, Mehr DR, Kruse RL, Sherman AK, Madsen RW, D'Agostino RB, et al. Predictors of mortality for lower respiratory infections in nursing home residents with dementia were validated transnationally. J Clin Epidemiol 2006;59:970–9.

The IDSA guidelines also include a recommendation for obtaining respiratory secretions for sputum culture, although the caveat to this recommendation is that not all residents have the ability to produce and expectorate an adequate sputum sample. Staff members at LTCFs are not generally trained or credentialed to obtain samples by any method other than collecting expectorated sputum; hence, the resident must be able to follow directions for this procedure. The sample should be evaluated to determine whether it contains adequate sputum or is mostly saliva. If the nursing staff cannot make this determination, laboratory personnel can. Clinical laboratory standards for the appropriate microbiological assessment of sputum state that the sample should be rejected if it does not contain adequate sputum, and the specimen should be cultured only if the Gram stain shows less than 25 squamous epithelial cells per low-power field.

Testing for influenza with throat or nasopharyngeal swabs in residents with active illness is recommended when there is a suspected outbreak within an LTCF. Because this procedure may not be routinely performed every influenza season in a given facility, it is recommended that this testing be coordinated with the assistance of the clinical laboratory. For facilities not associated with a hospital that has an on-site clinical laboratory, the swab samples will require special handling in a single tube containing temperature-controlled viral transport media. In the event of an outbreak, this testing can identify influenza A and other viruses and can differentiate whether acutely ill residents are appropriate candidates for antibiotic drug therapy or if antiviral interventions are more appropriate.

Skin and Soft Tissue Infection

Cellulitis and infected pressure sores are two of the most common skin and soft tissue infections seen in residents of LTCFs. For suspected cellulitis, skin culture does not yield useful information and is not recommended. Without a culture to indicate a specific organism, the fear of bacterial resistance increases the temptation to use broad-spectrum antibiotic drugs as empiric therapy. Such reliance on broad-spectrum antibiotic drugs should be discouraged. Instead,

tracking of the facility's history of skin infections and associated antibiotic drug outcomes can help determine the type of antibiotic drug coverage needed. Community-acquired skin infections are more likely to be caused by virulent organisms, but the rates of resistance to traditional antibiotic drugs tend to be lower than for organisms associated with health care–acquired skin infections. An LTCF resident may be susceptible to either community- or health care–associated skin infections, and so tracking of antibiotic drug treatment success or failure within a facility or even an individual nursing unit can help guide therapy. Review of the resident's medical history is also recommended. Residents with medical conditions such as diabetes mellitus may be more likely to experience infection with gram-negative bacilli. Fine-needle aspiration of the affected area rarely provides useful information and is not routinely recommended.

Pressure ulcers are a key indicator of the quality of care provided within nursing facilities. For this reason, LTCFs often initiate aggressive protocols to address pressure ulcers when they occur. If pressure ulcers do not respond to initial pressure relief and debridement, infection is often suspected. Cultures from the pressure ulcer are necessary if the ulcer is getting worse despite seemingly appropriate treatment; if the wound exudes persistent purulent drainage; or if the surrounding tissue shows signs of infection, such as erythema, inflammation, and warmth. If cultures are taken, they should be obtained from the drainage inside the wound or from deep tissue extracted at the time of debridement. Surface swabs of the skin are not recommended because a mixed flora is expected and will not accurately guide empiric therapy. Bacteremia is a common consequence of infected pressure ulcers. If the resident is showing signs of systemic infection such as fever, shaking, or chills with or without additional atypical signs of illness, wound cultures alone are not adequate, and blood cultures should be obtained.

Gastrointestinal Infection

When a resident presents with diarrhea, a drug regimen review should be performed to determine whether an antibiotic drug has been administered in the past 30 days. If so, stool samples should be obtained to test for *Clostridium difficile* toxin. The 2000 IDSA guidelines recommend that a single negative result not be used to exclude infection if diarrhea persists, and one to two additional stool specimens should be tested. If there is no history of antibiotic drug use, supportive care alone can be given. However, further evaluation may be indicated, because diarrhea can be associated with other infections, such as pneumonia and bacteremia. The evaluation should include the resident's oral intake and bowel sounds, and if diarrhea persists, more extensive evaluation is indicated. In the event that there is no history of antibiotic drug use and diarrhea is associated with fever, cramping, or red or white blood cells in the stool, a culture to identify other gastrointestinal pathogens is suggested.

Bacteremia

Most data describing the incidence and outcomes of bacteremia in institutionalized elderly people come from hospital-based LTCFs. Bacteremia is not a common type of infection in long-term care, occurring at a rate of 5 to 40 episodes per 100,000 resident-days. However, the mortality rate associated with bacteremia is significant, ranging from 20% to 50%. Bacteremia occurs as a secondary infection in about 6% of infections. The urinary tract is the most common primary site, although mortality risk is higher when pneumonia is the primary cause.

It is often difficult to identify bacteremia in a patient who is elderly. Predictive clinical signs include fever (85% of patients who are elderly with bacteremia will have a fever of at least 100°F [37.8°C]), lethargy, confusion, delirium, vomiting, diarrhea, abdominal pain, shaking, chills, and shock. In some studies, recent removal or replacement of a urinary catheter has been associated with increased risk of bacteremia. Some studies suggest that patients who are elderly will present with fewer of these symptoms than younger patients; however, it is possible that symptoms are present but go unrecognized until they become severe. About half of bacteremia-associated deaths occur within 24 hours of diagnosis, even with appropriate antibiotic drug intervention.

The utility of blood cultures is controversial. The IDSA guidelines do not recommend blood cultures because of the low yield of positive cultures and the lack of association between organism confirmation and improved outcomes. Because of the 24-hour mortality risk, empiric antibiotic drug intervention must be initiated without waiting for confirmation of an organism. In circumstances of rapid decline, it is likely that the utility of cultures is limited. In select circumstances, however, cultures may be useful. Blood and urine cultures can be paired for suspected urosepsis, particularly for patients with indwelling urinary catheters. Blood cultures may be recommended for identification of a clinically significant pathogen in a resident with pressure ulcers and signs of systemic infection. Lastly, one study suggested that patients who present with symptoms of severe pneumonia and who will not be transferred to the hospital are good candidates for blood cultures because of the high mortality risk associated with bacteremia as a secondary infection. For residents with suspected bacteremia, the 2000 IDSA guidelines suggest that transfer to an acute care facility is the best course of action; however, a specific level of evidence does not accompany this recommendation. Decisions regarding transfer are dependent on the resident's directives or their responsible party's wishes.

Selection of Appropriate Antibiotic Drug Therapy

Classification of Infection Etiology

Once infection is diagnosed, many factors must be considered when selecting and dosing antibiotic drug therapy. Even when culture and sensitivity data are ordered, initial antibiotic drug selection is empiric. Empiric therapy requires consideration of the most common causative organisms in a given infection; thus, a critique of the assumptions behind these considerations is important. There is controversy regarding whether infections in the LCTF should be classified as community acquired or nosocomial and which designation is more reliable. Nosocomial usually suggests a hospital-acquired infection, although the term *health care*

acquired is commonly used to include other health care institutions, particularly LTCFs. Classifying infections in the long-term care environment as health care acquired has implications for antibiotic drug selection, because it implies causative organisms and resistance patterns different from those suspected in community-acquired infections. In hospital-based LTCFs, empiric therapy selected on the basis of such assumptions may be appropriate. However, residents of community-based facilities may experience infectious exposures that more closely resemble the surrounding community at large, suggesting a different profile of causative organisms and resistance patterns. For instance, *Providencia* sp. as a cause of UTIs is almost exclusively found in the long-term care environment. It is important, therefore, to consider specific microbiologic data whenever possible. Assumptions about empiric therapy based solely on the classifications of community acquired or health care acquired can be misleading and inappropriate. There is no substitute for an individual facility's collection and tracking of its infection patterns and sensitivity. These data are the most reliable profile on which to base empiric antibiotic drug selections.

Application of Principles of Age-Related Changes in Pharmacokinetics and Pharmacodynamics to Drug and Dosage Selection

One of the most important age-related changes affecting antibiotic drug or dosage selection is declining glomerular function. There are few antibiotic drugs for which special precautions or dosing considerations are based on age alone, and in fact, most drug information resources that include sections for dosing in the elderly do not recommend routine adjustments for patients older than 65. However, these same resources provide dosage adjustment recommendations based on creatinine clearance parameters; thus, a significant proportion of this population will need drug dosages adjusted for declining kidney function. Although 30% of the population will have little or no deterioration in kidney function with aging, the majority of patients older than 40 will experience a 10% reduction in glomerular filtration rate per year, and 5% to 10% will experience loss at an accelerated rate. Calculated estimates of creatinine clearance, although inexact, are useful when determining the appropriate drug dosage for an LTCF resident. Dosage adjustment recommendations for the most common antibiotic drugs used in LTCF residents are compiled in Table 1-3.

Elderly residents are especially vulnerable to adverse reactions to antibiotic drugs. This vulnerability is not unexpected when there is exposure to excessive dosing caused by lack of dosage adjustment for renal function. Even with appropriate dosing, patients who are elderly may be more vulnerable to experiencing side effects, particularly central nervous system effects. Common side effects of antibiotic drugs in the elderly are listed in Table 1-3.

Route of Therapy

The route of anti-infective drug therapy to be used must also be considered. Most LTCF residents will receive drugs orally for infections treated within the facility. Intravenous antibiotic drug therapy is only an option in facilities with staff members who are trained in intravenous procedures. Long-term care regulations do not preclude licensed vocational nurses from administering drugs intravenously, but they do specify that personnel at this level must demonstrate competency with these procedures. Therefore, an LTCF resident's access to intravenous interventions of any kind may vary from facility to facility or even shift to shift depending on personnel. Drugs administered intramuscularly are an alternative, and ceftriaxone is the most common antibiotic drug administered by this route. Because of age-related changes in the ratio of lean muscle mass to total body fat, it has been suggested that 1-inch (25-mm) needles are preferable for intramuscular administration, although this may not be appropriate in a very frail, emaciated individual. Intramuscular injection of a cephalosporin can also be associated with a significant burning sensation, even when lidocaine is used as the diluent. Residents who experience significant discomfort or who become agitated with the injection may benefit from pretreatment with an analgesic such as acetaminophen.

Duration of Therapy

Duration of therapy is an important consideration when evaluating the appropriateness of an antibiotic drug regimen. For UTIs, the duration of therapy is usually dependent on whether the infection is uncomplicated or complicated. However, three things must be considered when determining the length of treatment for an LTCF resident with a UTI. First, definitions of complicated or uncomplicated UTI are gender-specific. All UTIs in male residents should be treated as complicated. Second, it may be difficult or even impossible to truly differentiate between a complicated and uncomplicated UTI in a patient with atypical symptom presentation. Third, elderly patients are not well represented in clinical trials of the short-course antibiotic drug regimens evaluated for uncomplicated cystitis. For these reasons, standard treatment durations of at least 7–10 days should be advocated in the long-term care setting. Some recommendations for men extend the standard treatment duration up to 14 days. Longer durations are also generally recommended when a known complicated UTI is caused by structural bladder abnormalities (10–14 days) or pyelonephritis (14–21 days). If recurrent infection occurs in a male resident or physical examination suggests the presence of prostate infection, treatment should continue for at least 4 weeks for acute bacterial prostatitis and 12–16 weeks for chronic prostatitis.

The optimal duration of treatment for the other types of infections discussed in this chapter is less clear. Pneumonia is usually treated in the inpatient setting until clinical indicators (e.g., temperature less than 100°F [37.8°C], pulse less than 100 beats/minute, respiratory rate less than 25 breaths/minute, systolic blood pressure greater than 90 mm Hg, oxygen saturation greater than 90%, ability to maintain oral intake) have been reached. Outpatient regimens are more empirically determined, usually 10–14 days, with the exception of azithromycin, which can be continued for only 5 days. Residents receiving treatment in the LTCF can be monitored following the inpatient criteria; however, drug orders are often written in more of an outpatient style, with a defined duration of 10–14 days, although intramuscular ceftriaxone injections are often prescribed for 5-day courses. In most cases, a 10- to 14-day regimen should be adequate because improvement should be expected within the first 2

Table 1-3. Antibiotic Drug Dosage Adjustments for Renal Dysfunction and Potential Adverse Effects

Antibiotic Drug	Creatinine Clearance (mL/min)	Initial Dosage Recommendation	Adverse Effects
Amoxicillin or amoxicillin/ clavulanate	< 30 < 10	250–500 mg every 12 hours 250–500 mg every 24 hours 875-mg dosage form should not be used	Nausea, vomiting, rash, fever, anxiety, confusion, headache
Azithromycin	< 10	Avoid use	Dizziness, nausea, cramping, vomiting
Cefazolin	< 55 < 35 < 10	Usual dose every 8 hours Usual dose every 12 hours Usual dose every 18–24 hours	Diarrhea, confusion, rash
Cefotaxime	< 50 < 20 < 10	Usual dose every 8–12 hours 50% dose reduction Extend interval to every 24 hours	Fever, rash, diarrhea, nausea, eosinophilia
Ceftriaxone	—	No dose adjustment for daily dosage < 2 g	Pain with injection (IM), diarrhea, rash, elevated LFTs, elevated BUN, eosinophilia, thrombocytosis, leukopenia
Cefuroxime	< 20 < 10	250 mg every 12 hours 250 mg every 24 hours	Nausea, diarrhea, dizziness, increased LFTs, decreased hemoglobin and hematocrit, eosinophilia, thrombophlebitis
Cephalexin	< 50	250–500 mg every 12 hours	Diarrhea, dizziness, fatigue, headache
Ciprofloxacin			
Oral	< 50 < 30	250–500 mg every 12 hours 250–500 mg every 18 hours	Nausea, diarrhea, rash, headache, dizziness, tremor, restlessness, confusion, tendon rupture
Intravenous	< 60 < 30	400 mg every 12 hours 400 mg every 24 hours	
Clarithromycin	< 30	250 mg every 12–24 hours after 500-mg loading dose	Headache, nausea, diarrhea, abnormal taste, dyspepsia, abdominal pain, ventricular tachycardia, torsades de pointes, mania, tremor, hypoglycemia, prolonged prothrombin time, leukopenia, neutropenia, elevated LFTs, and BUN
Clindamycin	—	No adjustments recommended	Nausea, vomiting, diarrhea, rash, hypotension, increased LFTs, pseudomembranous colitis, thrombocytopenia, eosinophilia, neutropenia
Trimethoprim/ sulfamethoxazole	< 30 < 15	50% dose reduction Avoid use	Nausea, vomiting, diarrhea, rash, skin reactions, photosensitivity, fever, dizziness, headache, elevated LFTs, BUN, and serums Cr, crystalluria, hyperkalemia, leukopenia, thrombocytopenia, neutropenia, serum sickness
Doxycycline	—	No adjustments recommended	Rash, photosensitivity, eosinophilia
Erythromycin	< 10	50% to 75% usual dose (maximum 2 g/day)	Abdominal pain, nausea, vomiting, oral thrush, hearing loss (doses > 4 g/day)
Gentamicin	< 50 < 10	30% to 70% dose every 12 hours 20% to 30% dose every 24–48 hours Multiple nomograms apply	Nephrotoxicity, ototoxicity, ataxia, vertigo, drowsiness, headache, nausea, vomiting, itching, rash, edema

Table 1-3. Antibiotic Drug Dosage Adjustments for Renal Dysfunction and Potential Adverse Effects (continued)

Antibiotic Drug	Creatinine Clearance (mL/min)	Initial Dosage Recommendation	Adverse Effects
Levofloxacin			
Uncomplicated	< 50	250 mg every 24 hours	Nausea, vomiting, dizziness, headache, tremor, insomnia, rash, arthralgias, increased LFTs thrombocytopenia, leukopenia
	< 20	250 mg every 48 hours	
Complicated	< 50	750 mg every 48 hours	
	< 20	500 mg every 48 hours	
Metronidazole	< 10	50% of usual dose	Nausea, vomiting, diarrhea, dizziness, ataxia, headache, seizures, neuropathy, metallic taste, disulfiram-like reaction with alcohol
Moxifloxacin	—	No adjustment recommended	Nausea, vomiting, anxiety, dizziness, insomnia, headache, tremor, nervousness, somnolence, vertigo, seizure, neuropathy, tachycardia, QT interval prolongation, eosinophilia, thrombocytosis, leukopenia
Nitrofurantoin	< 50	Avoid use	Nausea, vomiting, diarrhea, cough, dyspnea, fatigue, pulmonary fibrosis, loss of appetite, weakness, headache, neuropathy, chest pain
Norfloxacin	< 30	400 mg every 24 hours	Nausea, vomiting, diarrhea, dizziness, fatigue, headache, somnolence, depression, insomnia, heartburn, bitter taste, increased LFTs and BUN
Tobramycin	< 50	30% to 70% dose every 12 hours	Nephrotoxicity, ototoxicity, neurotoxicity, drowsiness, headache, tremor, weakness, hypotension, drug fever, nausea, vomiting, rash
	< 10	20% to 730% dose every 24–48 hours Multiple nomograms	
Vancomycin	< 50	500 mg every 24–48 hours	Rash, nausea, vomiting, chills, drug fever, bitter taste, nephrotoxicity, ototoxicity, eosinophilia, thrombocytopenia
	< 10	500 mg every 48–96 hours Multiple nomograms	

BUN = blood urea nitrogen; IM = intramuscular; LFT = liver function test; SCr = serum creatinine.

days of therapy, with resolution by 5–7 days and no longer than 10–14 days. If shorter courses of therapy are used, it is important to evaluate the patient for evidence that the above criteria for symptom resolution are met. Recommended treatment duration for bacteremia is similar to that for pneumonia. Ten- to 14-day courses of treatment are often advocated, but clinical parameters of improvement must be met.

The optimal duration of treatment for bacterial diarrheal illnesses depends on the organism being treated. The most common regimens, such as metronidazole for *C. difficile,* are 10 days or, for the alternative, oral vancomycin, 7–10 days. Courses of trimethoprim/sulfamethoxazole, macrolides, or fluoroquinolones for *Shigella, Salmonella, Campylobacter, Vibrio cholerae,* or *Escherichia coli* are often 3–5 days.

Cellulitis is usually treated for 7–14 days. Routine treatment of pressure ulcers with antibiotic drugs is usually discouraged, and treatment is reserved for situations in which the ulcer is associated with surrounding cellulitis, osteomyelitis, or bacteremia. In such cases, treatment recommendations defer to those of the associated condition. Some studies suggest the use of topical antibiotic agents, such as silver sulfadiazine, for up to 2 weeks.

Role of the Pharmacist

Prospective and Retrospective Drug Therapy Intervention

Pharmacists can provide prospective drug therapy intervention to optimize antibiotic drug selection and dosage in individual cases of infection. Such prospective evaluation is aimed at achieving a cure while avoiding adverse effects. Pharmacists can also provide retrospective evaluation of facility patterns of antibiotic drug usage. Retrospective evaluation is aimed at detecting facility-wide problems associated with suboptimal assessment and diagnostic procedures, unnecessary antibiotic drug use or inappropriate antibiotic drug selection, or facility resistance patterns. The extent to which both prospective intervention and retrospective evaluation can occur depends on the pharmacist's practice role in the LTCF.

There are two such pharmacist's roles. One role involves the dispensing of prescriptions, and the other involves clinical records review. If there is access to an on-site pharmacy, these roles could be provided by the same individual, but this is not the case for most LTCFs. When it comes to the evaluation of antibiotic drug therapy for acute infections, the pharmacist in the dispensing role has the advantage of being notified of the drug order at the time it is created. This time point would theoretically provide the best opportunity to make a prospective drug therapy intervention, because it would allow the order to be optimized before the first dose of antibiotic drug was administered. The disadvantage, however, is that the pharmacist in this position usually does not have access to the medical record and the documentation of clinical and laboratory data that support the diagnosis. The facility's consultant pharmacist, by contrast, does have full access to the clinical record and all other facility documentation and may therefore be in a better position to evaluate the appropriateness of antibiotic drug therapy. The disadvantage is that the consultant's reviews usually occur on a monthly basis and may not identify the presence of antibiotic drug therapy until well after it has been initiated, or even after it is completed. Therefore, both the dispensing and consultant pharmacists are presented with inherent barriers to achieving optimal antibiotic drug therapy outcomes.

Overcoming Potential Barriers to Optimal Pharmaceutical Care

Pharmacists receiving new orders to dispense antibiotic drug therapy can inquire about clinical data required to evaluate the appropriateness of antibiotic drug therapy. This information might allow drug therapy intervention between pharmacist and prescriber before the drug is dispensed. However, it is understood that this intervention often requires an extra step, because LTCF drug orders are increasingly transmitted by facsimile, which will not usually contain the data in question. Individual pharmacies or pharmacists may also face opposition when attempting to obtain these data, especially if the LTCF staff is not in the habit of providing this information to a pharmacist or if other pharmacies that serve the same LTCF do not uniformly request this information before prescription processing. In such circumstances, these well-meaning attempts can unfortunately be labeled as delays of care. Therefore, implementation of such a practice requires negotiation and coordination between the pharmacy and the facility's administration.

Another option is for the consultant pharmacist to negotiate a process that would provide notification when an infection is suspected or when a new antibiotic drug is prescribed. This process would require the nursing staff to call or page the pharmacist as well as the resident's physician or mid-level practitioner. Just as protocols can be developed to report appropriate data for diagnostic decision-making to the practitioner, protocols can be developed to report data for the assessment of antibiotic drug appropriateness to the pharmacist. Discussion between the pharmacist and the nurse can lead to drug therapy intervention, which can be communicated to the physician before the drug order is sent to the pharmacy. This strategy can also be effective in after-hours instances, when a pharmacist has the ability to provide intervention before the drug is taken from a night box or emergency kit. Such a service is not without significant time commitment. The consultant must negotiate what these services are worth and whether they will be reimbursed as part of the hourly rate or billed as a separate fee. The facility must value the pharmacist's input enough to incorporate notification of the pharmacist into operating procedures and to reinforce consistent performance by the staff.

Drug Regimen Review

In the absence of augmented services, there are other routine interventions and services a pharmacist can provide to improve antibiotic drug outcomes. The monthly drug regimen review already involves assessment of laboratory data to allow appropriate drug therapy monitoring. The pharmacist can provide documentation of the resident's estimated creatinine clearance as part of this review. Even though the pharmacist is not likely to be present when antibiotic drug therapy is being prescribed, the provision of easy access to the creatinine clearance will increase the likelihood that kidney function will be taken into consideration.

Monthly review can also identify antibiotic drug–prescribing patterns over time. Continuing quality assurance evaluations should track the most common infections, the most frequently selected antibiotic drugs, and the degree of adherence to culture and sensitivity data. To address recurrent problems, the pharmacist can collaborate with the facility's director of nursing or medical director to develop clinical pathways for in-house assessment and reporting or preprinted treatment orders that can be suggested to a prescriber at the time of illness notification.

Particular attention should be paid to infection clusters occurring with high frequency within a specific nursing unit or wing and to residents with recurrent antibiotic drug courses. Residents with multiple courses of antibiotic drugs for a period of several months or 1 year are candidates for case review. The resident's record should be evaluated to determine whether the clinical and laboratory data documented in each episode were adequate to support the diagnosis. When diagnostic criteria are not met, attention should turn to comorbid medical conditions or to current drugs that suggest ongoing symptoms of an undiagnosed comorbidity, because these may retrospectively suggest an alternate explanation of the illness presentation. When the same type of infection is implicated in each episode, recurrence and relapse must be differentiated. For each episode, the time between infections, the organism cultured, the sensitivity data associated with each culture, the antibiotic drug selected, and the dosage and duration of therapy should be considered.

Lastly, the pharmacist's records review can identify whether accurate vaccination histories are maintained. Many LTCFs have standing immunization orders, including annual influenza vaccination and pneumococcal vaccination on admission for residents who have not had it, who require a second vaccine, or who have an unknown immunization history. However, when vaccination frequency is longer than annually, as it is for the pneumococcal vaccine or for a tetanus booster, documentation of the facility's administration of the vaccine may be lost. This loss of documentation is also problematic for tuberculin skin test results. When the

method of documentation is a notation of administration in a doctor's order, medication administration record, history, and physical examination or progress note, these data are vulnerable to being thinned from the clinical record. Many facilities do not maintain a separate method of documenting vaccination history. In the absence of such, a periodic records audit is a useful way to determine ongoing facility compliance with these standards.

Conclusion

The risks associated with infections in long-term care are significant. One of the biggest challenges for achieving successful outcomes is misdiagnosis of infection. Although the pharmacist will not make the initial diagnosis, the accuracy of the diagnosis is fundamental to determining the appropriateness of antibiotic drug therapy. Therefore, pharmacists should be familiar with atypical disease presentations and the most reliable diagnostic criteria for infection. Pharmacists need to develop practical strategies for improving antibiotic drug outcomes that take into account logistical barriers within the long-term care environment. These strategies include not only resident-level drug therapy interventions to improve antibiotic drug selection and dosage, but also facility-level evaluations to identify problematic patterns of suboptimal infection assessment and poor treatment outcomes.

Annotated Bibliography

1. Bentley DW, Bradley S, High K, Schoenbaum S, Taler G, Yoshikawa TT. Practice guideline for evaluation of fever and infection in long-term care facilities. Clin Infect Dis 2000;31:640–53.

   This article is an excellent evidence-based review of the most common infections in the long-term care setting. Although published in 2000, it is the most contemporary guideline of its type. The primary authors are part of an expert panel that made up the practice guidelines committee of the IDSA. The guideline has been endorsed by the American Geriatrics Society and has been abstracted and published online as part of the American Geriatrics Society collection of clinical practice guidelines. This review describes infection presentation and evaluates methods of evaluation and diagnosis for UTIs, respiratory infections, skin and soft tissue infections, gastrointestinal infections, and bloodstream infections. The perspective of this practice guideline is somewhat limited, because the majority of data come from hospital-based LTCFs; however, this limitation is caused by the lack of data from community-based LTCFs and not to an intentionally narrow focus of the guideline. Therefore, despite these limitations, this practice guideline provides the best evidence-based recommendations possible.

2. Levy CR, Eilertsen T, Kramer AM, Hutt E. Which clinical indicators and resident characteristics are associated with health care practitioner nursing home visits or hospital transfer for urinary tract infections? J Am Med Dir Assoc 2006;7:493–8.

   This study identifies factors associated with hospital transfer or health care practitioner visits to the nursing facility for residents of a skilled nursing facility with suspected UTI. Long-term care regulations do not mandate practitioner visits more frequently than monthly in a Medicare skilled nursing facility, and IDSA recommendations do not specify whether suspicion of infection should warrant an in-person visit by a physician. It is likely that LTCF residents will not receive in-person attention, and in fact, this study demonstrated that less than one-third of residents with unstable vital signs were seen by a practitioner or transferred to a hospital. This study also evaluated whether the existence of "Do Not Resuscitate" orders had an influence on the receipt of this care, but there was no association between these orders and the frequency of personal visits.

3. Loeb M, Brazil K, Lohfeld L, McGeer A, Simor A, Stevenson K, et al. Effect of a multifaceted intervention on number of antimicrobial prescriptions for suspected urinary tract infections in residents of nursing homes: cluster randomized controlled trial BMJ 2005;331:669.

   This study evaluated the effect of an algorithm for the assessment and treatment of UTIs in LTCF residents. This article is interesting because it does not employ the use of a CBC for the purposes of identifying infection. This practice is in contrast to IDSA recommendations that suggest the CBC as the first-line laboratory test for suspected infection. This algorithm uses fever as the initial criteria and suggests urine culture only if symptoms localized to the urinary tract are present. Urine culture is not indicated if signs of another type of infection are present. Application of the algorithm was associated with a decreased rate of antibiotic drug prescribing, with no difference in hospitalization or mortality outcomes. There may be limitations of such an algorithm when illness presentation is atypical. Presumably, the CBC would still be required as the initial test to exclude the possibility of infection from any cause, although the algorithm does not specify this. Therefore, the utility of this algorithm may be limited to circumstances in which the illness presentation is associated with classic UTI symptoms.

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   In this prospective study, 2,334 illness presentations were evaluated among 1474 elderly residents of 36 nursing facilities in central Missouri. The objective of the study was to identify clinical signs of pneumonia that were associated with diagnosis confirmed by chest radiography. In 80% of the episodes of pneumonia, subjects had three or fewer respiratory symptoms; however, the study identified eight clinical variables that were independent predictors

of pneumonia. A simple score from −1 to 8 differentiated residents at low risk of pneumonia from those at high risk, although the predictive value was best for the residents at highest risk. The authors suggest that a high score identifies residents for whom treatment could be initiated without obtaining a chest radiograph. These findings require further validation, but the implications of this study are important in light of the numbers of LTCF residents who do not have easy access to radiographic testing.

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   This study group translated nationally published guidelines for nursing home–acquired pneumonia into practice protocols for implementation in a state veterans home. Previous data suggest that adherence to practice standards advocated by the guideline is associated with improved survival, and the intervention in this study operationalized the recommendations into a series of policies, procedures, and standardized orders. As a result of the intervention, improvements were seen in compliance with influenza vaccination, the timeliness of physician response to report of illness, the obtaining of chest radiographs for residents treated in-house, the use of appropriate antibiotic drugs, and the timeliness of access to antibiotic drugs for unstable patients. This study demonstrates the feasibility of implementing optimal practice standards for identifying and treating infection.

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   This study assessed whether colonization with methicillin-resistant *Staphylococcus aureus* (MRSA) was associated with morbidity and mortality among nursing home residents. A total of 2814 residents of 23 nursing facilities were followed for 3 years, and the occurrence of either hospitalization or death was evaluated. Carriers of MRSA were twice as likely to be hospitalized for respiratory tract infections, and death was also more likely in this group. The most significant association between MRSA colonization and risk of death was among residents with severe cognitive impairment. The rising incidence of resistant organisms, specifically MRSA, is well documented. This article highlights the particular vulnerability of long-term care residents with severe cognitive impairment.

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    This article describing the emergence of fluoroquinolone resistance in *E. coli* in long-term care residents is significant. Fluoroquinolones are commonly employed in long-term care, because they are broad-spectrum agents that have excellent oral bioavailability and cover the anticipated organisms in both urinary tract and respiratory tract infections. However, fluoroquinolones are overused in LTCFs. This study demonstrates that previous fluoroquinolone exposure is a significant risk factor for fluoroquinolone-resistant *E. coli*. Pharmacists should discourage the use of fluoroquinolones as first-line empiric therapy for uncomplicated infections, particularly UTIs, and this article provides excellent literature support for this position.

11. Meaume S, Vallet D, Morere MN, Teot L. Evaluation of a silver-releasing hydroalginate dressing in chronic wounds with signs of local infection. J Wound Care 2005;14:411–9.

    This clinical trial evaluates the effect of a silver-releasing dressing on the risk of local infection in individuals with chronic wounds. Previous studies have evaluated the benefit of topical silver, but this trial used a silver-releasing hydroalginate dressing. The wounds of patients in this study did not meet criteria for systemic infection but were associated with poor healing and serous exudate and were causing symptoms of pain, swelling, redness, and heat. Wound severity scores and wound closure rates were superior in the treatment group, but there were also fewer treatment group patients requiring systemic antibiotic drugs by the end of the 4-week follow-up period. This trial was small and included only 99 subjects, but an intervention that may reduce the likelihood of exposure to systemic antibiotic drugs is potentially significant.

12. O'Meara SM, Cullum NA, Majid M, Sheldon TA. Systematic review of antimicrobial agents used for chronic wounds. Br J Surg 2001;88:4–21.

    This article is a comprehensive review of 30 clinical trials evaluating antibiotic drug treatment for various types of chronic wounds including pressure ulcers, venous leg ulcers,

diabetic foot ulcers, and wounds of mixed etiologies. The results do not support the routine use of systemic antibiotic drugs for chronic wound healing, but they do provide some evidence for the utility of various topical antimicrobial treatments. Although this information is helpful, the review also illustrates the limited clinical trial data in this area. For instance, there were only two trials of pressure ulcer prevention and three for treatment. For wounds of mixed etiologies, there were only two trials of systemic therapy and five for topical therapies.

13. Drinka PJ, Gauerke C, Le D. Antimicrobial use and methicillin-resistant *Staphylococcus aureus* in a large nursing home. J Am Med Dir Assoc 2004;5:256–8.

    Infection caused by antibiotic-resistant organisms is a growing problem in LTCFs. Inappropriate antibiotic drug use is a major contributor to this phenomenon, and a primary focus of this chapter is to assist the clinician in accurately evaluating infection and determining optimal drug therapy. This article was selected for the annotated bibliography because it highlights the risks associated with inappropriate antibiotic drug selection. Investigators evaluated the sensitivity pattern for MRSA and methicillin-sensitive *S. aureus* and changes in facility use of antibiotic drugs. The results demonstrate that an 18% increase in MRSA infections was associated with a 42% increase in fluoroquinolone use and a 37% decrease in trimethoprim/sulfamethoxazole use. This article is an update to a previous analysis by the same investigators in 2002, which also demonstrated an association between antibiotic drug exposure and MRSA, with a strong association between fluoroquinolones and urinary or wound isolation of MRSA. Fluoroquinolones are often employed as empiric antibiotic drug therapy, but this practice should be discouraged. The use of this class of drugs is not only associated with increasing rates of fluoroquinolone-resistant *E. coli* but with MRSA as well.

14. Kreman T, Hu J, Pottinger J, Herwaldt LA. Survey of long-term care facilities in Iowa for policies and practices regarding residents with methicillin-resistant *Staphylococcus aureus* or vancomycin-resistant enterococci. Infect Control Hosp Epidemiol 2005;26:811–5.

    Despite concern over the prevalence of antibiotic-resistant infections, policies and practices in many LTCFs are not optimal to address this problem. In this study, the investigators evaluated the infection control policies and practices employed by 331 LTCFs in Iowa by a survey. Survey results showed prevalence rates of 13.4 infections per 1000 residents for MRSA and 2.3 infections per 1000 residents for vancomycin-resistant enterococci (VRE). Although statewide guidelines for the prevention and treatment of MRSA and VRE had been published by the Iowa Antibiotic Resistance Task Force, only 44.7% of survey respondents had heard of these recommendations. This suggests that dissemination of practice standards is not optimal. More troubling, the survey showed that some nursing facilities will actually deny admission to residents with known antibiotic-resistant infections, with 7.3% and 16.9% of responding facilities acknowledging that admission was denied on the basis of MRSA or VRE infection, respectively. For many LTCFs struggling with implementation or enforcement of infection control protocols, it may be tempting to keep the problem "out of the building" in this manner; however, this denies equitable access to care. Furthermore, it does not allow facilities to justify daily infection control procedures that are less stringent, because such criteria do nothing to address MRSA carriage.

15. Lucet JC, Grenet K, Armand-Lefevre L, Harnal M, Bouvet E, Regnier B, et al. High prevalence of carriage of methicillin-resistant *Staphylococcus aureus* at hospital admission in elderly patients: implications for infection control strategies. Infect Control Hosp Epidemiol 2005;26:117–20.

    When a known MRSA infection is present, most health care institutions will employ some kind of infection control protocol, including gloves, gowns, face masks, hand washing, or isolation. However, if individuals who are carriers of MRSA are not identified, the spread of antibiotic-resistant organisms can occur without such protocols being enforced. This study evaluated the utility of nasal cultures to screen for MRSA among 797 patients older than 75 years who were admitted to a large tertiary hospital in Paris, France. The authors determined that 84.1% of MRSA carriers would have been missed on admission without this screening. Based on the length of stay of MRSA carriers, it was calculated that without the screening, 81.1% of hospital days would have lapsed with no appropriate contact precautions taken. Although this was a hospital-based evaluation, its results are pertinent to LTCFs. Carriage of MRSA was associated with chronic wounds, previous stay in an LTCF or rehabilitation unit, and poor health status. Appropriate screening procedures may be more likely to be effective in preventing the spread of MRSA within an LTCF than denying admission to a resident with known infection.

16. Silverblatt FJ, Tibert C. Mikolich D, Blazek-D'Arezzo J, Alves J, Tack M, et al. Preventing the spread of vancomycin-resistant enterococci in a long-term care facility. J Am Geriatr Soc 2000;48:1340–2.

    Researchers evaluated the utility of identification of VRE with rectal swab and culture before admission. This study is similar in some ways to the MRSA screening study previously discussed, in that it identified individuals for whom contact isolation was appropriate before admission. In contrast to the MRSA screening study, patients were being admitted to an LTCF rather than a hospital, supporting the assertion that such screening procedures are appropriate on transfer of care venue in either direction. Of note, however, is that patients identified for screening in this study were admitted from an acute care facility with a high endemic rate of VRE. For those residents with VRE colonization, isolation precautions were implemented, and oral bacitracin was prescribed. Adherence to infection control protocols was associated with the absence of VRE transmission among facility residents. These findings support the success of appropriate infection control protocols. Admission to the LTCF need not be denied if colonized residents can be identified. This analysis also identified risk factors associated with VRE colonization, such as advanced age, prior antibiotic drug use, longer LTCF length of stay, prior hospitalization (within previous year), indwelling urinary catheters, fecal or urinary incontinence, and diarrhea. Such risk factors could be considered when designing admission protocols for LTCFs with increasing incidence of VRE among their residents.