Managing patients infected with antibiotic resistant bacteria is becoming one of the major clinical obstacles facing physicians who treat patients in long-term care facilities (LTCFs). Penicillin-resistant pneumococci (PRP), vancomycin-resistant enterococci (VRE), gram-negative bacteria that produce extended-spectrum and ampC-type \( \beta \)-lactamase enzymes, and quinolone-resistant gram-positive and gram-negative bacteria are the major resistant pathogens that are emerging in these settings. The mechanisms responsible for the evolution of these antibiotic resistant organisms (molecular rearrangement of penicillin binding protein genes, acquisition of a mobile genetic element, and point mutation that alter the active site) are reviewed. Vancomycin intermediate Staphylococcus aureus (VISA) and multidrug efflux pumps in gram-negative bacteria are also threatening our most potent antimicrobials. Aggressive screening, education, antibiotic-control measures, and immunization are advocated as important preventive measures. The combined efforts of the medical directors, infection-control personnel, and administrators are needed to stem this problem.

LONG-TERM care facilities (LTCFs) are becoming a major component in our health care delivery system (Figure 1). At present, approximately 2.5 million residents live in LTCFs, and it is estimated that 43% of the 2.2 million people who turned 65 years old in 1990 will enter a nursing home at least once before they die (1). These facilities provide a range of necessary services to elderly patients: rehabilitation, chronic care, adult day care, assisted living, and skilled nursing. As a result of intense economic and regulatory pressures, practitioners are using LTCFs as a less costly alternative to hospitalization (2).

Infections in LTCFs represent a major cause of morbidity and mortality (3–6). Because of the increased infection rate, antimicrobials are among the most frequently prescribed agents (7). Studies have shown that antibiotics account for 40% of all systemic drugs used in nursing homes (8). Unfortunately, indiscriminate and often inappropriate use of these medications has become commonplace. One of the major consequences of antimicrobial overuse is the promotion and transmission of antimicrobial resistance (9,10). Clinicians involved in the care of institutionalized elderly persons need to understand the origins and mechanisms underlying the most commonly encountered resistant pathogens in LTCFs so that effective strategies to prevent and treat these infections can be employed.

RISK FACTORS FOR INFECTION IN ELDERLY PERSONS

One of the major factors that contribute to acute infections in elderly persons is the use of devices that violate the natural mechanical barriers (indwelling bladder catheters and intravenous lines). Malnutrition, polypharmacy, multiple comorbidities, and diminished cognitive function also play major roles (11). Altered T-lymphocyte function, as measured by decreased cutaneous delayed-type hypersensitivity, diminished antibody production, and decreased interleukin-2 production, are immunologic changes that occur with aging (11). This impaired T-cell immunity is associated with increased mortality (12). Colonization of the oropharynx, perineum, and external nares by potential pathogens not normally found in community dwelling adults can also be a sign of significant immunologic and functional impairment (11).

ANTIBIOTIC-RESISTANT PATHOGENS IN LTCFS

The major antibiotic resistant bacteria of present concern to geriatricians in LTCFs are the: (i) penicillin-resistant pneumococci (PRP), (ii) aerobic gram-negative bacilli resistant to third-generation cephalosporins (the organisms that produce extended spectrum \( \beta \)-lactamases and AmpC \( \beta \)-lactamase), (iii) vancomycin-resistant enterococci (VRE), and (iv) quinolone-resistant gram-positive and gram-negative bacteria. Multi-drug resistant gram-negative bacilli and vancomycin intermediate Staphylococcus aureus (VISA) are significant potential problems for clinicians who care for patients in LTCFs affiliated with tertiary care centers, areas where antibiotic-resistant organisms are endemic. Colonization, infection, and eradication of methicillin-resistant S. aureus (MRSA) has been a persistent problem in LTCFs (13,14).

ORIGIN OF RESISTANT PATHOGENS IN LTCFS

Organisms carrying resistance determinants arise in nursing homes by one of two ways. First, multiresistant pathogens arrive when a colonized, or infected patient is transferred from hospital to LTCF. In the past this has been considered the primary route by which resistant organisms are introduced into the nursing home (15). Second, the excessive and inappropriate use of antibiotics selects for mutations in bacterial gene(s) that confer a selective advantage—antibiotic resistance. Recent analyses have shown that antibiotic resistant bacteria are becoming more prevalent in chronic care settings (16–20). Once endemic to a LTCF, the antibiotic resistance genes can be transferred from one species or genus to another (18). Moreover, the communal activities residents participate in, such as meals and physical therapy, can facilitate person-to-person transfer of resistant strains (10,11).
Penicillin-resistant Pneumococci (PRP)

In the first thirty years of its use, penicillin was exquisitely active in vitro against Streptococcus pneumoniae. By the late 1970s, isolates were discovered with decreased susceptibility to penicillin. This problem acquired world attention with the reports from South Africa by Jacobs and colleagues of serious infection with PRP (21). In the next decade, PRP was described in Hungary, Spain, United States, and Korea (22). In 1993, the prevalence of PRP in the United States approached 30% (23). A worrisome characteristic of PRP is the finding of resistance to erythromycin, tetracycline, quinolones, clindamycin, sulfia, and other antibiotics. Although many cases of PRP are reported in children who attend daycare, outbreaks of PRP have also been described in LTCFs (24).

Resistance to penicillin and other β-lactam antibiotics in the pneumococcus involves alterations in the penicillin-binding proteins (PBPs) (25). PBPs are bacterial enzymes that are responsible for cell wall synthesis. It is speculated that DNA from the PBP genes of relatively penicillin resistant streptococci that colonize the oropharynx (e.g., Streptococcus mitis) has been incorporated into the pneumococcal PBP genes, presumably by natural transformation and homologous recombination (Figure 2).

Penicillin resistance has occurred mainly in serotypes 6B, 9V, 14, 19A, 19F, and 23F (26). Because antibiotic resistance and pathogenicity are genetically separate processes, these PRP are as virulent as their penicillin susceptible counterparts. It is therefore logical to assume that one can partially protect against invasive infection by the strains which are penicillin resistant by immunizing with the pneumococcal polysaccharide vaccine. Hence, immunization of the elderly and other high-risk individuals in LTCFs assumes paramount importance. Despite substantial educational efforts, this practice has not gained universal acceptance. The documented difficulty in ascertaining correct immunization history has dampened enthusiasm for this practice. Hence, reimmunization with pneumococcal polysaccharide vaccine after 4 to 6 years remains an ideal, but elusive goal. This practice is relatively safe and has proven extremely beneficial (27). Nevertheless, there is still controversy regarding the efficacy of the pneumococcal vaccine (28).

Although retrospective studies indicate that penicillin is still adequate for moderately resistant (minimum inhibitory concentration [MIC] ≤ 1 µg/mL) pneumococcal pneumonia (29,30), concerns remain about the efficacy of penicillin in the treatment of nonmeningeal infections by strains expressing high-level resistance (30,31). A recent survey in 1997 has shown that 33.5% of pneumococcal isolates were resistant to penicillin (MIC ≥ 0.12 µg/mL) with 13.6% having high-level resistance ≥ 1.0 µg/mL (32). The concern raised by many regarding the increasing prevalence of high level penicillin (MIC ≥ 2.0 µg/mL) and cephalosporin (MIC ≥ 2.0 µg/mL) has focused attention to the use of the newer fluoroquinolone agents (grepafloxacin, trovafloxacin, sparfloxacin, and levofloxacin) in the treatment of pneumococcal pneumonia. These agents offer enhanced anti-pneumococcal activity when compared to ciprofloxacin. For a group, the newer fluoroquinolones have MICs between 0.25 µg/mL to 1.0 µg/mL (33, and references therein). Whether excessive use of these agents will impact on the colonizing flora of nursing-home residents remains to be seen.

Combination antibiotic therapy (cefotaxime or ceftriaxone with vancomycin with or without rifampin) for serious pneumococcal infections such as meningitis is still advocated (34). There is some laboratory experience using trovafloxacin in the treatment of meningitis (35). Meropenem, a carbapenem-type antibiotic, may prove eventually to be the treatment of choice (36).

Extended-spectrum β-Lactamases

β-Lactamase enzymes are the major mechanisms by which bacteria inactivate β-lactam antibiotics. Numerous cephalosporin and penicillin antibiotics have been developed to combat these enzymes. Although the third-generation cephalosporins promised to be the safest and most effective drugs against this problem, in the past 10 years, there have been described more than 50 extended-spectrum β-lactamases (ESBLs) able to inactivate many currently available penicillins and advanced-generation cephalosporins (37). Many of these β-lactam—inactivating enzymes are derived from the plasmid-borne TEM-1 and SHV-1 β-lactamases, the most common β-lactamases found in enteric bacilli. Horizontal transfer of β-lactam—resistance on plasmids in Escherichia coli and Klebsiella species has resulted in the dissemination of multiple antibiotic-resistant strains, because these mobile genetic elements often carry resistance determinants against many antibiotics (e.g., aminoglycosides) (38).

Point mutations in the plasmid determined β-lactamase genes are the major mechanism by which resistance to third-generation cephalosporin antibiotics develops in these ESBLs (38,39). These point mutations permit the enzymes to inactivate β-lactams before they reach the PBPs. The altered amino acids change the conformation of the active site such that third-generation cephalosporins can fit and be inactivated by these new en-
zymes. More recently, plasmid-encoded β-lactamases resistant to inactivation by β-lactamase inhibitors have also been described (39,40). The appearance of these newer enzymes is of significant concern. Most ESBL enzymes are highly susceptible to inactivation by β-lactamase inhibitors (clavulanate, sulbactam, or tazobactam). The clinical formulations, ampicillin-sulbactam, amoxicillin-clavulanate, piperacillin-tazobactam, and ticarcillin-clavulanate, can be used to treat infections by ESBL-producing enterics. To date, only one plasmid-determined β-lactamase resistant to inactivation by β-lactamase inhibitors and able to efficiently hydrolyze third-generation cephalosporins has been described in the clinic (TEM-50) (41). This unique β-lactamase enzyme has incorporated in its gene sequence the necessary mutations to confer resistance to β-lactamase inhibitors and to extend the substrate spectrum to include hydrolysis of third-generation cephalosporins.

Resistance to both third-generation cephalosporins and β-lactam–β-lactamase inhibitor combinations in clinical isolates has also been attributed to the production of more than one β-lactamase enzyme, hyperproduction of an ESBL, and the production of a chromosomal- or plasmid-mediated AmpC β-lactamase (39,42). The production of chromosomally mediated AmpC type β-lactamase confers β-lactam resistance to several clinically important gram-negative bacilli (Enterobacter, Citrobacter, Serratia, Pseudomonas). Elevated production of this β-lactamase can result from induction by exposure to cefoxitin, clavulanic acid, or imipenem (Figure 3). Mutations in the regulatory mechanism controlling expression of these AmpC β-lactamase enzymes are also well described (39,42). Important characteristics of these cephalosporinases are that they are able to inactivate all cephalosporins (with the possible exception of cefepime) and that they are generally resistant to inhibition by currently available β-lactamase inhibitors. The induction of β-lactamases and recycling of cell-wall materials are also related (43). Increased expression of the AmpC enzyme from Enterobacter species has been associated with the use of third-generation cephalosporins.

The clinical consequence of the induction of these chromosomal β-lactamases in Enterobacter has been examined by Chow and colleagues (44). In this prospective multicenter study, cefotaxime-resistant Enterobacter isolates were associated with a higher mortality rate. This increased mortality rate as a reflection of increased antibiotic resistance suggests somehow virulence and resistance are linked.

Recently, AmpC β-lactamases enzymes have been found on mobile, conjugative plasmids that can transfer between E. coli and Klebsiella pneumoniae species that normally do not produce AmpC-type β-lactamases in large amounts. The presence of these AmpC-type plasmid-mediated enzymes in E. coli and Klebsiella species result in resistance to penicillins, cephalosporins, β-lactam–β-lactamase inhibitor combinations, and cephemycins (45). In addition, if these AmpC-type plasmid β-lactamases are present in gram-negative bacteria that have lost an outer membrane protein, resistance even to imipenem can also be seen (46). The clinical impact of these plasmid-borne cephalosporinases that are found with outer membrane protein changes is not yet known.

Outbreaks of ESBLs have been reported in a number of nursing homes (17,19). Frequent use of third-generation cephalosporins has been blamed for the emergence of this problem (47). Successful treatment of these types of infections has required the use of imipenem and/or the combination of β-lactam–β-lactamase inhibitor (ampicillin-sulbactam, amoxicillin-clavulanate, piperacillin-tazobactam, ticarcillin-clavulanate). Experimental animal models are being actively studied to evaluate the most effective therapy (48,49). To date, of the β-lactam–type agents, the carbapenems (meropenem and imipenem) offer the most promise against ESBL and AmpC-type-producing enterics (38). The newer fluoroquinolones also are effective when the strain is susceptible in vitro (33).

**Vancomycin-Resistant Enterococci (VRE)**

Methicillin-resistant species of S. aureus (MRSA) and coagulate-negative staphylococci and enterococci have become the nosocomial gram-positive pathogens of the 1990s (50). To combat these infections, clinicians in the United States have depended upon the glycopeptide antibiotic, vancomycin. Vancomycin inhibits peptidoglycan cell-wall synthesis by hydrogen bonding with cell-wall precursors that terminate in D-alal-D-al, preventing formation of important cross bridges (51). Although antimicrobial resistance to β-lactams and aminoglycosides was widely reported in staphylococci and enterococci, resistance to vancomycin was not discovered in enterococci until 1986, almost 30 years after the release of the drug (51–54). Vancomycin resistance is dependent upon the activation of the AmpR gene, a gene present in all genera of enterics. This is a complex process that is precisely regulated. AmpC is under the control of AmpR, a transcriptional regulator. While β-lactam antibiotics accelerate cell wall breakdown, these products (cell wall peptides) are transported back into the bacterial cell by a permease (AmpG product). Normally, AmpD product (amidase) cleaves the tripeptide from N-acetylglucosamine or N-acetyl muramic acid residue (Mur-tripeptide). When the recycling process is saturated, the cell wall peptides are free to activate the AmpR transcriptional regulator. This increased AmpC transcription results in production of chromosomal β-lactamase (adapted from references 39 and 43).
tance is usually described in *Enterococcus faecium*. Fortunately, this organism is not as virulent as *E. faecalis* or *S. aureus.*

Four major phenotypes of VREs are described (Table 1) (54). Van A–resistant enterococci are characterized by high level resistance (minimum inhibitory concentrations, MICs > 64 µg/mL). Van B strains show variable resistance with MICs from 4–1000 µg/mL, whereas Van C strains are moderately resistant to vancomycin (MICs between 8 and 16 µg/mL). Both Van A and Van B have inducible resistance to vancomycin. This means that in the presence of vancomycin, the genes responsible for vancomycin resistance are expressed. Both Van A and Van B phenotypes are transferable; hence they can be disseminated easily on plasmids and transposons. Van D phenotype has also been reported. Its clinical significance is still not fully appreciated. The Van C phenotype is only found in *Enterococcus gallinarum* and *Enterococcus casseliflavus* and is not transferable.

The Van A phenotype is mediated by a complex 11-kb transposon (*Tn* 1546) that insures that the resistant organism will have the ability to synthesize cell wall in the presence of glycopeptide (51,54). The origin of *Tn* 1546 is still unknown. This transposon encodes nine genes; seven of which are responsible for glycopeptide resistance (Figure 4a). Two genes are responsible for sensing the presence of vancomycin in the bacterial environment (van R and van S). Two genes are responsible for the synthesis of d-alanine–d-lactate (van H and van A). d-alanine–d-lactate is attached to the growing pentapeptide essential for cross-linking of bacterial cell wall. van X is a dipeptidase that cleaves d-alanine–d-alanine, thereby decreasing the cellular pool of normal dipeptide precursors. With d-alanine–d-lactate incorporated in the cell wall, vancomycin binds with a significantly decreased affinity. Two subsequent genes on the transposon contribute in minor ways to glycopeptide resistance (van Y and van Z). Only van H, van A, and van X are required for expression of resistance.

Resistance conferred by the *van B* phenotype is also encoded by a large chromosomal segment. The *van B* operon is very similar in organization to *van A* (see Figure 4b) and can be transferred (51,54). It appears that in certain geographic locations either the *van A* or *van B* phenotype predominate. The significance of this finding is still not clear.

Identified risk factors for the emergence of VRE are: (i) the use of oral vancomycin and metronidazole to treat antibiotic induced colitis, (ii) excessive cephalosporin use, (iii) previous antibiotic use, and (iv) increased disease burden (55).

In a hospital-wide outbreak of VRE, up to 45 different strains were identified by pulse-field gel electrophoresis (56). This study suggests that there may be facile transfer of strains between institutions. Wells and colleagues reported that 209 patients were colonized, 75 were actively infected, and 31 were bacteremic (56). The authors of this study tried to abort the “outbreak” by restricting the use of intravenous and oral vancomycin. Despite these measures, there was no change in VRE prevalence once VRE became endemic. In another hospital-wide outbreak of VRE between 1990–1992, 64% of patients 60 years old and older became colonized or infected with VRE (57). These patients were hospitalized for a mean of 60 days, had been transferred from hospital ward to intensive care unit, and were considered “severely ill.” From these studies it appears that VRE can spread by direct patient-to-patient contact, indirectly via transient carriage on hands of personnel, contaminated environmental surfaces, and patient care equipment (57).

Why has VRE become a serious problem for geriatricians? Urinary tract infections (UTIs) and infected pressure ulcers are among the most common infections found in LTCFs. Many of these patients with pressure ulcers and UTIs receive multiple courses of antibiotics and are frequently hospitalized. Their translocation from tertiary care institutions to LTCFs and back can easily spread flora from the hospital to the nursing home (see Figure 1). Given that enterococci are one of the major causes of urine, wound, and blood stream infection in debilitated elderly persons, it is easy to understand why geriatricians are facing the problem of VRE infection and colonization in the nursing home.

Colonization by VRE presents a difficult problem for LTCF medical directors and infection control personnel. Immunocompromised and elderly patients are often transferred from tertiary care hospitals to nursing homes colonized with VRE in their stool. This is the primary mode of introduction of VRE into LTCFs (58,59). It is not known whether VRE patients require isolation in private rooms until this organism is “cleared,” usually two to three negative stool cultures 1 week apart (60,61). The Society Healthcare Epidemiology of America (SHEA) recommends modified contact isolation (gloves, gown, and private room if available) (62). It has been shown that LTCF patients have a prolonged carriage rate of VRE (58). More importantly, there are few specific prospective controlled studies that have proven guidelines in place that address the management of VRE in the nursing home. The recommendations for hospitals have proven to be impractical in nursing homes (Table 2). The financial, social, and psychological burdens associated with implementation of these guidelines are significant. Maintaining patient
Table 2. Recommendations for Control of VRE in LTCFs

1. Private room if possible. Barrier precautions. Roommates of patients with VRE should not be immunocompromised, have indwelling lines, open wounds, or be incontinent of stool.
2. Contain bodily secretions, but do not restrict activity. Limit patient transport.
3. Hand washing with chlorhexidine- or alcohol-based handwashing soap. Gloves when direct contact with body sites, secretions, and environment in room. Disposable gowns when contact with patient secretions or environmental surfaces.
4. Dedicated commode and patient care equipment (thermometers).
5. Education of staff about basic infection control policies regarding VRE.
6. Surveillance cultures in the event of an outbreak.
7. Restrict vancomycin use. Do not use vancomycin as first line therapy for Clostridium difficile colitis.

Adapted from references 61 and 62.

Drug specific and multidrug efflux pumps have emerged as a major problem in antibiotic resistance (75–77). Pathogenic bacteria have been described that possess increasing degrees of resistance to multiple antibiotics as well as topical antimicrobial compounds. The multiple antibiotic resistant locus (mar) conferring resistance to tetracycline, chloramphenicol, quinolones, and other bacterial efflux pumps exist in gram-negative bacteria and Mycoplasma genitalium (76,78). These drug-efflux pumps occur as four major families: the ATP-binding cassette superfamily, major facilitator superfamily, small multidrug resistance family, and the resistance-modulation cell division family (77). These transport proteins are nondiscriminatory and efficiently eliminate antibiotics before they reach their targets. Hence, the concern is that mar expression will diminish the efficacy of the quinolone antibiotics.

The target of quinolone action in gram-negative bacteria is the A subunit of DNA gyrase (79,80). DNA gyrase is a bacterial type II topoisomerase. It is made up of a tetramer of two parts, A2 and B2. This protein converts relaxed DNA into supercoiled DNA. The A subunit is responsible for breakage and rescaling of chromosomal DNA. The B subunit is responsible for energy transduction from ATP hydrolysis. Quinolones interrupt the rescaling of double stranded DNA by forming a quinolone-gyrase-DNA ternary complex. This inhibition is associated with rapid bacterial killing. Additional antibacterial activity is expressed through inhibition of topoisomerase IV. This enzyme is responsible for the separation of daughter DNA strands during bacterial cell division in gram-positive bacteria (80). Topoisomerase IV is likely to be the primary target for quinolone action in gram-positive bacteria. In addition to DNA gyrase and topoisomerase IV, quinolones are bactericidal by other mechanisms. Three mechanisms, A, B, and C have been proposed. Mechanism A requires RNA and protein synthesis as well as cell division for bactericidal action. Mechanism B is the
ability to kill nondividing cells without concomitant protein or RNA synthesis. Mechanism C is the bactericidal activity that occurs in the absence of multiplication, but in the presence of protein and RNA synthesis. Utilization of these mechanisms is organism specific (80).

Resistance to quinolone antibiotics is generally mediated by alterations in the chromosomal DNA of bacteria. In the main, most bacteria accumulate several mutations that affect both DNA gyrase and permeability (81). Mutations in the regulatory genes that govern permeability porins or efflux pumps are commonly found in quinolone resistant bacteria (see above). Point mutations in residues 67 to 106 of the A subunit of DNA gyrase, the quinolone resistance determining region (QRDR), result in resistance. Mutations in this region are associated with increased resistance to all quinolones (80).

Resistance to quinolone agents can emerge rapidly during therapy. Ciprofloxacin resistant *Pseudomonas aeruginosa*, *S. aureus*, *Staphylococcus epidermis* have been well described (82). Once these organisms develop resistance to quinolones, the therapeutic options are severely limited. Some of the newer generation quinolones (clinafloxacins) offer enhanced activity against ciprofloxacin-resistant organisms (83). The clinical efficacy and safety of the newer agents remains to be established.

**Infection Control and Antibiotic Use**

Recommendations regarding infection control measures to prevent the spread of multiresistant pathogens have been previously summarized (84). In general, methods proposed by the Society for Healthcare Epidemiology of America (SHEA) that are intended to help control antibiotic resistance in LTCFs and cross-infection include antibiotic restriction practices: surveillance, nontreatment of asymptomatic bacteruria, minimizing topical antibiotics, hand washing, and barrier precautions for wound care. We propose that for LTCFs, the following additional items be specifically stressed: (i) education, (ii) surveillance, (iii) antibiotic control, and (iv) immunization (Table 3).

Education concerning the enormity of the problem needs to be the first step. Alerting staff to the epidemiology of current outbreaks will help with enforcing infection control guidelines in the community. Regular instruction of the nursing staffs of the local resistance problems is imperative. We have found that nursing home personnel are extremely eager to learn about local trends in antimicrobial resistance. Education is also needed to determine if infection is really present.

As a guide we encourage the use of the definitions of infection in LTCFs developed by McGeer and colleagues (85). These are extremely useful in diagnosing infections in nursing homes, particularly when the decision to obtain laboratory tests or initiate empiric therapy must be performed by phone. Nursing personnel instructed in the use of these guidelines can assist physicians on determining if antibiotics are really necessary.

Infection control surveillance also helps to identify the presence and spread of resistance (86). Identifying patients coming from hospitals where PRP, VRE, and ESBLs are endemic should be a nursing home physician and Infection Control priority. Identifying nursing home residents who have been treated with multiple courses of antibiotics in hospital will alert health care workers to this potential problem. Although not proven in prospective studies, screening high-risk patients for colonization by antibiotic-resistant bacteria, particularly ESBLs, may help contain a potential outbreak.

Screening for VRE should also be a consideration in high risk LTCFs. We have observed that once these organisms are identified, practitioners are more conscious of antibiotic use in these facilities. Careful analysis of the demographics of patients colonized by antibiotic-resistant organisms can help uncover factors that could be modified to prevent this dilemma. This practice will need to be scrutinized before it is implemented.

Clinicians should be "ecologically responsible" in their prescribing of antibiotics. The unnecessary use of broad-spectrum antibiotics to treat susceptible organisms should be strongly discouraged. The control of antibiotic use in this population is critical. There should be clear guidelines in place for using vancomycin in the nursing home (MRSA, β-lactam allergy, metronidazole failures in treatment of *Clostridium difficile* colitis, or surgical prophylaxis in β-lactam allergic patients). Limits to the length of antibiotic administration should also be enforced. Guidelines should also be in place for the use of other parenteral antibiotics. Using third-generation cephalosporins in LTCFs only when they are absolutely necessary may limit the emergence of multiresistant gram-negative bacilli and VRE. Restricting antibiotic formulations for LTCFs has been suggested as a potential means to reduce colonization. We have also found it exceptionally rewarding to review the number, frequency, and type of antibiotics prescribed in our facility. Simply alerting physicians to the number of quinolones or advanced-generation cephalosporins unnecessarily used can stem overprescribing.

The choice of a specific antibiotic should include a thoughtful consideration of the most likely pathogens infecting that site. In each case, careful patient assessment and investigation should precede therapy (see above). When broad-spectrum agents are used, they should be prescribed only until culture data are known. Strict antibiotic monitoring should be part of infection control. Antibiotic order forms, automatic stop orders, and treatment algorithms are not yet a common practice in the nursing home and should be evaluated and developed.

Immunization of the elderly with pneumococcal polysaccharide vaccine should also be a clinical and administrative priority. The vaccine should be strongly encouraged in everyone older than 65 years admitted to a LTCF. It can be given at the time of influenza vaccine and should be part of a nursing home admission medical care regimen. Careful review of patient records should be undertaken to insure immunization when the patient's or family's recollection is not reliable. Once administered, the information can be entered in a patient log book which serves as a reminder for the next immunization. Pneumococcal polysaccharide vaccination is extremely safe and can and should be repeated every 6 years. It has been found that levels of serum vitamin B12 must be in the normal range for adequate response to the pneumococcal polysaccharide vaccine (87).

**Table 3. Infection Control Measures to Prevent Spread of Multiresistant Pathogens**

<table>
<thead>
<tr>
<th>Education</th>
<th>Antibiotic control policies</th>
<th>Immunization</th>
<th>Strict handwashing</th>
<th>Ecological responsibility</th>
<th>Surveillance</th>
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[80-87]
CONCLUSION

Antibiotic-resistant bacteria are becoming an increasingly important problem in LTCFs. The goal of each LTCF is to provide programs that will deliver quality care. Many of the issues discussed above address this. Once the frequency of antimicrobial resistance is known, our challenge is to reduce this threat. The cooperation of nursing home administrators, infection control nurses, medical directors, geriatricians, microbiologists, and patients need to be enlisted to help stem this problem. Interventional strategies are needed to help reduce this emerging problem.

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Address correspondence to Robert A. Bonomo, MD, Geriatric Care Center, 12200 Fairhill Road, Cleveland, Ohio 44120. E-mail: rab14@cwru.edu

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