Throughout the history of mankind, infectious diseases have remained a major cause of death and disability. Although industrialized nations, such as the United States, have experienced significant reductions in infection-related mortality and morbidity since the beginning of the “antibiotic era,” death and complications from infectious diseases remain a serious problem for older persons. Pneumonia is the major infection-related cause of death in older persons, and urinary tract infection is the most common bacterial infection seen in geriatric patients. Other serious and common infections in older people include intra-abdominal sepsis, bacterial meningitis, infective endocarditis, infected pressure ulcers, septic arthritis, tuberculosis, and herpes zoster. As a consequence, frequent prescribing of antibiotics for older patients is common practice. The large volume of antibiotics prescribed has contributed to the emergence of highly resistant pathogens among geriatric patients, including methicillin-resistant *Staphylococcus aureus*, penicillin-resistant *Streptococcus pneumoniae*, vancomycin-resistant enterococci, and multiple-drug-resistant gram-negative bacilli. Unless preventive strategies coupled with newer drug development are established soon, eventually clinicians will be encountering infections caused by highly resistant pathogens for which no effective antibiotics will be available. Clinicians could then be experiencing the same frustrations of not being able to treat infections effectively as were seen in the “pre-antibiotic era.”

**Key words:** aging; antimicrobial resistance; long-term care facility

**INFECTIONS AS A MAJOR CAUSE OF MORBIDITY AND MORTALITY IN OLDER PEOPLE**

Throughout the history of mankind, infectious diseases have remained a major cause of death and disablement. Today, infectious diseases account for one-third of all deaths in the world; the World Health Organization estimates that nearly 50,000 people die each day throughout the world from infectious diseases. However, in industrialized nations, such as the United States, infectious disease-related deaths have been substantially reduced since the advent of the “antibiotic era,” which began in the early 1950s. In 1900, at a time when infections were the leading cause of death in the United States, the average life expectancy at birth was approximately 47 (46 for men and 48 for women). Childhood deaths secondary to infections were very high. The major causes of death were smallpox, cholera, diphtheria, typhoid fever, plague, tuberculosis, typhus, scarlet fever, rheumatic fever, measles, mumps, pertussis, poliomyelitis, and syphilis. Many of these diseases also caused complications leading to severe disabilities (e.g., paralysis from polio, valvular heart disease from rheumatic fever, and neurological deficits and heart disease from syphilis).

The older population (aged 65 and older) was only 4% of the entire population in the United States in the early 1900s. Modern discoveries in medicine based on the germ theory provided the advances to reduce the morbidity and mortality from infectious diseases, especially in children. These advances included antibiotics, vaccination, antisepsis, public health measures, and public sanitation. As a result, average life expectancy at birth has dramatically increased over the past 50 years to approximately 75 in the United States, with older persons accounting for 13% of the total U.S. population. Moreover, the top 10 causes of death are no longer infections; cardiovascular diseases, cancer, and stroke are now the top three causes of death in adults, including older people, in the United States. Nevertheless, with aging, infectious diseases have re-emerged as important causes of death, disability, and functional decline. Pneumonia and influenza are the fourth-leading causes of death in older adults, and bacteremia is the ninth leading cause of death.

**SPECIAL PROBLEMS ASSOCIATED WITH INFECTIONS IN OLDER PEOPLE**

Not only are older persons at greater risk of dying from infections or suffering serious complications, they also have a higher susceptibility to select types of infections. Those infections associated with high mortality, morbid-
ity, and susceptibility include pneumonia, urinary tract infection (UTI), skin and soft tissue infections, bacterial meningitis, infective endocarditis, septic arthritis, tuberculosis, intra-abdominal infections (primarily cholecystitis, diverticulitis, perforated/ruptured appendicitis, and abscesses), and herpes zoster. It is well recognized that immune function, particularly cell-mediated immunity, decreases with aging. In addition, older people suffer more chronic diseases, some of which (e.g., cancers, connective tissue diseases) affect the integrity of host resistance. Thus, it is most likely the combined effects of age-related decline in host resistance and the presence of underlying diseases and disabilities that contribute to the greater vulnerability of older persons to infections and their complications.

With the rising numbers of older people, including those aged 80 and older, the incidence and prevalence of chronic diseases, physical disabilities, and cognitive impairment increase substantially. The demand and need for long-term care concomitantly rise. Presently, more than 1.5 million people live in nearly 17,000 nursing facilities in the United States. The skilled nursing facility (SNF) residents are generally very old (mean age 80–85) and frail, often cognitively impaired, physically dependent, and highly vulnerable to infections. Moreover, the setting of an SNF is favorable for regular exposure to microorganisms because of frequent contacts with other residents and staff in a closed environment; limited ventilation, filtration, and removal of recirculated air (which could contain pathogens); and free movement of other residents who may be harboring infections. Thus, the finding of fever and infection in residents of long-term care facilities (LTCFs) such as SNFs is a common occurrence. Infections are also the most common reason an SNF resident is transferred to an acute care facility. The most common infections encountered in residents of SNFs are pneumonia, UTI, and skin/soft tissue infections, which together account for approximately 75% of all nursing facility–acquired infections.

The difficulties in diagnosing infections in LTCFs are enormous because of atypical clinical manifestations of diseases in older people (to be discussed below), lack of an adequate number of highly-trained medical personnel in such facilities (predominantly nursing assistants) to make an appropriate assessment of the resident, limited contact by a primary care physician with the resident, minimal to no availability of on-site laboratory and radiology tests, and uncertainty of the primary clinician with respect to initiating diagnostic interventions in the absence of a clear-cut advance directive. Consequently, empirical antimicrobial therapy without microbiological data is common practice in the long-term care setting; the vast majority of prescribed antibiotics are ordered without direct examination of the resident by the primary care provider.

The clinical diagnosis of infection in older adults, especially very old and frail people, can often be challenging. Fever is the cardinal manifestation of infection, but, in approximately 20% to 30% of older persons with serious infections, fever is absent or blunted in comparison with younger adults. Suboptimal temperature response to an infection has been described in older patients with pneumonia, infective endocarditis, meningitis, tuberculosis, and bacteremia. Moreover, infection in geriatric patients may not elicit typical symptoms of a specific type of infection (e.g., cough and sputum with pneumonia, dysuria with UTI) and may manifest as cognitive impairment, decline in functional independence, falls, urinary incontinence, anorexia, weight loss, and weakness. These atypical presentations of infections in older patients cause delays in diagnosis and treatment and contribute to increased morbidity and mortality. Alternatively, experienced and knowledgeable clinicians may assume that older persons with such nonspecific symptoms may be harboring a serious infection and empirically initiate antimicrobial therapy without objective evidence for an infectious disease, which increases the prescribing of antibiotics in this population.

The causative pathogens of common infections in older people tend to be more diverse than in younger patients with the same disease. As examples, community-acquired pneumonia in younger adults is predominantly caused by Streptococcus pneumoniae, Chlamydia pneumoniae, and Mycoplasma pneumoniae, whereas older patients with pneumonia in the community and long-term care setting may have gram-negative bacilli as one of the causes of their lung infection. UTI in adults tends to be a disease of women and is caused by Escherichia coli in nearly 90% of uncomplicated infections. In contrast, E. coli accounts for approximately 60% to 70% of cases of UTI in older adults, with other gram-negative bacilli and enterococci often being isolated. Under these circumstances, antimicrobial therapy will often consist of broad-spectrum drugs with activity against both gram-positive and gram-negative bacteria. Broad-spectrum antibiotics will have a greater effect on indigenous microflora and promote colonization and growth of antimicrobial-resistant organisms.

FACTORS PROMOTING DEVELOPMENT OF ANTIMICROBIAL-RESISTANT PATHOGENS IN OLDER PATIENTS

The emergence of infections caused by antibiotic-resistant pathogens is a growing problem and has now become a major health issue in LTCFs. This is a major challenge to clinicians, given the problems encountered with attempting to diagnose and treat infections in LTCFs (as described earlier). Furthermore, with limited resources for implementing infection-control measures and procedures, such antibiotic-resistant organisms will be extremely difficult to control and contain.

Resistant organisms are found in healthcare facilities such as LTCFs probably because of transfer to the LTCF of patients who are colonized or infected with such pathogens at other institutions. Excessive and inappropriate use of antibiotics, especially broad-spectrum antimicrobial agents, select for the emergence of resistant pathogens. Prescribing antibiotics for unproven bacterial infections (e.g., upper respiratory viral infections) or “prophylactic” antibiotics for residents/patients with chronic urinary catheters are examples of inappropriate administration of these agents. Prolonged use of these drugs beyond the standard recommended duration for treating common infections (e.g., 7–10 days for UTI) increases the risk of selecting for resistant pathogens with each additional day of unnecessary treatment. Factors that increase the probability of microbial colonization (and subsequent infection)
are also common in residents of LTCFs (malnutrition, immunosuppressed state, urinary catheters, feeding tubes, pressure ulcers, and chronic immobility). Finally, inadequate adherence to infection-control measures such as frequent hand washing contributes to the spread of all types of microorganisms, including resistant pathogens, throughout the facility and to its employees and residents.

IMPORTANT RESISTANT PATHOGENS

The most frequently isolated resistant pathogens in the older population have been penicillin-resistant Streptococcus pneumoniae (PRSP), methicillin-resistant Staphylococcus aureus (MRSA), vancomycin-resistant enterococci (VRE), and multiple-drug-resistant gram-negative bacilli (MDRGNB). In a recent study of a skilled-care facility, 43% of 117 study participants were colonized with one or more resistant pathogens, which included MRSA (24% of participants), resistant gram-negative bacilli (33%), and VRE (3.5%).

Penicillin-resistant Streptococcus pneumoniae prevalence is the highest in the very young (under 5) and the very old (65 and older). In a recent surveillance study conducted in eight states by the Centers for Disease Control and Prevention, the prevalence of PRSP was 32.2% in children under 5 and 24.2% in adults aged 65 and older. More importantly, during 1995 to 1998, the proportion of PRSP increased from 21% to 25%, and PRSP resists to three or more classes of antibiotics increased from 9% to 14%.

Multidrug-resistant pneumococci have been reported as causes of serious infections in older residents of LTCFs. In one LTCF in Oklahoma, 23% of 74 residents were colonized with a pneumococcus resistant to penicillin, cefotaxime, cefaclor, erythromycin, trimethoprim-sulfamethoxazole, cindamycin, tetracycline, and chloramphenicol. Twelve residents of the same facility were hospitalized for pneumonia in 1996; three of the hospitalized residents with bacteremia died. In such cases, quinolones (e.g., levofloxacin, moxifloxacin) and vancomycin should be considered as potentially effective therapy.

MRSA was one of the earlier resistant pathogens that was described as a major clinical problem in LTCFs. They have been reported in a variety of LTCF settings in the United States, including community, Veterans Affairs, large, small, adult, pediatric, rural, and urban. Unfortunately, resistance to methicillin (nafcillin, oxacillin) is not the only issue; MRSA is generally resistant to all cephalosporins and quinolones as well. Vancomycin has become the mainstay of therapy for MRSA, but recent studies indicate the frightening evidence of emergence of Staphylococcus aureus with resistance to vancomycin (vancomycin-resistant intermediate Staphylococcus aureus (VISA)). Presently, it appears that the newer agents, quinupristin/dalfopristin (a streptogramin) and linezolid, may be active against MRSA and VISA.

VRE has also become a major concern for clinicians caring for patients in acute hospitals and LTCFs. Studies conducted primarily in older patients indicate that treatment with an anti-anaerobic antibiotic regimen promotes stool colonization with VRE. Agents lacking anti-anaerobic activity, such as dicloxacillin, levofloxacin, ciprofloxacin, and trimethoprim-sulfamethoxazole, had the least effect on increased VRE colonization in the stool. One study in a LTCF indicated that adherence to infection control practices by resident care staff of the LTCF was associated with absence of VRE colonization among the residents. Presently, the treatment of serious VRE infections is limited primarily to quinupristin/dalfopristin and linezolid. However, these drugs may not be available or practical for treating LTCF residents with VRE infections. In LTCF residents with uncomplicated UTI caused by VRE, nitrofurantoin and doxycycline maybe effective depending on the sensitivity of the organism to these agents.

A variety of gram-negative bacilli resistant to many antibiotics have been reported, especially in older patients being treated for UTI in LTCFs. Some common mechanisms of resistance include extended-spectrum beta-lactamases, which render many antibiotics inactive, including ceftazidime, inhibitor-resistant beta-lactamases (beta-lactamases produced by bacteria that are resistant to beta-lactamase inhibitors), and enzymatic inactivation of aminoglycosides (acetylation, phosphorylation, nucleotidylation). Such high prevalences of MDRGNB have limited the use of many beta-lactam agents and other antibiotics in the treatment of common infections such as UTI. In many instances, clinicians have opted to begin treatment with quinolones for serious UTI caused by gram-negative bacilli.

These examples of drug-resistant pathogens suggest a continuing growth in the numbers and types of microbial organisms becoming increasingly resistant to the effects of antibiotics. More importantly, the organisms are often resistant to multiple drugs and, in some instances, resistant to virtually every available antibiotic. Indeed, with essentially no effective antimicrobial agents against some of these pathogens, we would be returning to the “pre-antibiotic era.” Thus, strategies for the prevention of developing drug-resistant pathogens; limiting transmission of these resistant pathogens to highly vulnerable persons, such as older, frail, disabled, and immunocompromised people; careful and limited usage of drugs effective against such resistant pathogens (e.g., vancomycin, quinolones, streptogramins, linezolid); and development of newer and more effective agents against these organisms will be critical if we are to limit or eliminate morbidity and mortality from serious infections caused by resistant organisms.

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