

Infectious Diseases in Older Adults of Long-Term Care Facilities: Update on Approach to Diagnosis and Management

Robin L. P. Jump, MD, PhD,^{a,b,c} Christopher J. Crnich, MD, PhD,^{d,e,f} Lona Mody, MD, MSc,^{g,h} Suzanne F. Bradley, MD,^{i,j} Lindsay E. Nicolle, MD,^{k,l} and Thomas T. Yoshikawa, MD^{m,n,o}

The diagnosis, treatment, and prevention of infectious diseases in older adults in long-term care facilities (LTCFs), particularly nursing facilities, remains a challenge for all health providers who care for this population. This review provides updated information on the currently most important challenges of infectious diseases in LTCFs. With the increasing prescribing of antibiotics in older adults, particularly in LTCFs, the topic of antibiotic stewardship is presented in this review. Following this discussion, salient points on clinical relevance, clinical presentation, diagnostic approach, therapy, and prevention are discussed for skin and soft tissue infections, infectious diarrhea (*Clostridium difficile* and *norovirus* infections), bacterial pneumonia, and urinary tract infection, as well as some of the newer approaches to preventive interventions in the LTCF setting. *J Am Geriatr Soc* 66:789–803, 2018.

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From the ^aGeriatric Research, Education and Clinical Center; ^bSpecialty Care Center of Innovation, Louis Stokes Cleveland Department of Veterans Affairs Medical Center; ^cDivision of Infectious Diseases and HIV Medicine, Department of Medicine and Department of Population and Quantitative Health Sciences, Case Western Reserve University, Cleveland, Ohio; ^dSchool of Medicine and Public Health, University of Wisconsin; ^eWilliam S. Middleton Veterans Affairs Medical Center; ^fUniversity of Wisconsin Hospital and Clinics, Madison, Wisconsin; ^gGeriatric Research, Education and Clinical Center, Department of Veterans Affairs Ann Arbor Healthcare System; ^hDivision of Geriatric and Palliative Medicine, School of Medicine, University of Michigan; ⁱDivision of Infectious Diseases, Department of Veterans Affairs Ann Arbor Healthcare System; ^jSchool of Medicine, University of Michigan, Ann Arbor, Michigan; ^kDepartment of Internal Medicine; ^lMedical Microbiology, Health Sciences Centre, University of Manitoba, Winnipeg, Manitoba, Canada; ^mGeriatric and Extended Care Service, Geriatric Research, Education and Clinical Center; ⁿDepartment of Medicine, Department of Veterans Affairs Greater Los Angeles Healthcare System; and ^oDepartment of Medicine, David Geffen School of Medicine, University of California, Los Angeles, California.

Address correspondence to Thomas T. Yoshikawa, VA Greater Los Angeles Healthcare System, 11300 Wilshire Blvd, Building 158/GRECC (W-11G), Los Angeles, CA 90073. E-mail: toyoshikawa@cdrewu.edu

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Many of the clinical challenges and differences in epidemiology of, pathogenesis of, diagnostic approach to, treatment of, and prevention of infections in older adult, have been recently described,¹ but there is a subset of older adults who add another dimension of complexity, difficulties, and challenges to managing infections—those who reside in long-term care facilities (LTCFs), or more specifically, nursing homes, which are now more commonly referred to as nursing facilities. The 15,600 LTCFs in the United States provide daily medical and residential care for 1.4 million persons. Each year, 3.2 million persons reside in one of these facilities for some period of time.^{2,3} Although LTCFs may also refer to rehabilitation centers, assisted living facilities, and other forms of residential care, in this article, the term LTCF refers to nursing facilities. We will focus on providing an update on the approach to the most important infectious diseases, as well as the challenges clinicians encounter in diagnosing, treating, and preventing infections in older LTCF residents. A brief summary on managing infection outbreaks in LTCFs can be found in a recent publication¹ and thus will not be discussed in this review.

Individuals of a wide range of ages with a wide range of diseases and disorders are hospitalized needing acute (immediate) diagnosis and management and generally have a short stay of less than a week. In contrast, LTCF residents are almost exclusively aged 65 and older (average age about 80–85) and have multiple chronic diseases and disorders (with occasional acute exacerbations), physical disability, cognitive impairment, functional incapacity, and lengths of stay that are most often longer than 30 to 60 days, with many remaining in the LTCF for the rest of their lives. Consequently, the goals of care, approach, resources, environment, and staffing in LTCFs may be very different from those of an acute care facility. Standard hospital care in a ward setting generally requires a registered nurse-to-patient ratio of 1:5, but the registered nurse to patient/resident ratio is 1:25 in LTCFs. Acute care hospitals have physicians making daily rounds and onsite availability of laboratory and imaging studies, whereas LTCFs usually have no immediate access to such tests, and

physicians generally see each resident once a month (more often if the resident is not clinically well). In addition, infection is a major health concern in LTCF residents, and diagnosing an infection may be challenging in this population, given the atypical presentation commonly seen in older adults, which sometimes does not include fever.¹ With these major differences between a patient in an acute hospital setting and a LTCF resident, the approach to clinical and laboratory diagnosis, treatment, and prevention of serious infections in this setting is challenging.

ANTIBIOTIC STEWARDSHIP

Approximately 75% of residents who stay in a LTCF for 6 months or longer will receive at least one course of antibiotics.^{4–6} More than half of the antibiotic courses initiated in LTCFs are unnecessary, and even when the antibiotics prescribed are necessary, they are often excessively broad spectrum or administered for longer than necessary for treatment of the underlying infection. The overuse and misuse of antibiotics in LTCFs are major causes of adverse drug events and future infections such as those caused by *Clostridium difficile* and antibiotic-resistant bacteria. Once a resident acquires *C. difficile* or an antibiotic-resistant bacterium, it may then be spread to other residents and to patients in hospitals when resident illness requires a higher level of care.

Improving the quality of antibiotic prescribing in healthcare settings increasingly relies on development and expansion of antibiotic stewardship programs (ASPs), which are characterized by coordinated efforts to monitor patterns of antibiotic use and antibiotic-related outcomes, and to oversee identification and implementation of strategies to improve these measures.^{6,7} Implementation of ASPs in hospitals has been associated with significant reductions in use of targeted antibiotics, reductions in *C. difficile* and certain types of multidrug-resistant organisms (MDROs), and significant cost savings.⁸ Policy stakeholders have recommended expansion of ASPs into other healthcare settings,⁹ but their uptake in LTCFs remains limited.^{6,7} Nevertheless, this situation is poised to change rapidly with the recent release of regulations that require LTCFs to have ASPs in place by November 2017.¹⁰

Barriers to Antibiotic Stewardship

Antibiotic stewardship programs in hospitals and LTCFs share common goals, although their structure and process are different.⁷ ASPs in hospitals are typically organized around a team of individuals with expertise in infectious diseases, pharmacodynamics or pharmacokinetics, and informatics.⁹ Facility infection preventionists or directors of nursing most commonly direct stewardship programs in LTCFs. Medical directors and pharmacists are actively engaged in ASPs in fewer than half of LTCFs, and individuals with formal infectious disease training are involved in fewer than 15% of facilities.⁷ Most hospitals employ mature, sophisticated electronic record systems that permit efficient tracking and reporting of antibiotic use and antibiotic-related outcomes, but adoption of electronic health record systems has been slow in LTCFs, and most still rely on cumbersome manual methods of tracking and

reporting process and outcome measures. The most effective antibiotic improvement methods in hospitals, including prior authorization and post-prescriptive review and feedback, can be quite effort intensive.⁹ Although similar strategies have proven effective in LTCFs,¹¹ most facilities lack the resources and expertise to sustain these types of efforts. Consequently, efforts to improve the quality of antibiotic prescribing in LTCFs have primarily relied upon education, dissemination of guidelines, and introduction of decision-support tools.⁶

Implementing an ASP

Although implementing an ASP in a LTCF can be a daunting task, tools that the Centers for Disease Control and Prevention (CDC) have developed^{12,13} can help facilities structure their initial planning and implementation efforts (Table 1). Support from facility leadership, assembly of a team, and identification of a leader with overall accountability for the program are critical structural resources that LTCFs should have in place when first embarking on development of an ASP. Although it is unlikely that most LTCFs will have access to an ASP leader with specific antibiotic stewardship expertise, individuals with an understanding of facility clinical operations and data systems and experience with quality improvement activities should be accessible in most facilities. In most LTCFs, the infection preventionist or director of nursing is in the best position to assume this leadership role, although other individuals, such as the LTCF pharmacist, may also be appropriate. The medical director and director of nursing, even if they are not the designated ASP leaders, can assume a critical role in expanding the facility ASP by publicly affirming its importance and supporting improvement efforts.

Tracking and reporting antibiotic use and antibiotic-related outcomes (e.g., *C. difficile* and MDROs) is a core activity that the CDC recommends be performed¹² and will be required under new regulations.¹⁰ LTCFs perform infection surveillance and track residents who experience a change in condition, particularly those receiving antibiotics, as a routine practice in LTCFs.¹⁴ Adapting these existing processes to track antibiotic use and related outcomes should, therefore, be feasible in most LTCFs. At a minimum, facilities should periodically assess antibiotic use in the facility cross-sectionally (e.g., number of residents taking antibiotics during a given day, week, or month). To monitor the effects of improvement interventions and detect aberrant prescribing patterns, LTCFs should ideally track antibiotic starts or antibiotic days of therapy prospectively. Stratifying tracking measures according to indication (e.g., urinary tract infection (UTI)) and antibiotic class (e.g., fluoroquinolones) can help facilities better ascertain conditions in need of focused attention and follow the effects of condition-specific interventions. Supplementing usage measures with assessments of appropriateness (e.g., proportion of monthly antibiotic courses meeting explicit criteria or proportion of monthly antibiotic courses exceeding 7 days¹⁵) can provide additional insights into opportunities for improvement.

Once an ASP team and a system for monitoring antibiotic use are in place, LTCFs should focus on

Table 1. Core Elements of Antibiotic Stewardship in Nursing Facilities¹²

Component	Description	Comments
Leadership commitment	Dedicate support and commitment to safe and appropriate antibiotic use in facility	<ul style="list-style-type: none"> • Medical director and nursing leadership should provide visible support for the facility ASP • Leader of ASP should have dedicated time to perform stewardship duties • Structure, roles, and responsibilities of facility ASP should be clearly delineated in a policy that facility leadership reviews and approves • Facility ASP should periodically report to facility QAPI committee
Accountability	Identify which members of facility will be part of stewardship team and clearly delineate roles and responsibilities Assign administrative leadership of stewardship team to single individual	<ul style="list-style-type: none"> • Antibiotic stewardship is a team-based process that requires involvement and collaboration between leadership, providers, nursing staff, and pharmacy staff • Although responsibility for completing various ASP tasks may be delegated to different members of the team, administrative oversight should be assigned to a single individual • ASP team leader should have clinical background plus demonstrated capacity to work and communicate well with stakeholders in other disciplines who operate in the facility
Drug expertise	Ensure access to individuals with experience or training in antibiotic stewardship	<ul style="list-style-type: none"> • Individual selected to lead the facility stewardship team should have prior training or expertise in infectious diseases or antibiotic stewardship, although this will be unusual in most nursing facilities • In absence of local expertise, facility should provide support for stewardship team to attend stewardship training opportunities and pursue formal certification, if available, and identify and collaborate with experts in region (e.g., referring acute care hospital) who can help develop facility policies and guidelines and provide input on selection and implementation of different stewardship interventions
Action	Implement at least one policy or practice to improve antibiotic use in the facility	<ul style="list-style-type: none"> • Specific strategies should be chosen based on facility resources and needs identified through tracking measures • Strategies that focus on reducing unnecessary testing of urine samples and treatment of asymptomatic bacteriuria appear to have the greatest potential for immediate effect (see text)
Tracking	Monitor at least one antibiotic usage outcome and one clinical outcome measure of antibiotic use in facility	<ul style="list-style-type: none"> • At minimum, track facility-initiated antibiotic starts on monthly basis (ideally, denominate by resident-days) • Other usage measures to consider include proportion of antibiotic starts prescribed for >7 days and proportion of antibiotic starts that meet appropriateness criteria • Clinical outcomes that should be considered include monthly number of residents colonized or infected with different multidrug-resistant organisms (e.g., methicillin-resistant <i>Staphylococcus aureus</i>), <i>Clostridium difficile</i>, and the facility antibiogram
Reporting	Provide regular feedback of antibiotic use and antibiotic resistance to staff and providers in facility	<ul style="list-style-type: none"> • Antibiotic usage and clinical outcomes data should be presented at least quarterly at the facility QAPI meeting • Providing individual feedback to providers on their prescribing patterns relative to their peers may have beneficial normative influence on outliers
Education	Provide resources to staff, providers, and residents about risks of antibiotics and opportunities for improving antibiotic use	<ul style="list-style-type: none"> • Education on importance of antibiotic stewardship and strategies the facility is using to promote better antibiotic stewardship should be delivered at hire and periodically thereafter • Education should target nursing staff and prescribers

ASP = antibiotic stewardship program; QAPI = quality assurance and performance improvement.

developing policies and procedures that encompass prescribing etiquette (e.g., providing the indication, drug, dose, and duration with every antibiotic order), clinical indications for diagnostic testing, clinical indications for initiating antibiotic therapy, and preferred agents for treating commonly encountered infections. Education of facility staff and providers and residents' families¹⁶ is another foundational antibiotic stewardship strategy that has been shown to be effective in reducing inappropriate antibiotic use in LTCFs. Introduction of training and tools focused on improving resident assessments and interdisciplinary communication of residents' change in condition have been

associated with significant reductions in antibiotic use¹⁶ and may have benefits in other areas such as reducing hospital admissions. Given the outsized role that suspected UTIs play in antibiotic prescribing in LTCFs,^{6,17} implementation of protocols that restrict urine testing to residents with a high probability of having a UTI and similarly designed protocols to limit antibiotic therapy in residents without clear symptoms and signs of UTI^{18,19} would appear to offer a good return on investment. Strategies focused on promotion of self-directed stewardship, in which prescribers are trained or prompted to engage in review of empirically initiated antibiotics and

modify the therapeutic dose, spectrum, or duration when appropriate (antibiotic timeout), has been implemented successfully in hospitals,²⁰ and implementation of a checklist tool to promote this practice in LTCFs was associated with a significant reduction in systemic antibiotic use in intervention facilities in one study.²¹ Other improvement strategies, such as introduction of a facility-specific antibiogram and a pharmacist-led post-prescriptive audit and feedback, can be very effective but may require expertise and resources that are not widely available in most LTCFs.^{6,7}

Future Directions

The emerging crisis in antibiotic resistance will require a concerted effort to improve antibiotic stewardship across all healthcare settings. Considerable progress has been made in our understanding of the extent and determinants of inappropriate antibiotic use in LTCFs. Although there is accumulating evidence that interventions focused on processes (e.g., urine testing) associated with the initial antibiotic decision can reduce unnecessary antibiotic use, there remains a critical need to identify the effectiveness of interventions that target post-prescribing decision-making (e.g., review and de-escalation) and how these interventions can be delivered in a cost-effective manner. There is also a need for more research on how to implement stewardship interventions with fidelity and sustain them over time, particularly in LTCFs with limited quality improvement resources. Finally, there is a need for studies that evaluate the effects of stewardship interventions on facility and resident outcomes, including healthcare costs and rates of infections caused by *C. difficile* and multidrug-resistant bacteria.

SKIN AND SOFT TISSUE INFECTION

Clinical Relevance

Skin and soft tissue infections (SSTIs) are the third most common infection diagnosed in LTCF residents. Surveys of European and U.S. Department of Veterans Affairs LTCFs indicate that approximately 22% of infections are SSTIs.^{22,23} Routine infection surveillance in LTCFs does not require the monitoring of all SSTIs, so the prevalence of less severe infections may not be known,²⁴ but in Europe, it has been estimated that bacterial infections such as cellulitis and soft tissue and wound infections account for 87.4% of SSTIs.²² Fungal infections (8.3%), herpes simplex or herpes zoster infections (2.4%) and scabies (1.9%) account for the remainder.²²

Risk Factors for SSTIs in Older adults

Greater exposure to pathogens and conditions that promote changes in individuals' normal flora contributes to risk of SSTIs. Sharing living space exposes residents to various pathogens. Use of antibiotics and corticosteroids contributes to overgrowth of bacteria and fungi. Waning immunity is associated with reactivation of latent herpes infections in LTCF residents; 10,000 to 20,000 cases of herpes zoster occur annually.^{25,26}

Primary bacterial infections are frequently due to bacteria that asymptotically colonize human skin and mucosa, such as *Staphylococcus aureus* and group A beta-hemolytic streptococci. These bacteria can be easily spread to other residents and staff; outbreaks have been reported with high attack and fatality rates. These pathogens may also cause outbreaks of acute bacterial conjunctivitis. Epidemics of viral conjunctivitis due to adenovirus are also reported; contamination of ophthalmological equipment and medications facilitates spread.^{25,26}

Preexisting wounds can become secondarily infected through bacteria transfer from other patients on the hands of healthcare personnel or from the environment.^{25,26} Breaks in the skin can occur as a consequence of thinning of skin with age, pressure due to lack of mobility, maceration associated with incontinence, ischemia due to reduced blood flow, edema, and device use. Pressure ulcer risk increases with length of stay; it is estimated that one-fifth of LTCF residents will acquire an ulcer within 2 years. Almost 6% of pressure ulcers in LTCF residents will become infected.^{25,26} These infections are typically polymicrobial, involving aerobic and anaerobic flora, including *Escherichia coli*, *Proteus* species, *Pseudomonas* species, staphylococci, enterococci, anaerobic streptococci, *Bacteroides* species, and *Clostridium* species.^{25,26}

Clinical Presentation

Primary bacterial SSTIs can be categorized as erythematous with or without purulence (Table 2). Infections that involve deeper structures such as fascia occur less often and are typically more severe.^{25–27} *Candida* and *Tinea* species and dermatophyte (*Tinea*) infections also cause non-bacterial superficial mucocutaneous infections in LTCFs (Table 2). *Tinea unguium* has been reported to occur in 10% to 57% and *Tinea pedis* in 10% to 34% of residents. Scabies (*Sarcoptes scabiei*), lice (*Pediculus humanus capitis*, *P. humanus corporis*, *Phthirus pubis*), bedbugs (*Cimex lectularius*), and reactivation of herpesvirus infections (herpes simplex and herpes zoster) also cause rashes. Scabies has been reported in 3.3% of LTCF residents, with an attack rate of approximately 70%.^{25,26}

Diagnostic Approach

Initial evaluation of a possible SSTI should focus on the acuity of onset and whether symptoms and signs of systemic illness are present (Table 2).^{27,28} Pain out of proportion to clinical findings might suggest herpetic infection or necrotizing fasciitis. Distribution or location of skin lesions typically involve *Candida* or *tinea* infection (intertriginous areas)), herpes zoster (dermatomes) carbuncles (nape of the neck), and scabies (webs of the fingers). Characteristics of the skin lesions such as erythema, pustules, blisters, ulcerations, size, depth, and rate of spread should be described.

If the skin lesions have a characteristic appearance, further diagnostic testing may not be necessary. Painful or pruritic vesicles or ulcerations involving nasolabial, genital, or rectal skin and mucosa suggests herpes simplex, whereas a dermatomal distribution that does not cross the midline is diagnostic for herpes zoster.^{25,26} Typical scabies

presents with pruritus, intertriginous rashes, and burrows, although these features may be absent in older adults. Crusted scabies is more typical in this population, and the diagnosis is made only when usual features are seen in visitors or healthcare workers.^{25,26} Head and pubic lice may be found crawling in their respective hair bearing areas; their eggs (nits) may be found at the base of hair follicles. In the case of body lice, the louse or nits are found in the seams of clothing. Acquisition of bed bugs in the healthcare setting is rare because furniture in this setting is easily cleaned and disinfected. Red pruritic nodules may be noted in a linear distribution. Bed bugs are rarely found on the person; they infest clothing, mattresses, and overstuffed furniture. Adult bed bugs, which have a flat, red-brown, apple-seed appearance, run rapidly when they are seen.^{25,26,28}

If the clinical appearance is atypical or the individual is severely ill or is not responding to empirical therapy, further diagnostic studies are appropriate. Scrapings for fungal potassium hydroxide smear, Tzanck smear, and viral polymerase chain reaction (PCR) for herpesviruses or for ectoparasites, eggs, and feces can be done.^{25–28} Deep cultures of pus, aspirates, or tissue are recommended to confirm the cause of the infection and antimicrobial susceptibilities. It is likely that swabs of superficial ulcers reflect colonization and not the true cause of infection. MDROs frequently colonize or infect LTCF residents and can influence treatment choices.²² In the United States, overall rates of colonization of LTCF residents have varied from 11% to 59% for methicillin-resistant *S. aureus* (MRSA) (11–59%), 1% to 19% for vancomycin-resistant enterococci, and 23% to 51% for multidrug-resistant gram-negative organisms.⁵ Many residents are colonized with more than one organism, and new acquisitions may be frequent.⁵

Therapy

Residents with possible bacterial infections who do not have symptoms or signs of systemic illness may be managed in the LTCF. If the resident is systemically ill, and advance directives warrant aggressive care, transfer to hospital is appropriate for more intensive monitoring, urgent imaging, and surgical intervention.

One important consideration for SSTIs is when to begin antibacterial therapy. Minimum criteria to initiate an antibiotic for a SSTI have been established, including pus in a wound, skin, or soft tissue site or at least two of the following: fever or new or worsening redness, tenderness, warmth, or swelling at the suspected site. These criteria do not apply to nonbacterial infections or deep tissue or bone infection. Noninfectious causes such as burns, thromboembolic disease, and gout should be considered.²⁸ If a decision is made to begin treatment, the most likely underlying etiologies of the skin lesions, the clinical stability of the resident, and the route of antimicrobial administration should be considered in addition to risks for MDROs (Table 2).

Prevention

Prevention of SSTIs should focus on prevention of wounds by alleviating their underlying cause and using good

technique to keep wounds clean. Screening for neuropathy and use of appropriate footwear in individuals with diabetes is essential. Residents who are immobile should have optimal pressure relief with appropriate bedding and wheelchair cushions. Macrovascular disease should be evaluated and blockages relieved when feasible. Edema should be controlled with medications and compression wraps if there is venous insufficiency. Adherence to infection control procedures such as hand hygiene and glove use to prevent the spread of pathogens is essential. Limiting the use of unnecessary and overly broad-spectrum antibiotics may limit overgrowth of *Candida* species. Vaccination may also reduce herpes zoster infection.^{25,26}

INFECTIOUS DIARRHEA

Bacteria, viruses, and occasionally protozoa may cause outbreaks of infectious diarrhea in LTCFs. As discussed in detail below, *C. difficile* is the most important and most common bacterial cause of nosocomial diarrhea in this setting. Other bacterial pathogens include *Shigella*, *Salmonella*, and *Campylobacter* spp., as well as toxigenic enterohemorrhagic *Escherichia coli*.²⁸ Ingestion of food contaminated with enterotoxins produced by *S. aureus*, *Clostridium perfringens*, and *Bacillus cereus* may also lead to outbreaks of nausea and vomiting. A wide array of viruses from the families *Caliciviridae* and *Adenoviridae*, as well as enterovirus and rotavirus, may cause gastroenteritis in LTCF residents. Of these, norovirus, a member of the family *Caliciviridae*, is globally the leading cause of acute gastroenteritis and is discussed further below. Finally, protozoa such as *Giardia*, *Cryptosporidium*, and *Cyclospora* may cause diarrheal outbreaks in institutional settings, including those that care for older adults.

Clinical Relevance

C. difficile

Older adults are at high risk of infections caused by *C. difficile*, a gram-positive spore-forming bacillus.^{29,30} In 2010, more than 90% of deaths due to *C. difficile* infection (CDI) were in adults aged 65 and older. Age-specific risk factors for CDI include changes to the gut microbiome and immunosenescence. Aging and residence in a LTCF correlate with a less diverse gut microbiome at baseline. Subsequent exposure to antibiotics causes further disruption to the gut microbiome, rendering people exposed to *C. difficile* spores vulnerable to infection for up to 90 days after completion of the antibiotic.³¹ Once a vulnerable host ingests *C. difficile* spores, they germinate in the intestine to become toxin-producing vegetative bacteria. Robust antibody production against *C. difficile* toxins correlates with lower risk of CDI and recurrent disease. Older adults unable to mount a robust immune response may have diminished capacity to neutralize the effects of *C. difficile* toxins, correlating with greater disease severity and risk of recurrent disease. Moreover, CDI in LTCF residents is more severe and more likely to be associated with recurrent infection than in community-dwelling older adults with CDI.³²

Table 2. Empirical Treatment for Skin and Soft Tissue Infections in Long-Term Care Residents

Severity	Route	Antimicrobial	Minimum Duration	Typical Organisms	Comments
Primary bacterial infection					
Impetigo (nonbullous and bullous)					
Mild	Oral	Dicloxacillin or cephalixin Doxycycline, clindamycin, or TMP/SMX Penicillin	7 days	<i>S. aureus</i> ; MSSA most common MRSA	If many lesions, empirical therapy Culture known
	Topical	Mupirocin	5 days	GABHS Streptococci, <i>S. aureus</i>	Culture known Empirical therapy
Nonpurulent infection (cellulitis, erysipelas, necrotizing infection)^a					
Mild	Oral	Penicillin, dicloxacillin, cephalosporins, or clindamycin	5 days	Streptococci	Cultures; aspirates not routinely recommended
Moderate	IV	Penicillin, ceftriaxone, cefazolin, or clindamycin		Streptococci	Consider MSSA therapy; consider MRSA therapy if prior infection
Severe	IV	Vancomycin or piperacillin with tazobactam		GABHS, polymicrobial	Transfer to hospital; emergency surgery; deep tissue culture
Purulent infections (furuncle, carbuncle, abscess)^b					
Mild	N/A	None	N/A	<i>S. aureus</i> ; MSSA, MRSA	Incision & drainage; antibiotics if fails
Moderate	Oral	TMP/SMX or doxycycline	Minimum 5 days	<i>S. aureus</i> , MSSA, MRSA	Incision & drainage; culture & susceptibility
	IV/oral	Glycopeptides, daptomycin, ceftaroline, or linezolid As above			
Severe	IV	As above	N/A	<i>S. aureus</i> , MSSA/MRSA	Transfer to hospital; emergency surgery; deep tissue culture
Necrotizing fasciitis or gangrene					
Severe	IV	Vancomycin & piperacillin with tazobactam, or vancomycin & carbapenem, or vancomycin & metronidazole & ceftriaxone	N/A	Polymicrobial <i>S. pyogenes</i> <i>S. aureus</i>	Transfer to hospital; emergency surgery; deep tissue culture
Pyomyositis					
Severe	IV	Vancomycin	N/A	<i>S. aureus</i> MSSA/MRSA	Transfer to hospital; emergency imaging; deep tissue & blood culture
Secondary bacterial infections					
Surgical site infection >4 days postoperatively	IV	Vancomycin or ceftazolin	N/A	<i>S. aureus</i> MSSA/MRSA	Erythema >5 cm from incision; fever >38°C; high white blood cell count; begin dressing changes
Perineal wound or gastrointestinal/genitourinary surgery	IV	Cephalosporin & metronidazole, or levofloxacin & metronidazole, or carbapenem		Polymicrobial	

(Continued)

Table 2 (Contd.)

Severity	Route	Antimicrobial	Minimum Duration	Typical Organisms	Comments
Pressure ulcer infection: Stage III or IV					
	PO	Ciprofloxacin or levofloxacin & metronidazole or clindamycin		Polymicrobial aerobes & anaerobes	Optimize local care; debride necrotic tissue; deep tissue for culture; osteomyelitis evaluation
	IV	Piperacillin with tazobactam or carbapenem or cephalosporin & metronidazole, or quinolone & metronidazole or clindamycin If MRSA suspected, add vancomycin			
Superficial fungal infections (Candida and Dermatophytes)					
Intertrigo, vaginitis	Topical	Clotrimazole, nystatin		<i>Candida albicans</i>	Culture if no response
Thrush, paronychia, denture stomatitis	Oral	Fluconazole, terbinafine or itraconazole		<i>C. glabrata</i>	Drug interactions are common with azoles; monitor hepatotoxicity
Athletes foot, ringworm, onychomycosis, jock itch	Topical or oral	Clotrimazole, nystatin, itraconazole, or terbinafine		<i>Tinea pedis</i> <i>Tinea capitis</i> <i>Tinea unguium</i> <i>Tinea cruris</i>	Drug interactions are common with azoles; monitor hepatotoxicity
Herpesviruses					
Disseminated herpes; compromised hosts	IV	Acyclovir		VZV, HSV	Higher doses than VZV; adjust for renal function; treat VZV-related PHN
Localized shingles, oral or rectal herpes	Oral	Acyclovir, famciclovir, or valacyclovir		VZV, HSV 1 & 2	Higher doses for VZV; adjust for renal function; treat VZV-related PHN
Ectoparasites					
Scabies	Topical	Permethrin 5%	12 hours	Sarcoptes scabiei	Cover hairline to feet
Crusted scabies	Oral	Ivermectin			
Lice	Topical	Permethrin 5%	12 hours	<i>Pediculus capitis</i> <i>P. corporis</i> <i>Phthirus pubis</i>	Retreat 1 week later
Bedbugs	N/A	N/A	N/A	<i>Cimex lectularius</i>	Contact precautions; launder clothing; contact isolation; disinfect mattress; seek expert guidance

Adapted from (25–27).

^aMild = typical cellulitis or erysipelas without focus of purulence; moderate = typical cellulitis or erysipelas with systemic signs of infection (fever >38°C, heart rate >90 beats/min, respiratory rate >24 breaths/min, white blood cell count >12,000 or <400 cells/μL); severe = failure of oral therapy with systemic signs of infection, immunocompromise, or signs of deeper infection such as bullae, skin sloughing, hypotension, and organ dysfunction.

^bMild = purulent infection; moderate = purulent infection with systemic signs of infection; severe = failure of incision and drainage with oral antibiotics, systemic signs of infection, or immunocompromise.
IV = intravenous; MSSA = methicillin-susceptible *Staphylococcus (S.) aureus*; MRSA = methicillin-resistant *S. aureus*; GABHS = group A beta-hemolytic streptococci; TMP-SMX = trimethoprim-sulfamethoxazole; IV = intravenous; NA = not applicable.

Clinical Presentation

Clostridium difficile infection presents as watery diarrhea, sometimes accompanied by abdominal cramping and discomfort. Although some individuals may mount a fever, nausea and vomiting are not typical features of CDI. Disease manifestations may be mild to moderate, characterized by a white blood count of 15,000 cells/ μ L and a creatinine level less than 1.5 times the premorbid level. Severe disease, with a white blood cell count of more than 15,000 cells/ μ L or serum creatinine 1.5 times as great as the premorbid level, is best managed in acute care settings that can offer fluid resuscitation, electrolyte replacement, and for severe cases, parental therapy and possible colectomy.³¹ Severe disease may occasionally present with an ileus, leading to a clinical presentation of abdominal pain and distention without diarrhea. These individuals appear toxic, with hemodynamic instability.

After an initial episode of CDI, 20% to 30% of adults develop recurrent disease, most often within 1 to 2 weeks of completing therapy. Recurrent CDI is due not to resistance but to reexposure of a vulnerable host to *C. difficile* spores. These may be the same strain causing the initial infection (relapse) or a new strain of *C. difficile* (reinfection). In 2000, one study reported that of 93 people with recurrent CDI, relapse with the same strain caused approximately half of cases and reinfection with new strains the remainder of cases.³⁰ Risk of recurrence increases with age and, not surprisingly, with antibiotic exposure. Medications that suppress gastric acid production are a potentially modifiable risk factor for recurrent disease.³³ A retrospective study of 754 hospitalized individuals with CDI found that those taking a proton pump inhibitor were 1.5 times as likely to have recurrent CDI (hazard ratio = 1.5, 95% confidence interval (CI) = 1.1–2.0); fewer than half of those individuals had an indication for taking a proton pump inhibitor.³³

Diagnostic Approach

Clinical criteria for CDI are 3 or more unformed stools within 24 hours and a stool test positive for toxigenic *C. difficile* or demonstration of pseudomembranous colitis.^{31,34} The decision and selection of specific tests to support a laboratory diagnosis of CDI remains an area of controversy. A guidance document from the European Society of Clinical Microbiology and Infectious Diseases recommends a 2-step algorithm because no single commercial test has a sufficient positive predictive value when the prevalence of CDI is low.³⁵ Regardless of the diagnostic tests used, only unformed stools should be sent for clinical testing. Because *C. difficile* colonizes up to half of LTCF residents,³⁰ testing stools from asymptomatic individuals diminishes the specificity of diagnosing CDI. Similarly, because people may remain colonized with *C. difficile* for several weeks after resolution of clinical disease, tests of cure are not indicated.^{31,34} Finally, for individuals who may have an ileus, clinicians may consider sending a rectal swab, recognizing that this may lead to a false-negative result.

Therapy

In addition to supportive care, an important step in managing CDI is, whenever possible, to stop the inciting antibiotic and avoid subsequent antibiotic exposure. Metronidazole and oral vancomycin remain the mainstays of treatment for mild to moderate disease, including recurrent episodes.³⁴ For people with severe CDI, treatment with oral vancomycin significantly reduced the risk of 30-day mortality (adjusted relative risk (RR) = 0.79, 95% CI = 0.65–0.97).³⁶ Oral vancomycin is also the first-line agent for people taking warfarin. The risk of recurrent disease after treatment with metronidazole and oral vancomycin is similar.³⁶ Although fidaxomicin appears to reduce the risk of recurrent disease,³⁰ the cost of this agent is several times as high as that of metronidazole and oral vancomycin, the latter prepared by compounding the intravenous preparation.³⁴

Prevention

Reducing exposure to antibiotics and to *C. difficile* spores is the cornerstone of CDI prevention. Although any antibiotic may predispose an individual to CDI, a meta-analysis found clindamycin, fluoroquinolones, cephalosporins, monobactams, and carbapenems to be high risk.³⁷ In acute-care and LTCF settings, ASPs reduce the incidence of CDI.³⁰ (See also earlier section on Antibiotic Stewardship.) Infection prevention and control measures, discussed more extensively elsewhere,³⁰ seek to reduce contamination of health-care providers' hands and the environment with *C. difficile* spores. As long as people with CDI are symptomatic, they should remain on contact precautions, with health-care providers removing gowns and gloves before exiting the room, followed by hand washing with soap and water. (Alcohol gel is not sufficient to kill or remove spores.)^{31,34} After symptoms resolve, spores continue to be shed into the environment for several weeks,³⁰ which suggests that contact precautions should be extended. Finally, to reduce the burden of *C. difficile* spores, sporicidal agents that the Environmental Protection Agency has approved should be used to clean and disinfect the equipment and environment of people with current or recent CDI.

When administered concurrently with standard-of-care antibiotics, bezlotoxumab, a recently approved monoclonal antibody against *C. difficile* toxin B, reduced the rate of recurrent disease by 10% more than placebo.³⁸ Fecal microbiota transplant has proven to be an effective and safe intervention for recurrent CDI, including in older adults.^{30,34} Although clinical trials are underway, vaccines against *C. difficile* are not yet commercially available. A systematic review of randomized controlled trials investigating probiotics found moderate-quality evidence that probiotics prevent *C. difficile*-associated diarrhea (RR = 0.36, 95% CI = 0.26–0.51) but do not reduce the incidence of CDI (RR = 0.89, 95% CI = 0.64–1.24). Although subgroup analysis to examine older adults or LTCF residents or to evaluate specific species or combinations of microorganisms was not feasible, the authors conclude that probiotics are safe.³⁹

Norovirus

Norovirus is also a common cause of gastroenteritis in LTCF residents. A recent article reviewed this topic extensively; this section will highlight only the critical issues.⁴⁰ The majority of norovirus outbreaks occur in LTCFs, with 90% of norovirus-associated deaths occurring in adults aged 65 and older.⁴¹ Unlike CDI, norovirus infections present with acute-onset nausea, vomiting, and watery diarrhea. As few as 100 virions may lead to disease. Given that infected individuals may shed billions of virions in their stool and vomitus, norovirus spreads rapidly between LTCF residents and their healthcare providers. The incubation period for norovirus is 12 to 48 hours, followed by a self-limited illness that lasts 12 to 60 hours.

Early recognition and prompt implementation of infection prevention and control measures are central to limiting the severity of a norovirus outbreak. Some state public health laboratories will use reverse-transcription PCR to confirm norovirus, but more often, LTCFs will recognize a norovirus outbreak when 2 or more cases fulfill the Kaplan Criteria: vomiting in more than half of affected persons, mean (or median) incubation period of 24 to 48 hours, mean (or median) duration of illness of 12 to 60 hours, and no bacterial pathogen identified in stool culture.

In LTCFs, infection prevention and control measures must address residents and healthcare providers. Affected residents should be placed on contact precautions for at least 48 hours after symptom resolution. For norovirus, contact precautions entail gowns, gloves, hand hygiene with soap and water, and wearing a mask around vomitus or fecal material because norovirus may become airborne and cause infection. The facility should also minimize resident movements, suspend group activities, and consider restricting access to an affected ward. Healthcare providers with symptoms consistent with norovirus infection should be excluded from work and encouraged to stay home for 48 hours after symptom resolution. Upon returning to work, recently ill healthcare workers should care for symptomatic residents. A general framework is to group residents and staff into 3 clinical categories: symptomatic, asymptomatic and potentially exposed, and asymptomatic and unexposed. This framework can help with staff assignments that avoid having asymptomatic and potentially exposed staff interact with asymptomatic and unexposed residents.

BACTERIAL PNEUMONIA

Clinical Relevance

Infections of the lower respiratory tract, which include pneumonia and bronchitis, are leading causes of morbidity and mortality in older adults. Pneumonia in particular affects 1.4% to 2.5% of LTCF residents in the United States and is among the most common causes of hospitalization.⁴² Age-related changes to the respiratory system, including diminished cough and gag reflexes, impaired mucociliary clearance, poor respiratory muscle strength, and poor chest wall compliance and elastic recoil, serve to impair host defense mechanisms and allow pathogens to penetrate and infect the respiratory tract. This section will focus on bacterial pneumonia.

Recognition, diagnosis, and treatment of acute infections of the lower respiratory tract in LTCF residents present significant challenges. Comorbid conditions including congestive heart failure and chronic respiratory diseases may confound the clinical presentation, and aspiration of oral contents into the respiratory tract may lead to chemical pneumonitis, bacterial pneumonia, or both. Furthermore, although the vast majority of people with acute bronchitis have a viral infection, some may develop secondary bacterial pneumonia. Recent evidence implicates a viral pathogen in at least one-quarter of older adults presenting with community-acquired pneumonia.⁴³ Although the implications for the treatment of older adults with pneumonia, particularly LTCF residents, are not known, these data help to explain the similarity in clinical predictors of pneumonia with bacterial, viral, and mixed etiologies.⁴⁴ Finally, the high rate of colonization with MDROs in LTCF residents in general, coupled with a paucity of microbiological data from residents with suspected bacterial pneumonia, render selection of appropriate empirical antimicrobial therapy challenging.

Clinical Presentation

Clinical indicators of bacterial pneumonia include fever, pleuritic chest pain, respiratory rate of more than 25 breaths per minute, decline in functional status, new or increased cough, sputum production, shortness of breath, and physical findings upon chest examination. A retrospective review of nearly 300 LTCF residents admitted through the emergency department with a diagnosis of pneumonia described dyspnea as the most common presenting symptom (67%), followed by mental status change (51%), cough (49%), and fever (45%).⁴⁵ Another study reported on an attempt to develop a consensus of characteristics for the diagnosis of pneumonia in LTCF residents. Of the pulmonologists and geriatricians queried, 57% agreed that dyspnea, fever, decline in functional status, tachypnea, and crackles or rales on auscultation were important characteristics; they further agreed that at least two of these characteristics should be present to diagnose LTCF-acquired pneumonia. For aspiration pneumonia, 80% of the clinicians reached a consensus of dysphagia, choking incident, tube feeding, neurological disease, and cognitive impairment as risk indicators for aspiration pneumonia,⁴⁶ but with advanced age and decline in functional capacity, the presence of typical pneumonia symptoms decreases. Accordingly, atypical symptoms (e.g., change in mental status, loss of appetite) or exacerbation of chronic illnesses (e.g., congestive heart failure, chronic respiratory illness, diabetes mellitus) may be early clinical indicators of acute infection, including pneumonia.

Diagnostic Approach

In addition to assessing clinical changes, the diagnostic evaluation of a LTCF resident with suspected bacterial pneumonia should include measuring pulse oximetry and obtaining a chest radiograph. In LTCF residents, identification of low oxygen saturation using a bedside pulse oximeter may suggest pneumonia. A case-control study of residents in a veteran's nursing home found that a decrease

in oxygen saturation of more than 3% from baseline or of less than 94% suggested pneumonia.⁴⁷ Chest radiographs revealing a new infiltrate also indicate pneumonia, but obtaining a chest radiograph of sufficient quality to make this determination may be challenging in LTCFs because of the limitations of portable films, inability of an ill resident to maintain a suitable position, and interpretation, including delays or lack of comparative radiographs. In the study of individuals hospitalized for LTCF-acquired pneumonia, the authors found that fewer than 20% of chest radiographs obtained in the emergency department indicated possible pneumonia.⁴⁵ These data suggest that, during the initial phase of illness, a “negative” chest radiograph is not sufficient to exclude lower respiratory tract infection.

Although sputum culture results are consistently challenging to obtain and sometimes to interpret, the findings can help direct appropriate antibiotic therapy. A study found that, microbiological culture results were available for just 12% of 56 residents hospitalized with LTCF-acquired pneumonia.⁴⁸ This unfortunate paucity of sputum cultures increases the need to use rapid diagnostic tests. Positive tests for *Streptococcus pneumoniae* antigen in urine or for influenza in nasopharyngeal swabs can inform the choice of therapeutic agent and length of therapy used to treat LTCF residents. Similarly, multiplex panels that test for several respiratory pathogens may help improve the diagnosis of bacterial pneumonia, although their cost makes routine use of these impractical for most LTCF settings. Finally, although procalcitonin has the potential to identify bacterial infections, further studies are needed to understand whether testing for it has a role in the clinical evaluation of frail older adults or LTCF residents with suspected pneumonia.

Therapy

The Loeb Minimum Criteria offer a concise set of recommendations for starting antibiotic treatment in LTCF residents in whom there is a concern about bacterial pneumonia.⁴⁹ Evidence-based recommendations for empirical agents and length of therapy are less clear. Despite the prevalence of MDROs colonizing LTCF residents, recent literature suggests that using antibiotics recommend for community-acquired pneumonia are sufficient to treat most cases of LTCF-acquired pneumonia (Table 3).^{45,50} Although there are few data specifically on older adults or LTCF residents with bacterial pneumonia, recommendations for treating community-acquired and hospital-acquired pneumonia indicate that, in most instances, the length of antibiotic therapy should be 5 to 7 days.^{51,52} In general, a short, fixed course of antibiotics results in fewer adverse events related to antibiotics, including CDI, emergence of resistant bacteria, and costs, than a longer course, without reducing the benefits of antibiotic therapy. For residents with immunocompromising conditions, structural lung disease, or a delayed response to empirical therapy, a longer course of antibiotics (7–10 days) may be warranted. Hospitalization should be considered in residents with respiratory compromise, cardiovascular instability, worsening of preexisting noninfectious comorbidities, poor oral intake, or inadequate nutrition.

Table 3. Suggested Empirical Antibiotic Therapy for Nursing Home-Acquired Bacterial Pneumonia

Clinical Context	First Line	Second Line
Mild to moderate pneumonia symptoms	Cefpodoxime or amoxicillin with clavulanic acid (first choice if aspiration suspected)	Doxycycline or levofloxacin
Severe pneumonia symptoms or failure to improve with appropriate empirical therapy	Ceftriaxone and azithromycin	Ertapenem or levofloxacin
Severe pneumonia symptoms and concern for methicillin-resistant <i>Staphylococcus aureus</i> in respiratory tract	Consider adding vancomycin or doxycycline	Consider adding linezolid
Known history or strong suspicion of <i>Pseudomonas</i> or resistant Gram-negative bacteria in respiratory tract	Cefepime or piperacillin with tazobactam	Levofloxacin or carbapenem (other than ertapenem) or aztreonam

Prevention

Vaccination against *S. pneumoniae* and influenza remain central to reducing the risk of lower respiratory tract infection in LTCF residents. Although dysphagia is a risk factor for developing LTCF-acquired pneumonia, efforts directed at minimizing the risk of aspiration have not reduced the incidence of respiratory illness.⁵³ (See Preventative Interventions for a more detailed discussion.)

URINARY TRACT INFECTION

Clinical Relevance

Urinary tract infection is one of the most common infections diagnosed in LTCF residents.⁵⁴ The high frequency of infection is largely attributable to comorbidities that affect normal voiding, such as urological abnormalities and chronic neurologic diseases. There is also a very high prevalence of asymptomatic bacteriuria (35–50% of residents without indwelling urethral catheters) in this population. Although asymptomatic bacteriuria is benign, the common finding of a positive urine culture leads to frequent overdiagnosis of symptomatic UTI. As many as 75% of prescriptions for UTI in LTCF residents are given to individuals who do not meet criteria for UTI.⁵⁵ This is a major contributor to inappropriate antimicrobial use in LTCFs and promotes antimicrobial resistance and CDI in residents.^{55,56} The important clinical factors for optimizing management of UTI are ascertainment of symptomatic infection and nontreatment of asymptomatic bacteriuria.

Bladder emptying is managed using a chronic indwelling catheter in 5% to 10% of LTCF residents.⁵⁷ Bacterial biofilm formation along the internal and external catheter surfaces is universal, so polymicrobial bacteriuria is the

norm for residents with chronic catheters. The presence of a catheter is associated with greater incidence of symptomatic UTI, and catheter-associated UTI (CAUTI) is the most frequent source of bacteremia in LTCFs.^{54,57}

Clinical Presentation

Residents with UTI may present with typical clinical symptoms.⁵⁴ Bladder infection is manifested by acute onset of lower urinary tract irritative symptoms of frequency, urgency, slow and painful urination (stranguria), dysuria, or new or increased incontinence. Upper urinary tract (kidney) infection presents as pyelonephritis with costovertebral angle pain or tenderness, usually with fever, and variable accompanying lower urinary tract symptoms. Ascertainment of symptoms in many residents is problematic because of impaired communication, functional disability, and chronic genitourinary symptoms attributed to comorbidities.^{24,54} Residents without acute localizing genitourinary findings but with clinical deterioration and non-specific symptoms or signs are frequently diagnosed with and treated for UTI, often because a urine culture is positive,^{24,54–56} but evidence does not support attributing non-localizing and nonspecific symptoms to UTI, even with a positive urine culture.^{24,58} Mental deterioration (e.g., delirium)⁵⁹ or falls,⁶⁰ by themselves, are generally not presentations of UTI.

Residents with CAUTI usually present with fever alone, although localizing symptoms including catheter obstruction, acute hematuria, and suprapubic or costovertebral tenderness may occasionally be present.⁵⁷ Determinants of symptomatic infection are not well described, but catheter obstruction and catheter trauma are potential antecedents of symptomatic infection.

Diagnostic Approach

Guidelines for diagnosing symptomatic UTIs in residents without indwelling catheters require the presence of localizing genitourinary symptoms or signs^{24,28,49,54} (Table 4). An evidence-based diagnostic approach to UTI was recommended in the 2009 Infectious Diseases Society of America guidelines for evaluation of fever and infection in older LTCF residents.²⁸ For residents in whom a diagnosis of UTI is considered, a urine specimen for determination of pyuria should be obtained. If a voided urine specimen cannot be collected, an in-and-out catheter specimen should be collected, whenever possible. A urine culture is requested only if the urinalysis is positive. A screening test for pyuria has a negative predictive value of more than 95% for UTI, so UTI is excluded if pyuria is not present,²⁸ although pyuria accompanies asymptomatic bacteriuria and is also found in as many as 30% of residents without bacteriuria. Thus, pyuria by itself does not diagnose bacteriuria or differentiate symptomatic from asymptomatic infection.⁵⁴

The most common clinical presentation of CAUTI is fever alone (Table 4). When fever is the only sign, infection at other sites must always be considered and excluded. Replacement of the catheter is recommended if it has been present for 2 weeks or longer, because the biofilm contaminates urine specimens collected through the catheter.

Obtaining a urine specimen through a freshly inserted catheter provides a more valid specimen to identify bladder bacteriuria and infecting organisms and susceptibilities.⁵⁷ Blood cultures are indicated for severely ill individuals with or without catheters. Residents with indwelling catheters are more likely to experience urosepsis.

Some residents present with a clinical syndrome consistent with severe sepsis, including one or more of fever or hypothermia, hemodynamic instability, acute delirium, and respiratory distress. If no source of infection is apparent, these residents should be managed as if they had sepsis syndrome, considering urinary infection as one potential site, pending results of cultures and other investigations.

Therapy

When the presenting symptoms are mild, initiation of antimicrobial therapy should await urine culture results. If the urine culture is subsequently positive, antimicrobial therapy should be initiated only if symptoms have persisted. When fever alone is present in residents with chronic indwelling catheters, clinical monitoring without initiation of antimicrobial therapy may also be appropriate. As many as two-thirds of febrile episodes in residents with long-term catheters are attributed to urinary infection, but most resolve in less than 24 hours without intervention.⁶¹ In residents with severe symptoms including sepsis, immediate empirical therapy is indicated. Asymptomatic bacteriuria should be treated only before an invasive urological procedure that is likely to be associated with mucosal bleeding. A single dose of an effective antimicrobial given immediately before the procedure is usually effective for prophylaxis.⁵⁴

Clinical presentation, resident tolerance, and known or suspected susceptibilities of the infecting organism determine the choice of antimicrobial regimen, including oral vs intravenous therapy and duration.⁵⁴ Susceptibility of organisms isolated in prior urine cultures from the resident and the resistance prevalence of uropathogens in the facility should guide selection of initial empirical therapy. The specific antimicrobial choice is similar to that in other populations with UTI and may include nitrofurantoin (for cystitis only), trimethoprim with sulfamethoxazole, ampicillin, cephalexin, and when indicated, fluoroquinolones, oral extended-spectrum cephalosporins, or amoxicillin with clavulanic acid.⁵⁴ When resistant organisms are isolated, susceptibility determined antimicrobial selection, and aminoglycosides, carbapenems, and beta-lactam/beta-lactamase inhibitor combinations may be appropriate. For residents requiring parenteral therapy, transfer to an acute care facility may be necessary.

Prevention

For residents with frequent recurrent symptomatic infection, especially when the clinical presentation is severe, urological abnormalities, which are potentially correctable, such as obstruction, should be excluded. Prophylactic antimicrobial therapy for residents with recurrent infection should be avoided, because this promotes emergence of resistant organisms without decreasing the frequency of

Table 4. Guidelines Providing Criteria for Clinical Diagnosis of Urinary Tract Infection (UTI) in Long-Term Care Facility (LTCF) Residents

Reference	Proposed Use	Residents without Indwelling Catheters	Residents with Indwelling Catheters
Loeb et al. ⁴⁹	Minimum criteria for the initiation of antibiotic therapy for urinary infection	Acute dysuria alone or fever (>37.9°C (100°F) or ≥1.5°C (≥2.4°F) above baseline) and one or more of new or worsening urgency, frequency, suprapubic pain, gross hematuria, costovertebral angle tenderness, urinary continence	Presence of ≥1 of fever (>37.9°C or ≥1.5°C above baseline), new costovertebral angle tenderness or rigors (shaking, chills) with or without identified cause, new-onset delirium
High et al. ²⁸	Evaluation of fever and infection in older LTCF residents	Acute onset of UTI-associated symptoms and signs (e.g., fever, dysuria, gross hematuria, new or worsening urinary incontinence, suspected bacteremia)	Suspected urosepsis (fever, shaking, chills, hypotension, delirium), especially in context of recent catheter obstruction or change
Stone et al. ²⁴	Surveillance definitions for infection in long term care	At least one of the following symptoms or signs: <ul style="list-style-type: none"> • Acute dysuria or acute pain, swelling, or tenderness of testes, epididymis, or prostate • Fever or leukocytosis (single oral temperature >37.8°C (>100°F), repeated oral temperature >37.2°C (>99°F) or rectal temperature >37.5°C (>99.5°F), or single temperature ≥1.1°C (≥2°F) over baseline from any site); leukocytosis, neutrophilia (>14,000 leukocytes/μL) or left shift (>6% bands or 1,500 bands/μL)] and at least one of the following localizing subcriteria: acute costovertebral angle pain or tenderness, suprapubic pain, gross hematuria, new or marked increasing incontinence or urgency or frequency, urgency • In absence of fever or leukocytosis, ≥2 of above localizing urinary tract subcriteria 	≥1 of the following signs or symptoms: <ul style="list-style-type: none"> • Fever, rigors, new onset of hypotension with no alternate source of infection • Acute change in mental status or acute functional decline with no alternate diagnosis and leukocytosis • New-onset suprapubic pain or costovertebral angle pain or tenderness • Purulent discharge from around catheter or acute pain, swelling, or tenderness of testes, epididymis, or prostate

symptomatic infection. Cranberry products do not decrease the frequency of infection.⁶² The most effective means of preventing CAUTIs is to remove the catheter whenever possible. When this is not possible, resident care practices to identify catheter obstruction early and to avoid trauma to the catheter should be implemented and followed.

PREVENTIVE INTERVENTIONS

Clinical Relevance

Similar to cardiovascular disease and cancer, prevention is critical to reducing the risk of infection, particularly in LTCFs, which have a high prevalence of MDROs. Influenza vaccination of older adults and healthcare personnel lowers infection rates, saves lives, and reduces complications.⁶³ Recommended vaccinations in older adults include yearly influenza vaccine; one dose of pneumococcal conjugate vaccine (PCV13); and at least one dose of pneumococcal polysaccharide vaccine (PCV23), herpes zoster vaccine, and tetanus-diphtheria and acellular pertussis (Tdap) vaccine if there is anticipated contact with a child

younger than 12 months old. Tetanus-diphtheria vaccine can replace Tdap if there is no anticipated infant contact. Optimal management of chronic diseases; prevention of pressure ulcers; attention to infection prevention practices, such as hand hygiene for healthcare professionals, caregivers, residents, and families; appropriate gown and glove use; and judicious antibiotic usage are all important preventive measures to reduce infections and enhance quality of care of older LTCF residents.

Emerging Evidence

Several recent randomized controlled trials have identified preventive interventions that are shown to be of benefit and those that are not. Next we provide a brief overview of some recent studies.

URINARY TRACT INFECTIONS

Use of Cranberry to Prevent UTIs

In a recent randomized controlled study, investigators asked whether two oral cranberry caplets per day lead to

lower rates of bacteriuria plus pyuria in noncatheterized older women in LTCFs.⁶² In a double-blind, placebo-controlled, randomized trial focused on older long-term female residents, consenting participants were randomized to 2 cranberry capsules per day (equivalent to 72 mg of proanthocyanidins) or placebo for 360 days. Surrogate consent was required in 94% of the instances, highlighting challenges in conducting research in these settings. Twenty-six percent of urine specimens in the treatment group and 30% in the control group had pyuria with bacteriuria. In other words, cranberry capsules did not have any effect on the primary outcome. Furthermore, cranberry capsules had no effect on secondary outcomes. This study helped disprove the long-held pervasive practice of using cranberry capsules to prevent UTI.⁶⁴

Multicomponent Interventions to Prevent CAUTI

In a recent cluster-randomized interventional study, investigators evaluated the effect of a targeted infection-prevention multimodal intervention program in reducing MDRO prevalence and device-associated infections in a group of southeast Michigan LTCFs.⁶⁵ The intervention included a structured interactive educational program for frontline healthcare personnel, hand hygiene promotion, preemptive barrier precautions when assisting with high-risk activities of daily living (e.g., bathing, dressing, grooming, toileting, feeding, ambulation), and active surveillance for MDROs and infections with monthly data feedback. Interactive educational modules incorporating adult learning theory were presented to healthcare personnel at intervention sites in 10 in-service trainings on a broad range of topics, including overview of infection prevention practices, hand hygiene, barrier precautions, infection recognition, and care of indwelling devices, with content following evidence-based guidelines. This approach was shown to reduce overall MDRO prevalence by 23%, new MRSA acquisition by 22%, and clinician-diagnosed CAUTIs by 31%.⁶⁵

Lessons learned from the targeted infection prevention study and the Agency for Healthcare Research and Quality (AHRQ) Safety Program for Reducing Catheter-associated UTI in Hospitals⁶⁶ were then implemented in nearly 500 NHs in 48 states through the AHRQ Safety Program in Long-Term Care: HAI/CAUTI project.⁶⁷ Using a combination of technical and socio-adaptive interventions, the program emphasized professional development in urinary catheter use, catheter care and maintenance, and antimicrobial stewardship and promoted a LTCF resident safety culture, team building, and leadership engagement. CAUTI rates decreased by 54% (incidence rate ratio = 0.46, 95% CI = 0.36–0.58, $P < .001$) during the project. The number of urine cultures ordered for all residents decreased by 15%.⁶⁷ These studies provide evidence that multicomponent interventions can reduce CAUTI in LTCF populations.

RESPIRATORY TRACT INFECTIONS

Use of High-Dose Vitamin D in Pneumonia Prevention

In order to evaluate effectiveness of high-dose Vitamin D in pneumonia prevention, investigators conducted a major

randomized controlled trial to determine the efficacy and safety of high-dose vitamin D to prevent acute respiratory tract infections in NHs.⁶⁸ The study involved 25 Colorado-based LTCFs and residents aged 60 and older. Participants were randomized to a high-dose group that received 100,000 IU of vitamin D monthly and a standard dose group that received placebo if already on supplementation of 400 to 1,000 IU/d of vitamin D or 12,000 IU of vitamin D if taking anything less than 400 IU/d. The high-dose group experienced 0.67 acute respiratory tract infections per year, and the standard-dose group experienced 0.6 infections per year; the difference was clinically insignificant. Furthermore, falls were more common in the high-dose group (1.47/person-year) than in the standard-dose group (0.63/person-year), although fractures were uncommon. Thus, the role of high-dose vitamin D in preventing infections remains unclear.

Chlorhexidine-Based Oral Care in Aspiration Pneumonia

Several preliminary studies suggest that adequate oral hygiene using mouth rinses, toothpaste, brushing, and feeding in an upright position mitigates the risk of pneumonias attributed to aspiration.⁵³ Another major cluster-randomized study assessed older LTCF residents in 36 LTCFs in Connecticut with impaired oral hygiene or swallowing difficulty according to clinical assessment. The intervention comprised manual tooth and gum brushing along with a chlorhexidine rinse twice a day and upright positioning. The primary outcome was time to first chest radiograph-confirmed pneumonia and secondary outcomes included development of first lower respiratory tract infection. The study was terminated for futility and ineffectiveness (primary outcome of time to first pneumonia: HR = 1.12, 95% CI = 0.84–1.50, $P = .44$), because this chlorhexidine-based intervention was not effective in reducing lower respiratory infections, thus calling into question the utility of this enhanced oral care protocol in LTCF populations.

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