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Preventing Transmission of Multidrug-Resistant Pathogens in the Intensive Care Unit

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INTRODUCTION

Intensive care unit (ICU) beds in the United States are increasing as a proportion of all hospital beds, reflecting increasing need for critical care, particularly among neonates and the elderly.¹ Although nosocomial infections complicate 4% of overall hospital admissions,² 9% to 20% of critically ill patients develop infections while in the ICU.^{2–4} Nearly half of all health care–associated infections that occur in hospitals are attributable to the ICU.² At the same time, the proportion of nosocomial infections caused by multidrug-resistant organisms is increasing, limiting treatment options and increasing length of stay, mortality, and cost.⁵ Increasing use of critical care resources and high risk of nosocomial infection in the context of increasing antimicrobial resistance make infection prevention a leading priority in the ICU.

Guidelines from the Centers for Disease Control and Prevention (CDC) from 2006,⁶ and the Society for Hospital Epidemiology of America from 2003,⁷ provide infection control guidance to prevent the spread of multidrug-resistant pathogens. This article examines more recent evidence for methods of preventing the transmission of multidrug-resistant pathogens in the ICU.

Importance of Preventing Transmission of Resistant Organisms

ICU patients are highly vulnerable to nosocomial infection because of invasive devices, immune compromise caused by underlying diseases or medications, poor nutritional states, uncontrolled hyperglycemia, and sepsis, which can lead to a paradoxical immune suppression.⁸ Multidrug-resistant pathogens represent a substantial proportion of nosocomial infections in the ICU, including 10% to 16% of US device-related infections.⁹ Infection with multidrug-resistant organisms causes significant mortality in hospitalized

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patients. Approximately 23,000 persons in the United States die each year from these organisms, most of which are acquired in health care settings.¹⁰ Nosocomial bloodstream infections with resistant gram-negative organisms can have mortality as high as 80% to 85%.^{11,12}

In addition to host susceptibility, the logistics and complexity of critical care medicine put patients at risk of acquiring nosocomial organisms. Invasive procedures and indwelling devices, often essential to providing supportive care to critically ill patients, serve as portals of entry for pathogens. Lifesaving critical care treatment requires the concurrent contributions of many health care team members and the use of many patient care devices, potentially posing additive risk of transmission from personnel or fomites. Infection control precautions may not be the predominant priority in situations in which seconds matter, such as resuscitating patients suffering trauma, sepsis, cardiac arrest, and other emergencies. Antimicrobial use may select out resistant strains that are potentially transmissible from patient to patient.

Transmission of Resistant Organisms in the intensive Care Unit

Bacterial pathogens of epidemiologic concern in the ICU tend to inhabit specific sites on or in the human body, or in the hospital environment, that serve as reservoirs for transmission. The reservoirs of resistant organisms include niches in the human microbiome. The microbiota of skin, respiratory epithelium, and the gastrointestinal tract are altered within a few days in the hospital. Patients' flora can be deranged by antibiotics, chemotherapy, or acquisition of nosocomial organisms, among other sources. Patients who are colonized with resistant bacteria serve inadvertently as potential reservoirs for transmission. Colonization pressure, or the proportion of patients in a given unit who are colonized with resistant bacteria, is an independent risk factor for transmission.^{13,14} Resistant organisms are generally thought to be transmitted from person to person via the hands of health care personnel, or from contaminated patient care equipment or contaminated surfaces in the health care environment. Antimicrobial stewardship, hand hygiene, and proper disinfection of equipment and hospital surfaces are thus important means of preventing spread.

Hospitals should have policies and procedures in place that outline clear infection control guidelines, along with contingency procedures for special situations. ICU staff must receive periodic training and education in infection control, which should be informed by data on infection rates, hand hygiene rates, and other relevant outcome measures. In addition, compliance with infection control procedures requires adequate staffing, infrastructure (such as handwashing sinks), and supplies (such as gloves, masks, and alcohol-based hand gel).

ANTIMICROBIAL STEWARDSHIP

Antimicrobial stewardship has an important and distinct role to play in the ICU, and has been shown to improve the treatment of critically ill patients and reduce antimicrobial resistance.^{15,16} The goals of antimicrobial stewardship are to improve the quality of care and avert adverse outcomes, including antimicrobial resistance, by optimizing dosing and selection of drugs, along with reducing duration of therapy.¹⁷ Intensivists face a challenge of balancing the need to administer broad antibiotic coverage for the immediate welfare of

critically ill patients, particularly those with undifferentiated shock, with the short-term potential for drug toxicity and *Clostridium difficile* infection and the longer-term potential for generating antimicrobial resistance in individual patients and the ICU population.

The initial antimicrobial management of sepsis is critical. In patients with septic shock, delays in empiric antimicrobial administration are highly correlated with mortality.¹⁸ The selection of appropriate initial antimicrobial therapy is also associated with a mortality benefit.¹⁹ Empiric therapy for sepsis should consider the most likely source and pathogens, the local antibiogram, and the local epidemiology of multidrug-resistant organisms in the ward, institution, or community from which the patient arrived.

In the ICU, antimicrobial stewardship favors prospective audit and feedback by pharmacists and physicians trained in antimicrobial stewardship, reevaluating empiric therapy after 48 to 72 hours to consider deescalation if a diagnosis has been established.²⁰ In addition, formulary restriction of select antimicrobials and therapeutic drug monitoring are also integral to minimizing selection pressure and optimizing antimicrobial therapy in the ICU. Rapid diagnostic methods, such as matrix-assisted laser desorption ionization—time of flight (MALDI-TOF) mass spectrometry, can expedite diagnosis and thus deescalation of empiric therapy to optimal therapy.²¹ In addition, guidance from serial serum concentrations of procalcitonin, a biomarker with increased levels in patients who have bacterial infections, has been shown to reduce the duration of antimicrobial therapy in ICU patients.²² A successful antimicrobial stewardship program requires not only education of physicians, nurses, and other health care staff but also culture change, such that the program is embraced as a critical patient safety measure.

Hand Hygiene

ICU personnel who perform inadequate hand hygiene may carry multidrug-resistant organisms on their hands. Although carriage may be transient, many organisms can survive long enough to be spread to the ICU environment or directly to patients. Personnel can have longer-term carriage of bacterial pathogens in rings²³ or under long or artificial fingernails, and the recurrent role of long and artificial nails in outbreaks has led the CDC to recommend against them.²⁴

Hand hygiene, prioritized as an overriding infection control goal by the CDC and the World Health Organization (WHO),²⁵ is one of the most challenging measures to follow consistently in the ICU. The WHO's Five Moments for Hand Hygiene is a simple, precise schema for hand hygiene opportunities, or transitions in patient care at which hand hygiene should be done in order to prevent cross-transmission.²⁵ Despite evidence that hand hygiene prevents nosocomial infections²⁶ and extensive research efforts to boost hand hygiene compliance rates in hospitals, adherence remains as low as 40% to 60%, and in some studies is lower in the ICU than in other wards.^{27,28}

Investigators have attempted to understand the basis for uneven compliance in order to identify opportunities for improvement. In a recent German study, investigators measured the number of hand hygiene opportunities per ICU patient and the mean duration of hand hygiene.²⁹ Among an estimated 218 to 271 daily hand hygiene opportunities per patient,

overall compliance was 42.6%, with an average 6.8 seconds spent on each hand hygiene episode. The investigators concluded that if hand hygiene were performed in compliance with WHO guidelines (including 20–30 seconds per hand hygiene episode), each nurse would spend an estimated 58 to 70 minutes on hand hygiene for each patient during a 12-hour shift.²⁹ This study shows the predicament faced by ICU personnel when patient care workload conflicts with commitment of time to meticulous hand hygiene.

Recent research studies to improve hand hygiene compliance have focused on improving monitoring of compliance and addressing behavioral and psychological barriers to consistent hand hygiene. Investigators at the University of North Carolina addressed both goals by opening compliance measurement to frontline health care personnel in a broad range of disciplines, thereby generating more robust monitoring data and improving compliance in the involved disciplines.³⁰ Early-generation electronic monitoring systems have had mixed results, showing that there is room for improvement in the automated systems and the study designs used to evaluate them.^{31,32}

In an era in which some classes of antibiotic-resistant organisms have diminishing treatment options, hand hygiene remains the simplest and possibly the most important intervention to limit the human toll of infections caused by these organisms in the ICU. Achieving better hand hygiene compliance is a major infection control goal.

MANAGEMENT OF ANTIBIOTIC-RESISTANT ORGANISM COLONIZATION

Microbial Screening

Identification and isolation of colonized patients are standard infection control measures to reduce the risk of patient-to-patient transmission. The goal of screening patients for microbial colonization is to identify those who are carriers of antibiotic-resistant organisms and could serve as reservoirs for transmission. Such information theoretically provides an opportunity to interrupt spread through isolation precautions or decolonization. However, the efficacy of microbial surveillance as a horizontal strategy to minimize transmission of resistant pathogens is controversial. Although screening and isolation have been effective in some models and clinical settings,^{33,34} widespread implementation is costly and laborious, and carries the inherent negative of placing more patients in isolation for uncertain benefit to the patient population.

In one study that shows the potential pitfalls of such an approach, investigators assessed the effect of daily surveillance cultures among ICU patients for *Staphylococcus aureus* (including methicillin-resistant *S aureus* [MRSA]), but did not report either negative or positive culture results to ICU staff, or place MRSA-colonized patients on isolation precautions.³⁵ Surveillance cultures and genotyping showed no cross-transmission, despite the presence of several patients colonized by methicillin-sensitive *S aureus* and MRSA, but the absence of spread was not caused by the surveillance cultures. The investigators concluded that “reporting culture results and isolating colonized patients, as suggested by some guidelines, would have falsely suggested the success of such infection control policies.”³⁵

The effectiveness of screening and isolation has been examined in several recent large, cluster-randomized trials. In a US cluster-randomized trial, Huskins and colleagues³⁶ screened patients using standard cultures for MRSA and vancomycin-resistant *Enterococcus* (VRE) within 2 days of admission, weekly thereafter, and within 2 days before or after transfer out of the ICU, with contact isolation of carriers. Control and intervention ICUs followed the same screening procedures, but control ICUs did not receive the results of their patients' screening tests. Despite more frequent identification and isolation of carriers in the intervention ICUs, there was no difference in the rate of acquisition of MRSA or VRE. Confounding the interpretation of this study, some patients' screening results may not have been available before their transfer out of the ICU, because the mean turnaround time for the screening cultures was 5.2 days.

In a large European interrupted time series trial, improved hand hygiene compliance and implementation of daily chlorhexidine baths reduced acquisition of MRSA and reduced ICU length of stay. In the next phase of the study, rapid chromogenic screening for highly resistant Enterobacteriaceae and conventional or polymerase chain reaction (PCR) screening for VRE and MRSA were implemented in intervention ICUs within 2 days of admission, twice weekly for 3 weeks, then weekly, with subsequent contact isolation of carriers. Screening, even with rapid PCR testing, and isolation did not significantly reduce acquisition of those resistant organisms in the intervention ICUs.³⁷ This trial is the only rigorously designed, published study that has addressed screening for resistant gram-negative pathogens.

Some hospitals have reported that ICU screening for carbapenem-resistant gram-negative bacteria as part of a larger infection control program has reduced transmission of, and clinical infections with, these organisms.^{38,39} On a larger scale, Israel has achieved remarkable nationwide declines in rates of transmission of these organisms, thanks to a centralized infection control program that involves active surveillance and isolation of carriers in all health care facilities.⁴⁰ Further prospective studies are needed to better understand the benefits of screening for carbapenem-resistant bacteria in regions with low and high endemicity.

Isolation Precautions

Despite long-standing recommendations to care for patients who are known to be colonized or infected with multidrug-resistant organisms under barrier precautions,⁴¹ there remains controversy about the benefits of isolation. As described earlier, several approaches to screening and isolating patients have shown no change in acquisition of the multidrug-resistant organisms for which they were screened,^{36,37,42} which is likely to be due to a combination of colonization that screening cultures failed to detect and cross-transmission between patients.

Given the pitfalls of strategies of screening and isolation, Harris and colleagues⁴³ studied whether universal barrier precautions could reduce acquisition of VRE and MRSA in ICUs. In their cluster-randomized trial, personnel in intervention ICUs used gowns and gloves for all patient care, whereas control ICUs used barrier precautions only per CDC guidelines for known colonized or infected patients. Universal gowning and gloving reduced acquisition of

MRSA but not VRE. Analysis of trial data showed that hand hygiene compliance improved in the intervention ICUs, and despite a lower number of health care personnel interactions with patients there was no increase in adverse events when all patients were managed under barrier precautions.⁴³ Implementation of universal contact isolation may be a useful intervention during an ICU-based outbreak, as suggested in several outbreak reports.^{12,44,45}

Empiric Isolation

In order to be optimally effective, patient isolation should be implemented not only for confirmed transmissible infection or colonization but also for cases in which a patient is suspected of having communicable disease. For example, droplet isolation should be used when a patient has respiratory symptoms that may be consistent with influenza, airborne isolation in a negative-pressure room when a patient is being tested for pulmonary tuberculosis or chickenpox, and contact isolation when a patient has diarrhea that may be caused by an infectious pathogen. Empiric isolation is recommended until the results of diagnostic tests can confirm or counter the need for ongoing isolation. This strategy helps prevent transmission during the interval while diagnostic tests are pending.

Decolonization and Skin Antisepsis

The aim of decolonization is to eradicate carriage of potential pathogens and reduce the risk of developing invasive infections from those pathogens. Although decolonization regimens have been tested in clinical trials for several epidemiologically important pathogens, *S aureus* (susceptible or resistant to methicillin) is the organism for which the strongest evidence exists.⁴⁶

Chlorhexidine gluconate baths are a widely studied strategy to reduce the microbial burden colonizing patients' skin. In addition to reducing central line-associated bloodstream infection (CLABSI) rates and MRSA in the ICU,⁴⁷ 2% chlorhexidine gluconate daily baths have been shown in some clinical trials to reduce rates of acquisition of other multidrug-resistant organisms, particularly VRE. In a study involving community hospital ICUs in North Carolina, the treatment reduced rates of all CLABSI, CLABSI caused by VRE, and total VRE infections.⁴⁸ A cluster-randomized crossover study similarly found reduced rates of CLABSI and VRE during the intervention period when chlorhexidine daily baths were used.⁴⁹ However, another such study found no reduction in CLABSI or other health care-associated infections, or occurrence of clinical cultures growing multidrug-resistant bacteria.⁵⁰

Although the benefits of chlorhexidine baths for reducing the incidence of resistant gram-positive infections is arguable, the treatments have shown even less convincing effects on resistant gram-negative organisms in ICU patients. In a single-center, ICU-based study of 4% chlorhexidine baths, Borer and colleagues⁵¹ reported a reduced incidence of multidrug-resistant *Acinetobacter* bloodstream infections. Chung and colleagues⁵² reported reduction in acquisition of multidrug-resistant *Acinetobacter* in a single ICU with high endemicity of the organism. Rigorous, multicenter studies of the effects of chlorhexidine daily baths on multidrug-resistant gram-negative organisms are needed, involving hospitals with varying prevalence of these pathogens.

Daily baths with 2% chlorhexidine gluconate are an effective public health measure in the ICU. The antiseptic solution is applied on each patient from jaw to toes, avoiding mucous membranes and breaches in the skin, and left on to dry. The residual antimicrobial effect reduces skin colonization with epidemiologically important, antibiotic-resistant organisms, including MRSA, VRE, and carbapenemase-producing Enterobacteriaceae.^{42,53,54} Because of strong, but not uniform,⁵⁰ evidence from multiple clinical trials showing reduction in CLABSI rates, chlorhexidine daily baths have become standard of care in ICUs.⁵⁵ At the present time, despite 1 study to the contrary, there are sufficiently robust data to recommend chlorhexidine daily baths as a universal, or horizontal, intervention in ICUs for prevention of bloodstream infections and reduction in gram-positive infections.⁴⁶

Preventing transmission from the intensive care unit environment

A recent study showed that 40% of patient rooms in the hospital contained environmental contamination with multidrug-resistant organisms, most frequently VRE.⁵⁶ The viability of resistant organisms on fomites in the hospital environment is estimated from experimental studies, but is likely affected by many confounding factors (eg, organism burden and strain, temperature, moisture). Some resistant nosocomial pathogens are notoriously hardy on dry surfaces, including VRE and MRSA. Their prolonged viability presents a protracted opportunity for spread from contaminated sites. Researchers at the CDC recently found that *Acinetobacter baumannii* inoculated on steel and plastic remained cultivable at high concentrations that were undiminished throughout the 28-day study period. VRE had a 4-log reduction in concentration but remained cultivable at 28 days.⁵⁷ Organisms that prove resilient on hospital surfaces may spread to patients long after they are shed, leading to a protracted transmission cycle.

Less hardy but highly concerning pathogens such as carbapenemase-producing Enterobacteriaceae have also shown remarkable tenacity under dry conditions in experimental studies. The CDC study showed that *bla*_{KPC}-carrying *Klebsiella pneumoniae* was cultivable on plastic and steel for up to 5 to 6 days, and thereafter viable but noncultivable.⁵⁷

Standard, approved hospital disinfectant cleaners are generally effective against these organisms, provided that they are applied thoroughly to contaminated surfaces and allowed to dwell for an adequate time. Patient care equipment used for patients who are known to harbor multidrug-resistant organisms should, to the greatest extent possible, be disposable to reduce the risk of cross-transmission. Equipment that is shared among patients, such as blood pressure devices, cooling blankets, and portable radiology cassettes, should be disinfected thoroughly between patients. Items like fabric privacy curtains, which are readily and widely contaminated with resistant organisms,⁵⁸ can be removed or replaced with disposable curtains.

Adjunctive methods of disinfection, such as ultraviolet light and hydrogen peroxide vapor, have been studied in experimental settings and in clinical trials.⁵⁹ Both methods reduce the burden of bacterial pathogens, including spores, in the environment. Hydrogen peroxide vapor is highly effective for eliminating pathogens that are on surfaces out of the line of sight, but takes hours and requires sealing of a patient room, including temporary closure of

air supply and return. It has been used to good effect to decontaminate hospital wards undergoing outbreaks,¹² and for decontamination in the setting of high-concern pathogens.⁶⁰ Ultraviolet light is logistically easier, less time consuming, and less dependent on technical expertise to operate, but is less effective at killing organisms that are in shadows outside the path of the light.

A cluster-randomized, multicenter trial led by investigators at Duke University compared terminal cleaning with standard hospital disinfectants, enhanced cleaning with bleach-containing disinfectant, and standard or bleach cleaning in combination with ultraviolet C treatment. Despite a high rate of compliance with environmental disinfection and documented reduction in VRE and MRSA environmental contamination in bleach and ultraviolet light-treated rooms, the study results showed the complexity of linking environmental disinfection with patient outcomes. MRSA was reduced among patients who occupied rooms disinfected with ultraviolet light, VRE was reduced among those whose rooms had been treated with bleach, and *C difficile* infection was not reduced by any of the interventions.⁶¹

Some organisms reside in moist locations in the environment, and may inhabit biofilms from which they can potentially be transmitted to patients. Examples include waterborne bacteria such as species of *Stenotrophomonas*, *Pseudomonas*, *Aeromonas*, and *Sphingomonas*, which can colonize plumbing fixtures. In multiple reported ICU outbreaks, multidrug-resistant outbreak organisms have been identified in the biofilms of sink drains, faucets, or aerators. Although circumstantial evidence may implicate the sink drain colonization in the outbreak, it is difficult to determine whether drains were truly sources of transmission or just became colonized during the course of an outbreak.

Preventing transmission from contaminated plumbing is an area of uncertainty in hospital infection control, and the subject of active research.⁶² Some basic steps include ascertaining adequate levels of free chlorine in hospital water,⁶³ selecting sinks that have low-splash design, and avoiding placement of patient care supplies around handwashing sinks, where they could be contaminated by splash-back from the drain. In an outbreak setting in which plumbing fixtures are implicated, plumbing might require disassembly, special cleaning and disinfection procedures, or even replacement.

Preventing transmission of methicillin-resistant *Staphylococcus aureus*

S aureus, an important cause of severe infections in ICU patients, is carried on skin and mucous membranes in up to half of hospitalized patients.⁶⁴ MRSA causes community-acquired infections (eg, skin and soft tissue infections, endocarditis, pneumonia) that can require ICU care, and nosocomial infections (eg, wound infections, device-associated bacteremia, pneumonia) that can complicate ICU care.

Because of extensive MRSA transmission in the community, a significant proportion of patients are colonized on admission. Patients who are colonized and/or infected with MRSA can serve as reservoirs for transmission in the hospital. A long-term study showed that 22% of MRSA acquisition in a neonatal ICU could be traced to MRSA carriers in the same

unit.⁶⁵ As with many other nosocomial bacteria, MRSA are thought to be spread on the hands of health care personnel, and on contaminated equipment and surfaces.

Some institutions have implemented programs of large-scale MRSA screening and isolation to reduce transmission. The Veterans Affairs hospitals began such a program in 2007, and reported sustained declines in MRSA transmission and health care–associated infections in ICUs over the subsequent 8 years. Transmission of MRSA in the ICU, defined as a newly positive screening test or clinical culture after hospital day 2, declined by 36.6%, and nosocomial MRSA infections in the ICU declined by a stunning 87%.⁶⁶ The program notably includes culture change among health care personnel around infection prevention as a major goal, in addition to tracking and quantifying preventive efforts.

Other approaches include attempts at decolonization of MRSA carriers using nasal mupirocin and chlorhexidine baths. A cluster-randomized trial by Huang and colleagues⁴² showed that a strategy of screening cultures for MRSA in ICUs and isolation of carriers was less effective for reducing the incidence of MRSA than either targeted or universal decolonization with nasal mupirocin and chlorhexidine daily baths. The 2 decolonization strategies were compared in an attempt to settle controversy about whether the intervention should target those who are colonized and at high risk of infection, or should be used as a blanket public health intervention in ICUs.⁴⁶ In the study by Huang and colleagues⁴² universal decolonization led to a 44% reduction in bloodstream infections caused by any pathogen and a 37% reduction in MRSA-positive clinical cultures.⁴² Universal decolonization in the ICU has been shown to be a cost-effective strategy,⁶⁷ and the practice can decrease endogenous infection along with patient-to-patient transmission; however, there are concerns about development of antibiotic resistance with widespread use of chlorhexidine.^{46,68}

Preventing transmission of vancomycin-resistant *Enterococcus faecium*

Colonization with VRE is common in the ICU, especially among patients who are immunocompromised or chronically ill, have prolonged hospital stays, and have received broad-spectrum antimicrobials. Development of VRE colonization in the ICU is associated with prolonged hospitalization and receipt of metronidazole.⁶⁹

Although VRE bacteremia has a low attributable mortality in ICU patients, on par with that of coagulase-negative staphylococci, it does cause nosocomial infections that can be difficult to treat.⁷⁰ In VRE-colonized patients, the organisms are found primarily in the fecal flora, are shed in high numbers, and can be found on skin and throughout the patient's hospital room.⁷¹ Because VRE can be carried on health care personnel hands and survive well on inanimate surfaces, the organisms are easily transmitted via the health care environment.

Hayden and colleagues⁷¹ found that VRE was highly prevalent in their ICU environment, and showed that reducing environmental contamination had a marked effect on the spread of VRE in their ICU. Patients who occupy ICU rooms that previously housed patients colonized with VRE are at increased risk of acquiring VRE themselves. That risk is only partially mitigated by enhanced environmental cleaning.⁷²

Preventing transmission of resistant gram-negative bacteria

Multidrug-resistant gram-negative bacteria have long posed a threat to critically ill patients. Resistant *Pseudomonas aeruginosa* and *A baumannii*, extended-spectrum β -lactamase–producing Enterobacteriaceae, and carbapenemase-producing and colistin-resistant strains of gram-negative bacteria can cause a wide range of nosocomial infections that can be difficult to treat. The most prevalent bacterial causes of nosocomial bloodstream infections have shifted from gram-positive to gram-negative organisms, with a high proportion of multidrug-resistant gram-negative strains.⁷³ Intensivists have a shrinking antibiotic armamentarium when patients develop device-related infections, including bacteremia and pneumonia, or other severe infections with these organisms.

Over the past 15 years, gram-negative bacteria carrying a variety of carbapenemase enzymes have emerged and disseminated around the globe, profoundly changing the epidemiology of nosocomial infections in many countries. Carbapenemase genes are often found in organisms that already harbor other significant resistance genes, such as extended-spectrum β -lactamases, and are thus extensively resistant or even pan-resistant to antibiotics.¹² Clinically significant carbapenemase genes include *bla*_{KPC}, *bla*_{OXA-48}, and *bla*_{OXA-48-like} family, and the *bla*_{NDM-1}, *bla*_{VIM}, and *bla*_{IMP} metallo- β -lactamase genes. Although plasmid-borne genes for carbapenemase enzymes can be found in a broad array of gram-negative species, *K pneumoniae* and *Enterobacter* species are the most common in North America.⁷⁴ Globally, *P aeruginosa* and *A baumannii* are often multidrug resistant because of carbapenemase genes, chromosomal resistance genes (such as multidrug efflux pumps), or both. Spread of the recently discovered plasmid-borne *mcr-1* gene conferring colistin resistance may further complicate epidemiology and management of nosocomial gram-negative infections.

Like other nosocomial bacteria, resistant gram-negative organisms are likely spread on the hands of health care personnel, with contamination of the dry environment of the hospital likely playing a lesser role in nosocomial spread than is thought to occur with gram-positive bacteria. Long-term acute care hospitals serve as a deep reservoir of resistant gram-negative bacteria, in part because of poor control of transmission in those facilities, chronic illness and immunocompromised states, long-term invasive devices such as ventilators, and repeated exposure to antibiotics. Patients transferred to the ICU from these facilities are at high risk of being colonized or infected on transfer with resistant gram-negative organisms. Many hospitals target this patient population for admission surveillance with rectal or perirectal swabs to detect colonization with carbapenem-resistant or carbapenemase-producing bacteria and prevent their transmission within the ICU.

In the wake of a 2011 to 2012 outbreak of carbapenemase-producing *K pneumoniae*, our hospital conducts admission surveillance on patients of all ages, apart from those on behavioral health wards. Patients undergo carbapenemase surveillance cultures from perirectal swabs on admission, and twice weekly while in the ICU. Patients who are in the CDC's high-risk categories (those hospitalized in the United States in the previous week or outside the United States in the previous 6 months) are placed in contact isolation on admission and undergo 2 perirectal cultures to increase the sensitivity of screening. Patients who are found to be colonized with carbapenemase-producing bacteria are cohorted, or

housed in a designated section of the ICU, and cared for by nurses who are assigned only to their care. An additional measure is the use of adherence monitors, staff members who are trained to observe all health care personnel and visitors who enter and exit the cohorted patient's room and ensure that all infection control precautions are followed meticulously. These measures are intended to reduce the risk of cross-transmission to other critically ill patients.⁷⁵

Multidrug-resistant *Acinetobacter baumannii*

A baumannii is a nosocomial menace whose high-level resistance and worldwide dispersal have earned the bacteria the distinction of being the WHO's top antimicrobial-resistant pathogen of concern.⁷⁶ *A baumannii* is a particular problem in ICUs, where it causes device-related infections, pneumonia, bloodstream infections, and wound infections that can be extremely difficult to treat because of the paucity of effective antibiotic choices.⁷⁷ In a large international study, *Acinetobacter* species were responsible for an average of 8.8% of gram-negative ICU infections on all continents, and more than 19% in Asian ICUs.⁷³ More than 80% of *A baumannii* isolates are multidrug resistant,⁷⁸ with the highest rates of resistance found in residents of nursing homes.⁷⁹ Surveillance cultures for colonization can be collected from the groin, which is the most sensitive site for detection,⁸⁰ and the throat.

A baumannii develops antimicrobial resistance rapidly via chromosomal mutations and mobile genetic elements, including plasmids carrying carbapenemase genes. As noted earlier, *A baumannii* is able to withstand long periods of desiccation and can persist on ICU surfaces and equipment. The organism readily adheres to protective equipment; in one study, nearly 40% of interactions with ICU patients colonized by *A baumannii* resulted in contamination of health care personnel gloves, gowns, or both.⁸¹ The lack of treatment options for multidrug-resistant *Acinetobacter* underscores the critical role of hand hygiene and painstaking environmental infection control in preventing spread of what is often a nearly untreatable pathogen. The authors have used the same control measures for carbapenemase-producing organisms described earlier to contain highly resistant *A baumannii* in the ICU.⁴⁴

Candida auris

C auris is a newly emerging, global microbial threat in ICUs. *Candida* species are the most common health care-associated fungal infection and an important cause of bloodstream infections in ICU patients. Outbreaks of *C auris* have been reported in ICUs in the Americas, Europe, Africa, and Asia.^{82,83} Like *A baumannii* and distinctly unlike most nosocomial *Candida* species, *C auris* tends to be multidrug resistant, spreads from colonized patients to other patients within the ICU, and contaminates surfaces with marked longevity and tenacity.^{82–84} The organism has been cultured from the skin of both asymptomatic patients and health care personnel.⁸⁵ The CDC in 2016 issued a clinical alert requesting that all health care facilities report cases of *C auris*, isolate patients colonized or infected with the organism, and redouble efforts at disinfection and cleaning of their rooms.⁸⁶ This organism deserves the attention of infection control and intensive care staff, because it seems to have all the features of a fierce nosocomial pathogen.

SUMMARY

Infection control in the ICU has seen many advances, including rapid molecular screening tests for resistant organisms and chlorhexidine use in daily baths. Although these developments advance the cause of infection prevention, compliance with some of the most basic measures remains elusive. Hand hygiene, antimicrobial stewardship, and reduction in device use remain the low-technology interventions that could have a major impact on nosocomial transmission of antimicrobial-resistant organisms. Although continued research is needed on new and old ways of preventing nosocomial infections, ICU staff must persevere in improving adherence with the measures that are known to be effective.

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KEY POINTS

- Multidrug-resistant organisms (MDRO) pose an increasing threat to critically ill patients.
- Patients, healthcare personnel, and the built environment of the intensive care unit are potential reservoirs for transmission of MDRO.
- Meticulous hand hygiene, environmental disinfection, chlorhexidine baths, and other infection control measures can interrupt spread of MDRO.
- Antimicrobial stewardship is an essential tool for improving quality of care and reducing selective pressure that promotes emergence of multidrug resistance.
- While infections with MDRO are becoming more difficult to treat with available antimicrobial drugs, intensive care unit staff can combat their spread by optimizing basic measures that are known to be effective.