Infection Prevention and Control in the Intensive Care Unit

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KEYWORDS

• Infection prevention • Infection control • Health care–associated infection
• Multidrug-resistant organism • Transmission • Outbreak

KEY POINTS

- The Intensive care unit is the most common site for health care–associated infection identification in the hospital setting and thus is an excellent target for prevention efforts.
- Prevention of Healthcare-associated infection (HAI) is a multidisciplinary endeavor that plays to the strengths of the ICU team-based care model.
- HAI transmission is an interplay between infectious agents, susceptible hosts and opportunity in both exposure and vulnerability (loss of barriers) to infection.
- ICU patients are likely to receive antibiotics during their stay, and antibiotic stewardship improves patient outcomes and reduces HAI.
- The ICU is the clearinghouse for both known and unknown (future pandemic) organisms. Fastidious compliance with prevention and preparedness/surveillence for what's next and key activities all ICUs should engage in.

INTRODUCTION

Health care–associated infections (HAIs) in the intensive care unit (ICU) are common, costly, and clinically deleterious. In a global point-prevalence study of 15,000 ICU patients across 88 countries, 22% of patients had an ICU-acquired infection.[1] In the United States, the total cost of HAIs is estimated at $9.8 billion, with surgical site infections and ventilator-associated pneumonia (VAP) accounting for the highest expenses.[2] ICU-acquired infections are associated with prolonged length of stay and increased mortality with the risk of death significantly higher when antibiotic-resistant pathogens are involved.[3,4] The Center for Disease Control and Prevention (CDC) highlight the growing threat of antimicrobial resistance in their 2024 report

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Abbreviations	
AI	artificial intelligence
BMI	body mass index
CDC	Center for Disease Control and Prevention
CDI	*Clostridioides difficile* infection
CRE	carbapenem-resistant *Enterobacteriaceae*
CRAB	carbapenem-resistant *Acinetobacter baumannii*
CVC	central venous catheters
CLABSI	central line–associated blood stream infection
CAUTI	catheter-associated urinary tract infection
HAIs	health care–associated infections
ICU	intensive care unit
IVAC	infection-related ventilator-associated complication
LTCF	long-term care facility
MDR	multidrug-resistant
MDROs	multidrug-resistant organisms
MRSA	methicillin-resistant *Staphylococcus aureus*
NHSN	National Healthcare Safety Network
PPE	personal protective equipment
PICC	peripherally inserted central venous catheter
PVAP	possible/probable ventilator-associated pneumonia
PsA	*Pseudomonas aeruginosa*
SARS-CoV-2	severe acute respiratory syndrome coronavirus 2
VAE	ventilator-associated event
VAP	ventilator-associated pneumonia
VAC	ventilator-associated condition
VRE	vancomycin-resistant *Enterococcus*
WGS	whole genome sequencing

which noted that antimicrobial-resistant HAIs increased by 20% during the COVID-19 pandemic compared to the prepandemic period, peaking in 2021 and remaining above prepandemic levels in 2022. Infection prevention and control measures can improve outcomes by limiting the incidence and spread of HAIs and multidrug-resistant organisms (MDROs). The goal of this article is to review core infection prevention strategies in the ICU, discuss risk factors and prevention strategies for ICU-associated HAIs, highlight efforts to prevent and control MDROs, and describe innovations in infection prevention.

CORE INFECTION PREVENTION STRATEGIES

There are 3 essential elements for the transmission of pathogens in a health care setting: (1) an infectious agent (virus, bacteria, or fungus), (2) a host susceptible to that pathogen, and (3) a mechanism by which the pathogen enters the host.[5] Effective infection prevention hinges on disrupting this triad. The most fundamental and significant strategy for reducing HAIs is hand hygiene. Yet, more than 175 years since Semmelweis first demonstrated its lifesaving importance, compliance with hand hygiene recommendations remains suboptimal.[6] Health care worker hands harbor pathogenic organisms, even after glove removal. Over a 24-hour period, ICU patients may undergo an average of 178 interventions, all of which may require hand hygiene.[7] Missing even one of these opportunities creates an opening for the transmission of clinically significant pathogens, and a single lapse can lead to a life-threatening infection.

Health care facilities inherently contain patients with transmissible pathogens, and ICUs concentrate individuals who are either intrinsically vulnerable or rendered more susceptible by critical illness, immunosuppression, or invasive therapies. Preventing

the transmission of these potentially infectious pathogens forms the foundation of standard and transmission-based precautions. Standard precautions must be applied to the care of all patients, recognizing that the pathogens they harbor may be unknown until after transmission has occurred. A central tenet of standard precautions is that blood, bodily fluids, secretions, excretions, nonintact skin, and mucus membranes may contain high concentrations of infectious organisms. In addition, patients may be vulnerable to infection from their own colonizing flora if introduced through the entry point of a medical procedure such as central line placement or surgical incision. Any potential contact with blood or bodily fluids should prompt the use of appropriate personal protective equipment (PPE), such as gloves when touching nonintact skin, and a gown when anticipating contact with soiled linens. The use of PPE does not abrogate the need for hand hygiene after PPE removal.[5]

Transmission-based precautions are implemented in addition to standard precautions when a specific pathogen is known or suspected. These include contact, droplet, and airborne precautions (**Table 1**).[5] Respiratory isolation precautions are particularly relevant in the ICU, where patients frequently require mechanical ventilation or noninvasive respiratory support. Droplet transmission occurs via respiratory particles $\geq$5 microns that typically travel short distances before settling from the air. Exposure occurs within three to six feet of the source and can be prevented by wearing a surgical mask and eye protection.[5] Pathogens transmitted primarily by droplets include *Neisseria meningitidis*, *Bordetella pertussis*, influenza, and others (see **Table 1**).

In contrast, airborne transmission involves respiratory particles less than 5 microns, which remain suspended in the air for prolonged periods.[5] Pathogens requiring airborne isolation include *Mycobacterium tuberculosis,* disseminated herpes zoster, varicella zoster (chickenpox), measles (rubeola), and severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) during aerosol-generating procedures (see **Table 1**). ICU patients requiring airborne isolation should be placed in a private, negative pressure room

Table 1
Pathogens requiring contact, droplet, or airborne precautions

Precaution Type	Pathogen[a]	Notes
Contact	*C difficile*, *Norovirus*, RSV, *Scabies,* and certain MDRO (eg, CRE)	Use gown and gloves; *C difficile* and *Norovirus* require soap and water hand hygiene; MDROs are judged by institutional infection prevention team
Droplet	*B pertussis, N meningitidis*, Hib, *Mycoplasma pneumoniae*, Group A *Streptococcus* invasive disease, influenza, rhinovirus, parainfluenza, mumps, and rubella	Use surgical mask and face shield or goggles when within 6 feet of a patient infected with known pathogen
Airborne	*M tuberculosis,* disseminated herpes zoster, varicella zoster (chickenpox), measles (rubeola), and SARS-CoV-2[b]	Use contact precautions and an approved N95 respiratory mask; isolate patient in negative-pressure room

Abbreviations: Hib, Haemophilus influenzae type b; RSV, Respiratory syncytial virus.
[a] Pathogen list is not comprehensive. Please review guidance from the CDC for complete details on pathogen transmission-based precautions.
[b] Airborne isolation should be prioritized for patients with SARS-CoV-2 undergoing aerosol-generating procedures.

(airflow directed into the room from the corridor), with a flow rate of 6 to 12 air changes per hour, and exhaust vented outdoors or filtered through a high-efficiency particulate air filter before recirculation.[5] Personnel entering the room should wear gown, gloves, face/eye protection, and a fit-tested N95 respirator to prevent transmission.

Building on the principles of airborne isolation, enhanced biocontainment units are specialized rooms designed for the management of high-consequence infectious diseases such as viral hemorrhagic fevers or novel pathogens of uncertain transmissibility.[8] These units incorporate advanced environmental engineering (eg, independent air handling and waste management protocols), specialized staff training and full-barrier PPE with trained observer oversight during donning and doffing.[8,9] Though rarely needed, awareness of these distinctions is critical for ICU preparedness, staff safety, and system-level infection prevention planning.

While standard and transmission-based precautions mitigate many sources of transmission, the ICU remains uniquely prone to HAIs because of the frequent use of invasive devices, high colonization pressure from broad-spectrum antimicrobial use, and physiologic vulnerability of critically ill patients.

PREVENTING HEALTH CARE–ASSOCIATED INFECTIONS IN THE INTENSIVE CARE UNIT

Central Line–Associated Bloodstream Infections

Central venous catheters (CVCs) provide reliable venous access for the administration of intravenous fluids, vasoactive medications, broad-spectrum antibiotics, total parenteral nutrition, and renal replacement therapy. While often necessary for the delivery of life-sustaining therapies, CVCs are associated with an increased risk of bloodstream infection. Bloodstream infections related to CVCs are classified according to the CDC's National Healthcare Safety Network (NHSN) definition of a central line–associated blood stream infection (CLABSI): a laboratory-confirmed bloodstream infection in a patient with a CVC in place for more than 48 hours before blood culture collection, with no alternative source of bacteremia or fungemia.[10]

Risk Factors

The risk of CLABSI is high among ICU patients because of frequent placement of multiple catheters, often under emergent conditions, combined with daily access requirements and prolonged catheter dwell times.[11–13] Risk factors for CLABSI can be categorized into patient, provider, and device-related factors (**Table 2**). Patient-related risks include immunocompromised states such as neutropenia, severe burns, malnutrition, a body mass index (BMI) over 40, receipt of total parenteral nutrition, and prolonged hospitalization before catheter placement.[14–16] Provider-related risks entail emergent insertion, breaches in aseptic technique, low nurse-to-patient ratios, delayed catheter removal, and frequent catheter manipulation.[17,18] Device-related factors include site of insertion, insertion technique, the number of lumens, and the indication for use.

Prevention Strategies

CLABSIs are associated with increased length of stay, higher health care costs, and considerable morbidity and mortality.[3,19,20] In response to the substantial clinical and economic burden of CLABSI, health care institutions and regulatory bodies have prioritized the implementation of standardized, evidence-based prevention strategies.[13,21] These strategies include the following:

- Perform hand hygiene immediately before and after inserting, replacing, accessing, or dressing a CVC. Acceptable methods include washing with antiseptic

Table 2
Risk factors for common health care–associated infections in the intensive care unit

Infection Type	Risk Factor Category	Specific Risk Factors
CLABSI	Device-related	Site of insertion, insertion technique, number of lumens, and indication for use
	Provider-related	Emergent insertion, breaches in aseptic technique, low nurse-to-patient ratios, delayed catheter removal, and frequent catheter manipulation
	Patient-related	Immunocompromised, severe burns, malnutrition, BMI > 40, total parenteral nutrition, and prolonged hospitalization before catheter placement
VAP/VAE	Device-related	Prolonged mechanical ventilation, mandatory modes of ventilation, and reintubation
	Provider-related	Use of neuromuscular blocking agents and sedative exposure (eg, benzodiazepine, propofol, and fentanyl)
	Patient-related	Positive fluid balance
CAUTI	Device-related	Prolonged catheterization and use of nonclosed drainage system
	Patient-related	Female sex, advanced age, diabetes mellitus, and prolonged hospitalization
CDI	Medication-related	Antibiotic exposure and gastric acid suppression
	Patient-related	Advanced age and prolonged hospitalization

soap or using an alcohol-based hand rub. For hands that are not visibly soiled, alcohol-based formulations are preferred. The use of gloves does not eliminate the need for proper hand hygiene.[22]

- Use insertion checklists that outline the steps required for optimal CVC insertion using aseptic technique. These checklists should be completed by a trained observer who monitors adherence to sterile practices and is authorized to stop the procedure in the event of a protocol breach.[23]
- Use a comprehensive catheter insertion cart or kit that contains all components necessary for sterile CVC placement.[24]
- Cleanse the insertion site with an alcohol chlorhexidine containing a minimum of 2% chlorhexidine gluconate.[25,26] Allow the site to fully dry before skin puncture to maximize efficacy.
- Use maximal sterile barrier precautions during CVC insertion including mask, cap, sterile gown, sterile gloves, and a large sterile drape the covers the entire patient.[27]
- Prefer the subclavian vein for CVC placement in ICU patients, unless contraindicated. Individualize site selection by weighing the risks of infectious and noninfectious complications. For example, while the subclavian site reduces infection risk, it increases the risk of pneumothorax and is generally avoided for hemodialysis catheters because of the potential for central vein stenosis.[15,28–30] Consider the availability of ultrasound guidance and operator experience when selecting an insertion site.
- Avoid peripherally inserted central venous catheters (PICCs) as a CLABSI prevention strategy, as the infection risk associated with PICCs in hospitalized patients is comparable to that of other CVCs.[31]

- Apply chlorhexidine-containing dressings to reduce CLABSI risk.[32,33]
- Disinfect catheter hubs and injection ports with an alcoholic chlorhexidine solution before each access.[34]
- Perform daily chlorhexidine bathing for ICU patients to reduce microbial skin colonization and associated blood stream infections.[35]
- Assess the necessity of each catheter daily and remove any catheter that is no longer clinically indicated.[36]
- Maintain appropriate nurse-patient ratios and limit the use of float or traveling nurses in ICUs to support adherence to infection prevention protocols.[13,17]

Prevention Practices to Avoid and Areas of Uncertainty

- Do not routinely replace CVCs or arterial catheters.[13]
- Do not use systemic antibiotic prophylaxis for short-term or tunneled catheter insertion.
- Consider using antiseptic- or antimicrobial-impregnated CVCs in ICUs with persistently elevated CLABSI rates, despite adherence to standard prevention measures.[13]

In addition to effective prevention strategies, it is essential to provide regular education and training to all ICU staff on the indications for intravascular catheter use, aseptic techniques for insertion and maintenance, and appropriate infection control measures. Fostering a culture of safety and interdisciplinary collaboration centered on commitment to best practices is critical for sustained CLABSI prevention.

Ventilator-Associated Pneumonia and Ventilator-Associated Events

VAP is defined as a pneumonia that occurs 48 hours or more after endotracheal intubation.[37] Clinically, pneumonia is diagnosed based on the presence of a new or progressive radiographic infiltrate accompanied by worsening oxygenation and systemic signs of infection such as fever, purulent secretions, and leukocytosis. These criteria are neither sensitive nor specific and often fail to correlate with histopathologic findings at autopsy.[38,39] The subjective nature of this clinical definition contributes to significant interobserver variability and unreliable administrative diagnostic coding data.[40,41]

Due in part to limitations in pneumonia surveillance definitions, reported reductions in VAP incidence have not consistently correlated with meaningful improvements in patient outcomes.[42] In response, the CDC developed the ventilator-associated events (VAEs) surveillance definition to facilitate more objective and automated detection of clinically significant events.[43]

VAEs are categorized into ventilator-associated condition (VAC), infection-related ventilator-associated complication (IVAC), and possible/probable ventilator-associated pneumonia (PVAP). A VAC is identified when there is an increase in the daily minimum positive end expiratory pressure of $\geq$3 cm H_2O or an increase in the fraction of inspired oxygen (Fio_2) of $\geq$20 points sustained for $\geq$2 calendar days following $\geq$2 days of stability or decrease in these parameters. An IVAC is defined as a VAC with concurrent signs of infection (temperature <36°C or >38°C or white blood cell count $\leq$4000 or $\geq$12,000 cells/mm^3) and the initiation of antibiotics that continues for $\geq$4 days. A PVAP requires additional microbiologic evidence of infection in a patient meeting IVAC criteria.

VAEs are frequently attributable to etiologies other than VAP, such as pulmonary edema, atelectasis, and acute respiratory distress syndrome.[44,45] Consequently, the prevalence of PVAP has been shown to diverge from traditional VAP. Nevertheless, both VAP and VAEs have been independently associated with prolonged mechanical ventilation, increased hospital length of stay, and higher mortality.[46]

Risk Factors

A fundamental, and perhaps self-evident, risk factor for VAP and VAEs is prolonged mechanical ventilation.[47,48] Accordingly, factors that contribute to extended ventilator dependence such as positive fluid balance, use of mandatory modes of ventilation, reintubation, and exposure to sedative agents (eg, benzodiazepines, propofol, and opioids) or neuromuscular blocking agents are associated with increased VAE risk (see **Table 2**).[49–51] Conversely, interventions that shorten the duration of mechanical ventilation are associated with a reduced VAE incidence. These include spontaneous awakening trials, spontaneous breathing trials, and conservative fluid management strategies.[52–54] A comprehensive review of prevention strategies follows.

Prevention Strategies

- Avoid intubation and reintubation when clinically safe and feasible.[55] Use high-flow nasal oxygen and noninvasive positive pressure ventilation to prevent intubation in patients with hypoxemic respiratory failure and reduce the risk of reintubation following extubation in critically ill patients.[56]
- Minimize sedation of mechanically ventilated patients. Employ multimodal analgesia and prioritize sedatives other than benzodiazepines. Perform daily spontaneous awakening trials in patients without contraindications.[57,58]
- Assess readiness to extubate daily by performing spontaneous breathing trials.[58,59]
- Elevate the head of the bed to 30° to 45° to reduce the risk of aspiration.[60]
- Provide daily oral care with toothbrushing. Avoid routine use of chlorhexidine because of potential harm and lack of consistent benefit.[61,62]
- Initiate early enteral nutrition rather than parenteral nutrition.[63] In patients at high risk for aspiration, use postpyloric feeding over gastric feeding.[64]

Prevention Practices to Avoid and Areas of Uncertainty

- Stress ulcer prophylaxis may be indicated for prevention of gastrointestinal bleeding, but randomized trials show no benefit in reducing nosocomial pneumonia.[65]
- Routine monitoring of gastric residual volumes is not recommended.[66]
- Endotracheal tubes with subglottic secretion drainage may be considered in patients anticipated to require mechanical ventilation for more than 48 to 72 hours.[67]
- Consider selective oral or digestive decontamination in settings with a low prevalence of antibiotic-resistant organisms.[55]
- Early tracheostomy may reduce VAP rates, shorten the duration of mechanical ventilation, and decrease ICU length of stay; however, evidence does not consistently demonstrate a mortality benefit.[68]

Preventing VAP and other VAE requires a coordinated, multidisciplinary effort focused on consistent adherence to evidence-based practices, often in the form of *prevention bundles*. Implementation of prevention bundles has been associated with reductions in VAP rates and, in some studies, improvements in ICU length of stay and mortality.[69,70] While no single prevention bundle has universal consensus, interventions such as staff education, performance feedback, sedation minimization, head-of-bed elevation, toothbrushing, and daily assessment for extubation are among the most consistently supported strategies.[55] Regular monitoring of bundle compliance and VAE outcomes with transparent reporting to clinical teams and senior hospital leadership cultivates shared accountability, promotes continuous quality

improvement, and helps sustain long-term success. Although the task is challenging, examples of successful programs show that sustained improvement is achievable.[71]

Catheter-Associated Urinary Tract Infections

Catheter-associated urinary tract infection (CAUTI) is defined as the presence of bacteriuria in a patient who has had an indwelling urinary catheter in place for more than 48 hours, accompanied by signs or symptoms suggestive of a urinary tract infection. According to NHSN surveillance criteria, a CAUTI requires significant bacteriuria ($\geq 10^5$ colony forming units [CFU]/mL) with no more than two organisms, along with at least one of the following clinical findings: fever, suprapubic pain, or costovertebral angle tenderness.[72]

Although CAUTIs account for over 40% of all hospital-acquired urinary tract infection (UTIs),[73] they represent up to 95% of UTIs occurring in ICUs.[74] In the United States, approximately 12% to 16% of hospitalized patients will have an indwelling urinary catheter during their admission, and the risk of developing bacteriuria increases by an estimated 3% to 7% with each day the catheter remains in place.[75] An estimated 65% to 70% of CAUTI cases are considered preventable with appropriate catheter use and evidence-based infection prevention strategies.[74]

Risk Factors

Prolonged duration of catheterization is the most significant and modifiable risk factor for CAUTI, with the risk of infection increasing incrementally each day the catheter remains in place (see **Table 2**). Additional risk factors include female sex, advanced age, diabetes mellitus, nonclosed drainage systems, and extended hospitalization.[76]

Prevention Strategies

- Avoid unnecessary catheterization: Before placement, clinicians should consider alternative strategies such as intermittent straight catheterization or external urinary devices.[77]
- Standardize indications: Institutions should establish clear criteria for appropriate use of indwelling catheters. Accepted indications may include perioperative use for selected surgical procedures, accurate urine output monitoring in ICU patients guiding therapy (eg, fluid resuscitation or vasopressors), management of acute urinary retention, promotion of wound healing in patients with incontinence and open pressure ulcers, and end of life care aligned with patient goals.[72] Notably, ICU admission alone should not justify catheter use without a specific clinical indication.
- Implement a catheter insertion policy emphasizing aseptic technique: Provide education and periodic competency assessments for health care personnel on catheter insertion, maintenance, and removal.[78]
- Maintain a closed, drainage system with unobstructed urine flow.[72]
- Evaluate the necessity of indwelling catheters daily and establish nurse-driven protocols to promptly remove catheters that are no longer indicated.[79,80]

Prevention Practices to Avoid and Areas of Uncertainty

- Routine use of antimicrobial- or antiseptic-impregnated catheters is not recommended.[72]
- Do not screen for or treat asymptomatic bacteriuria except in the few patient populations where benefits may exceed harms (eg, pregnant patients and patients undergoing urologic procedures associated with mucosal trauma).[81]

Despite the success of collaborative, multidisciplinary efforts in reducing CAUTI rates on medical-surgical floors, similar progress in the ICU has been more limited.[79] This may stem from the assumption that critical illness justifies prolonged indwelling urinary catheter use, as well as the common practice of pan-culturing in response to fever which often includes unnecessary urine cultures. These patterns underscore the potential harm of urinary catheterization in critically ill patients, including impaired mobility, urethral trauma, heightened delirium risk, asymptomatic bacteriuria leading to inappropriate antibiotic use, and ultimately CAUTI. Given these risks, timely removal of the catheter should be a priority once the original indication has resolved. In many cases, catheter removal is not only a step toward reducing infection risk, but also a meaningful milestone on the path to ICU recovery.

Clostridioides difficile Infection

Clostridioides difficile infection (CDI) is defined by presence of clinically significant diarrhea or toxic megacolon without other cause and either a stool test positive for *C difficile* toxins or toxin-producing *C difficile* organism or findings of pseudomembranous colitis on colonoscopy or histopathology.[82] Nosocomial diarrhea is a common complication of hospitalized patients, and although CDI is a frequent focus, less than 20% of cases are attributable to CDI.[83] Nevertheless, CDI is associated with approximately half a million infections and roughly 30,000 deaths annually in the United States.[84,85] In part because of greater emphasis on infection prevention measures, the incidence of health care–associated CDI has declined substantially over the last decade.[86]

Risk Factors

The most important modifiable risk factor for CDI is antibiotic exposure (see **Table 2**). Almost all antibiotics have been associated with CDI; however certain classes including third-/fourth-generation cephalosporins, fluroquinolones, carbapenems, and clindamycin are most implicated.[87] Advanced age and prolonged duration of hospitalization are additional, important risk factors.[88] Gastric acid suppression, particularly use of proton pump inhibitors, has been associated with increased risk of CDI; however, restriction of gastric acid suppression has not been established as an effective CDI prevention measure.[88,89]

Prevention Strategies

Prevention of CDI focuses on the following 2 methods: (1) protecting patients from initial *C difficile* acquisition and (2) limiting pathogen transmission between patients with CDI and health care practitioners and other patients. Because antibiotic exposure contributes to disruption of the intestinal microbiota and subsequent development of *C difficile*, avoiding unnecessary antimicrobial use through implementation of an antimicrobial stewardship program is an important measure to curtail initial *C difficile* acquisition. Large meta-analyses suggest that restrictive antimicrobial stewardship programs, particularly when paired with infection prevention measures, can reduce CDI incidence by 30% to 50%.[90,91] Additional prevention measures focusing on curtailing spread once a patient has been found to have CDI are as follows.

- Place patients with CDI on contact precautions, preferably in a single-patient room to help reduce patient-to-patient spread of the organism. Contact precautions should be continued for at least 48 hours after diarrhea has resolved.[87]
- Providers should don gown and gloves upon entry to the patient's room, and these should be removed before exiting the room.

- Perform hand hygiene immediately before donning and after removing PPE. Using soap and water is preferred over alcohol-based hand hygiene, particularly during CDI outbreaks.[82,87]
- Use disposable patient equipment (ie, stethoscope) when possible and ensure reusable equipment is thoroughly cleaned and disinfected, preferentially with a sporicidal disinfectant.[82]
- Conduct terminal ICU room cleaning with a sporicidal agent and incorporate measures of cleaning effectiveness to ensure quality of environmental cleaning.[82]

Prevention Practices to Avoid and Areas of Uncertainty

- Consider oral vancomycin prophylaxis in patients with a history of CDI who require systemic antibiotics and are at high risk for recurrence.[87,92]
- Probiotics are not recommended for routine primary or secondary CDI prophylaxis.[92]

Prevention of CDI in the ICU relies on a close working relationship between ICU health care personnel and the infection prevention team. Integrating and measuring best practices that focus on antimicrobial stewardship, hand hygiene, adherence to contact precautions, and effective environmental cleaning can help prevent the spread of *C difficile* and ensure the ICU remains a safe environment for patients.

Adherence to the above principles provides a strong foundation for preventing most HAIs; however, critical care physicians must remain adaptable to emerging and uncommon pathogens, as exemplified by the SARS-CoV-2 pandemic. In such scenarios, identify, isolate, and inform paradigm remains essential.[93] Prompt recognition of patients with concerning clinical symptoms, timely isolation with appropriate PPE, and immediate notification of infection prevention teams are critical steps to limiting nosocomial transmission. These same principles underpin efforts to prevent and control outbreaks of MDROs, which represent an ongoing and increasingly complex challenge in the ICU.

Prevention and Control of Multidrug-Resistant Organisms in the Intensive Care Unit

MDROs are defined as pathogens resistant to one or more classes of antimicrobial agents.[94] In the ICU, clinicians frequently encounter such organisms, including methicillin-resistant *Staphylococcus aureus* (MRSA), vancomycin-resistant *Enterococcus* (VRE), multidrug-resistant (MDR) *Pseudomonas aeruginosa* (PsA), carbapenem-resistant *Enterobacteriaceae*, and *Candida auris* (**Table 3**). According to the CDC, HAIs caused by MDROs increased approximately 20% during the COVID-19 pandemic compared to the prepandemic period.[95]

Infections with MDROs are linked to worse clinical outcomes including increased mortality, prolonged length of stay, and higher costs.[96,97] Risk factors for MDRO acquisition in the ICU include prolonged critical illness, exposure to broad spectrum antibiotics, mechanical ventilation, higher severity of illness, and recent surgical or invasive procedure (see **Table 3**).[98] Moreover, the ICU environment exerts multiple stressors on the patient's microbiome such as disruption of the gastrointestinal tract, artificial nutrition, antibiotic exposure, and dysglycemia, which collectively diminish microbial diversity, facilitating colonization by resistant organisms.[99] As colonization with MDROs increases, so too does the risk of transmission, most commonly via the hands of health care personnel or through contact with contaminated equipment and surfaces in the patient care environment.[100] Effective infection prevention and control strategies are therefore essential to interrupt transmission and mitigate the impact of MDROs in the ICU.

Table 3
Multidrug-resistant organisms in the intensive care unit

Pathogen	Common Risk Factors	Source/Reservoir	Key Infection Prevention Strategies[a]
MRSA	Indwelling devices, prolonged hospitalization, and immunosuppression	Skin, nares, and environmental surfaces	Active surveillance, universal decolonization with CHG bathing, and contact precautions (debated)
VREs	Prior antibiotic exposure, prolonged hospitalization, immunosuppression, and prior enterococcal infection	Skin, GI tract, and environmental surfaces	Antimicrobial stewardship and contact precautions (debated)
MDR PsA	Mechanical ventilation, prior antibiotic exposure, and immunosuppression	Hospital water sources: sinks, plumbing, hospital equipment, and endotracheal tube	Water management protocols, antimicrobial stewardship, and contact precautions
CRE	Prior antibiotic exposure, prolonged ICU stay, and LTCF residence	GI tract, environmental surfaces	Antimicrobial stewardship, active surveillance, contact precautions, patient isolation, and staff adherence monitoring
CRAB	Indwelling devices, mechanical ventilation, and prior antibiotic exposure	Skin, environmental surfaces, hospital equipment, and endotracheal tube	Equipment decontamination, antimicrobial stewardship, contact precautions, patient isolation, and staff adherence monitoring
C auris	Prior antifungal exposure, indwelling devices, and LTCF residence	Skin and hospital equipment	Registered sporicidal equipment disinfection, contact precautions, and patient isolation

Abbreviation: CHG, chlorhexidine; GI, gastrointestinal.
[a] Rigorous hand hygiene and thorough environmental cleaning are considered essential measures.

Prevention of MDRO transmission in the ICU involves both horizontal and vertical strategies.[98] Horizontal strategies are non–pathogen-specific aimed at reducing the overall risk of transmission. These include hand-hygiene, environmental cleaning, universal decolonization (eg, chlorhexidine gluconate bathing), and antimicrobial stewardship. In contrast, vertical strategies are pathogen-specific and focus on identifying and managing carriers of MDROs through active surveillance and targeted interventions such as decolonization protocols or implementation of contact precautions.

KEY MULTIDRUG-RESISTANT ORGANISMS PATHOGENS

Methicillin-Resistant Staphylococcus aureus

Although the incidence of MRSA infections in the United States has declined since the early 2000s, MRSA remains one of the most prevalent health care–associated

pathogens in the ICU.[101] In addition, it carries a substantial mortality burden, with one US study reporting an unadjusted in-hospital mortality rate of 29% for hospital-onset MRSA bloodstream infections from 2012 to 2017.[102] Current guidelines recommend that acute care hospitals implement MRSA surveillance programs to evaluate the effectiveness of infection control measures and track hospital-onset cases to assess transmission risk.[101] Among the strategies shown to reduce MRSA transmission and infection in the ICU, universal decolonization, using daily chlorhexidine bathing and intranasal mupirocin for all ICU patients, has demonstrated the most consistent benefit.[103] Although current guidelines continue to recommend contact precautions for patients colonized or infected with MRSA,[101] this practice has been the subject of debate.[104] A recent systematic review article found no significant difference in hospital-associated MRSA infection rates after discontinuing contact precautions.[105]

Vancomycin-Resistant Enterococci

Enterococci are commensal organisms of the human gastrointestinal tract that can cause invasive infections, particularly in critically ill patients. A meta-analysis reported that 8.8% of patients are colonized with VRE upon ICU admission.[106] This finding becomes clinically significant when considering that 8% of colonized patients may develop an invasive infection within 30 days.[107] In a large ICU point prevalence study, VRE infections were independently associated with increased mortality compared to infections with other microorganisms.[1]

Risk factors for VRE colonization include exposure to antibiotics (particularly vancomycin, third-generation cephalosporins, and metronidazole), prolonged hospitalization, immunosuppression, severe comorbidities, and previous enterococcal infection.[108,109] VRE is frequently shed in feces and can colonize the skin and contaminate surrounding patient care surfaces. Its hardy nature on environmental fixtures was highlighted by an observational study that identified VRE as the most frequently recovered MDRO, detected in 19% of routine and terminally cleaned patient rooms.[110]

Effective strategies to prevent VRE transmission in the ICU primarily rely on horizontal approaches, including strict hand hygiene adherence and comprehensive environmental cleaning.[111,112] As with MRSA, the role of contact precautions is controversial. Although historically recommended for VRE,[5] more recent studies suggest that discontinuing contact precautions does not lead to increased rates of hospital-acquired VRE.[113,114]

Multidrug-Resistant Pseudomonas aeruginosa

PsA is a nonfermenting gram-negative rod that is ubiquitous in the environment and commonly acts as an opportunistic pathogen in critically ill patients with impaired host defenses. A well-known cause of HAIs, PsA ranked as the fifth most common overall HAI pathogen, the second most common cause of VAP, and the third most common cause of CAUTI based on NHSN data from 2018 to 2021.[115] During this period, an average of 11.9% of PsA HAI isolates were MDR. However, in 2020, coinciding with the onset of the COVID-19 pandemic, MDR rates increased by 32% and have remained elevated compared to prepandemic levels.[95]

Mechanisms of antibiotic resistance in MDR PsA are often multifactorial and include the production of ambler class C (AmpC) and extended-spectrum beta-lactamases, overexpression of efflux pumps, porin mutations, and biofilm formation.[116] Its capacity to rapidly acquire chromosomal mutations further contributes to resistance, underscoring the importance of antimicrobial stewardship in minimizing the selective pressure that drives resistance.[91] PsA is frequently found in water sources, including hospital sinks and plumbing, which then serve as persistent environmental reservoirs

in ICUs. Notably, several ICU outbreaks of MDR Pseudomonas have been stymied only after identifying and addressing a contaminated water source for PsA.[117,118]

Carbapenem-Resistant Enterobacteriaceae and Acinetobacter baumannii

Both carbapenem-resistant *Enterobacteriaceae* (CRE) and carbapenem-resistant *Acinetobacter baumannii* (CRAB) are classified as urgent threats by the CDC's 2022 Antimicrobial Resistance Report.[95] These pathogens can strike fear in intensivists because of their multifactorial resistance mechanisms, limited therapeutic options, and high-associated mortality.

CRE include members of the *Enterobacterales* order—most notably *Klebsiella pneumoniae*, *Escherichia coli*, and *Enterobacter* spp—that have developed resistance to carbapenems either through carbapenemase production or other mechanisms such as porin loss and efflux pump overexpression.[119] In the United States, 35% to 83% of CRE cases are caused by carbapenemase-producing isolates.[119] The most common carbapenemases include *K pneumoniae* carbapenemase, followed by New Delhi metallo-β-lactamase, and oxacillinase-48-like carbapenemases.[120,121]

Risk factors for CRE colonization include prior antibiotic exposure, presence of indwelling catheters or devices, prolonged hospital or ICU stay, residence in long-term care facilities (LTCFs), and cocolonization with other MDROs.[122] Active surveillance using rectal swabs can detect asymptomatic CRE colonization and is particularly valuable during outbreak investigations and in endemic settings, including ICU populations and recent long-term care transfers.[123]

CRAB presents even greater clinical challenges than CRE because of the extreme paucity of effective antimicrobials. MDR, extensively drug-resistant and pan-drug–resistant strains have been reported globally.[124] CRAB thrives in ICU settings because of its ability to form biofilms and adhere to endotracheal tubes, CVCs, and hospital surfaces. It can survive desiccation for prolonged periods, contributing to its environmental persistence.[100,125] Once patients are colonized, transmission to health care workers is common; one study found that nearly 40% of interactions with colonized ICU patients resulted in contamination of personnel hands, gloves, or gowns.[100,126]

Preventing transmission of nosocomial CRE and CRAB requires a comprehensive approach that includes rigorous adherence to horizontal strategies, contact precautions for all patient room entry, isolation of colonized or infected patients, and adherence monitoring to ensure compliance with infection prevention and control (IPC) measures.[127,128]

Candida auris

First identified in 2009, *C auris* has emerged as a serious global health threat, causing multiple ICU outbreaks worldwide.[129] In the United States alone, the CDC reported a fivefold increase in cases from 2019 to 2022.[95,130]

Risk factors for *C auris* colonization and invasive infection mirror those of other MDROs, such as prior antibiotic exposure, presence of indwelling devices, and residence in LTCF, with the additional risk of recent antifungal exposure.[131] Outbreaks of *C auris* are especially difficult to control because of its ability to persistently colonize the skin, sometimes indefinitely. Colonized patients shed the organism into the health care environment, where it can survive on surfaces and act as a reservoir for transmission.[132]

Infection prevention strategies for *C auris* align with those used for other MDROS but require special attention to reusable equipment such as temperature probes, which have been implicated in previous outbreaks.[133] Standard disinfectants, such

as quaternary ammonium compounds, are ineffective against *C auris*. The CDC recommends using an Environmental Protection Agency–registered hospital-grade disinfectant that is also effective against *C difficile* spores.[134] Laboratories that identify *C auris* should notify state or local health departments and the CDC to facilitate contact tracing and a broader public health response.

Managing an Multidrug-Resistant Organisms Outbreak in the Intensive Care Unit

Managing an MDRO outbreak in the ICU requires prompt intensification of infection control measures to prevent further spread, and a focused epidemiologic investigation to identify and eliminate the source and mode of transmission.[135] The most important role of ICU providers is to ensure adherence to foundational infection control interventions including the following:

- Meticulous hand hygiene
- Contact precautions
- Removal of unnecessary indwelling devices
- Universal chlorhexidine skin bathing
- Intensified environmental cleaning and disinfection of rooms and equipment
- Adherence monitoring to ensure compliance with infection prevention measures

Concurrently, infection prevention teams should guide ICU leadership on active surveillance strategies to identify colonized patients for isolation, perform decolonization when appropriate, and verify successful outbreak containment. Screening methods and sites should be selected based on how the MDRO is acquired and shed by patients (eg, nares for MRSA and rectal for VRE). While there is no universal consensus on the timing of active surveillance, common strategies include screening upon ICU admission and weekly thereafter.[136]

During an outbreak investigation, active surveillance helps define cases by identifying patients colonized or infected with an MDRO. Case definitions can be based on positive laboratory results or epidemiologic links, such as shared units, equipment, or procedures and tracked using spatiotemporal clustering and contact tracing. Environmental screening of shared equipment and high-touch surfaces can reveal reservoirs of transmission requiring targeted intervention.[117,133] Whole genome sequencing (WGS) is an invaluable tool in outbreak investigations, providing high-resolution data to identify clonal spread and map transmission pathways.[137] For hospitals without access to WGS, traditional infection prevention practices remain essential, and several CDC resources offer practical guidance and tools.[138] Ultimately, successful containment hinges on robust infection control practices and a coordinated, data-driven response to halt further transmission and prevent recurrence.

Innovations in Infection Prevention and Control: A Focus on Artificial Intelligence

Although still in its early stages, artificial intelligence (AI) has emerged as a promising tool in infection prevention, offering the potential for earlier detection, more accurate surveillance, and improved prediction of infectious disease outbreaks and HAIs. These capabilities are largely driven by advanced algorithms and machine learning models, which enable computational systems to simulate aspects of human cognition when analyzing complex medical data.[139]

A compelling example of AI's utility lies in its application to hospital outbreak investigations.[140] Traditionally, outbreak detection has relied on manual surveillance and contact tracing through exhaustive chart reviews and environmental sampling.[141] WGS enhances this approach by revealing the genetic relatedness between pathogen isolates, helping to identify clusters of potential transmission. However, WGS alone

cannot determine the specific mechanism of transmission, which requires complementary epidemiologic and environmental data.

To overcome these limitations, Sundermann and colleagues integrated WGS with a machine learning tool capable of automatically mining a patient's electronic health record for epidemiologic data to support outbreak investigations.[140,142] In 1 case, surveillance data signaled a PsA outbreak involving 6 patients who were separated in both time and space. The machine learning algorithm identified a contaminated gastroscope as the common source of a transmission; an insight that would have been difficult to discern through traditional methods alone.[141] Cost-benefit analyses suggest that this AI-enhanced approach may yield substantial savings, whereas improving clinical outcomes.

AI is also transforming HAI surveillance. Historically, surveillance for these infections required time-intensive manual chart review but is now increasingly being automated. Automated surveillance offers several advantages, including freeing infection preventionists to focus on higher-value tasks, improving detection accuracy, and enhancing interfacility reliability.[139,143] In the future, as machine learning and predictive analytics continue to evolve, infection prevention practices may shift from reactive HAI detection to proactive prediction, identifying high-risk patients before infection occurs and targeting them for intensified preventive strategies.[144]

SUMMARY

Infection prevention and control in the ICU have assumed renewed importance following the COVID-19 pandemic, which was accompanied by a significant global rise in HAIs and MDROs. Although advances in infection control strategies continue to emerge, sustained improvement is contingent on the rigorous implementation of established, evidence-based interventions, including hand hygiene, timely removal of invasive devices, daily reassessment bundles, antimicrobial stewardship, and continuous staff education. Effective infection prevention in the ICU necessitates a coordinated, multidisciplinary effort to safeguard patients from preventable harm, whereas delivering optimal critical care.

CLINICS CARE POINTS

- The ICU one of the first places new pathogens are identified, and a potential hotbed of HAI.
- Addressing HAI is a group project. Collaborate with key players including Infection Prevention, Infectious Diseases, and Microbiology.
- A key strategy in preventing device-associated infections is discretion in device placement and prompt removal when the device is no longer needed.
- Restrictive antimicrobial stewardship results in significant reduction in CDI.

DECLARATION OF AI AND AI-ASSISTED TECHNOLOGIES IN THE WRITING PROCESS

During the preparation of this work the authors used ChatGPT in order to revise and edit the article. After using this tool/service, the authors reviewed and edited the content as needed and take full responsibility for the content of the publication.

DISCLOSURE

The authors have nothing to disclose.

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